Tehran University of Medical Sciences
Vice Chancellor for Global Strategies
and international Affairs
International Campus

Periodical Collection of Research Projects Conducted by IC-TUMS

(From Nov 2014 - July 2017)

Compiled and produced by:

The office of IC-TUMS Vice Dean for Research Affairs

July 2017

In the Name of

GOD

the Merciful and the Compassionate

Tehran University of Medical Sciences
International Campus (IC-TUMS)

Vice Chancellor for Global Strategies and International Affairs

PERIODICAL COLLECTION OF RESEARCH PROJECTS CONDUCTED BY IC-TUMS

(Articles published from Nov 2014 to July 2017)

JUly 2017

Compiled and Produced by the office of IC-TUMS Vice Dean for Research Affairs:

- **Dr. M.R. Hadian**
- **Behnam Izadyar**
- **Behnaz Salehi-Rad**
- **Sepideh Zamiri**

Contents:

Message from Vice Chancellor for Global Strategies and International Affairs

Tehran University of Medical Sciences (TUMS), in addition to an educational organization, is a *research*-led university with a reputation for world class research in select areas of medical and health sciences.
TUMS is also recognized as the Iran's leading research university in medical sciences.

The international campus of TUMS began admitting international students in 2008, and as of then, a significant number of research projects have been conducted by students.

The purpose of producing this periodical book is to collect and introduce the publications of the research activities carried out by IC-TUMS researchers and students. Of course, this collection includes the articles which have been published in the accredited journals.

In this book, we have provided a collection of the article abstracts published by our

students which are arranged by school.

I hope publishing this book outlines the main research activities conducted at IC-TUMS.

Ali Arabkheradmand, MD,
Vice Chancellor for Global
Strategies & International Affairs

Message from Vice Dean for Research Affairs

IC-TUMS is home to a growing body of scholars recognized nationally and internationally for the significance of their contributions to the medical, paramedical, and health sciences. IC-TUMS researchers and students are making a difference across our campus, our nation and globally. We are also advancing our understanding of the world around us, maximizing benefits to society, and enhancing quality of life today and tomorrow through academic and research activities.

Given our strategic research priorities and geographic location, IC-TUMS academic departments and research institutes/centers are unambiguously determined to address the crucial national and regional demands. We are committed to training highly qualified personnel who will become our next-generation scholars, leaders, scientists and industrial entrepreneurs, and also advancing the research enterprise of the TUMS Schools by providing input on research and research related policy matters. By collaborating with institutional, government and industrial stakeholders, we are making significant improvements to fundamental knowledge and understanding in these fields. Our researchers are safeguarding the health of our environment, and the social, cultural and economic framework of our communities by developing policy and technologies that enhance the human experience.

I hope this book gives the readers an idea of the wide variety of studies conducted by our academics and students in the last few years.

M. R. Hadian, PhD,
Vice Dean for Research Affairs

Chapter One

Number of Published Articles at a Glance

(by schools & departments)

School	Department	Number of Published Articles
Public Health	Health Management	11
	Medical Parasitology	1
	Medical Entomology	4
	Disaster and Emergency Health	7
	Health Education	4
	Occupational Health	4
	Immunology	8
	Epidemiology	5
Total		44

School/ Center	Department	Number of Published Articles
Pharmaceutical Sciences Research Center	Pharmacology	29
Total		29

School	Department	Number of Published Articles
Medicine	Physiology	5
	Pharmacology	8
	Bacteriology	4
	Medical Physics	1
	Medical Genetics	2
	Immunology	2
Total		22

School	Department	Number of Published Articles
Rehabilitation	Physiotherapy	9
Total		9

School	Department	Number of Published Articles
Nursing and Midwifery	Medical Surgical Nursing	8
	Reproductive Health	1
Total		9

School	Department	Number of Published Articles
Nutritional Sciences	Clinical Nutrition	3
	Community Nutrition	4
	Cellular and Molecular Nutrition	2
Total		9

School	Department	Number of Published Articles
Pharmacy	Drug and Food Control	5
	Clinical Pharmacy	2
Total		7

School	Department	Number of Published Articles
Advanced Technologies in Medicine	Medical Biotechnology	5
Total		5

School	Department	Number of Published Articles
Dentistry	Prosthodontic Technology	2
	Endodontics	1
	Oral and Maxillofacial Pathology	1
Total		4

School	Department	Number of Published Articles
Allied Medical Sciences	Medical Informatics	1
Total		1

Chapter Two

School of Public Health

1- Aymen Elsous

First Name	Last Name	Program	Level	School
Aymen	Elsous	Health Policy	Ph.D.	Public Health

Published Articles:

	Title of the Article
1	Nursing perceptions of patient safety climate in the Gaza Strip, Palestine
2	Prevalence and Microbiological Profle of Catheter Associated Urinary Tract Infections: A Survey in Secondary Care Hospital in Gaza Strip
3	Nurses and Physicians Attitudes toward Nurse-Physician Collaboration: A Survey from Gaza Strip, Palestine
4	A cross-sectional study to assess the patient safety culture in the Palestinian hospitals: a baseline assessment for quality improvement
5	Psychometric Properties of an Arabic Safety Attitude Questionnaire (Short Form 2006)
6	Medications adherence and associated Factors among Patients with Type 2 Diabetes Mellitus in the Gaza Strip, Palestine
7	Psychometric Soundness of an Arabic Version of the Jefferson Scale of Attitude toward Physician and Nurse Collaboration (JSAPNC): A Preliminary Study

Original Article

Nursing perceptions of patient safety climate in the Gaza Strip, Palestine

A. Elsous[1,2] **BSc, MScIH, A. Akbari Sari**[2,3] **MD, PhD, Y. AlJeesh**[4] **BSc, PhD & M. Radwan**[2,5] **BSc, MPH**

1 PhD Candidate, **5** PhD Candidate, **3** Professor, **2** Department of Health Management and Economics, School of Public Health, International campus - Tehran University of Medical Sciences, Tehran, Iran, **4** Professor, Dean, Faculty of Nursing, Islamic University of Gaza, Gaza Strip, Palestine

ELSOUS A., AKBARI SARI A., ALJEESH Y. & RADWAN M. (2017) Nursing perceptions of patient safety climate in the Gaza Strip, Palestine. *International Nursing Review* **00**, 000–000

Aims: This study was undertaken to assess the perception of nurses about patient safety culture and to test whether it is significantly affected by the nurses' position, age, experience and working hours.

Background: Patient safety has sparked the interest of healthcare mangers, yet there is limited knowledge about the current patient safety culture among nurses in the Gaza Strip.

Methods: This was a descriptive cross-sectional study, administering the Arabic Safety Attitude Questionnaire (Short Form 2006) to 210 nurses in four public general hospitals.

Results: Job Satisfaction was the most highly perceived factor affecting patient safety, followed by Perception of Management. Safety culture varied across nursing position, age, work experience and working hours. Nurse Managers had more positive attitudes towards patients than frontline clinicians did. The more experience nurses had, the better their attitudes towards patient safety. Nurses who worked the minimum weekly required hours and who were 35 years and older had better attitudes towards all patient safety dimensions except for Stress Recognition. Nurses with a positive attitude had better collaboration with healthcare professionals than those without a positive attitude.

Limitation: Generalization is limited, as nurses who worked in private and specialized hospitals were excluded.

Conclusion: Evaluation of the safety culture is the essential starting point to identify hindrances or drivers for safe patient care. Job Satisfaction, Perception of Management and Teamwork necessitate reinforcement, while Working Conditions, Stress Recognition and Safety Climate require improvement.

Implications for nursing and health policy: Ensuring job satisfaction through adequate staffing levels, providing incentives and maintaining a collegial environment require both strategic planning and institutional policies at the higher administrative level. Creation of a non-punitive and learning environment, promoting open communication and fostering continuous education should be fundamental aspects of hospital management. A policy of mixing experienced nurses with inexperienced nurses should be considered.

Keywords: Cross-Sectional, Gaza Strip, Nurses, Palestine, Patient Safety, Perceptions, Safety Culture

Correspondence address: Aymen Elsous, Department of Health Management and Economics, School of Public Health, International Campus – Tehran University of Medical Sciences, Tehran, Iran; Tel: +970-598-926886; Fax: +970 8 2827711; E-mail: aymenelsous65@gmail.com.

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Research Article
IJHR
Open Access

Prevalence and Microbiological Profile of Catheter Associated Urinary Tract Infections: A Survey in Secondary Care Hospital in Gaza Strip

Aymen Elsous[1,2*], Mahmoud Ouda[2], Samah Mohsen[2], Mohammed Al-Shaikh[2], Siham Mokayad[2]

[1] Department of Health Management and Economics, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran. [2] Quality Improvement and Infection Control Office, Shifa Medical Complex, Ministry of Health, Gaza Strip, Palestine.

First Published online June 30, 2016

Abstract

Background and Objectives: Healthcare-associated infections is a major health care concern posing potentially serious negative impact on patient safety and outcome. In this paper, we report this microbiological profile and the prevalence of catheter associated urinary tract infections (CAUTIs).

Methods: This was a prospective observational study for 60 inpatients from 8 wards among patients having indwelling catheter for at least 48 hours. Urine cultures were taken in initial phase within 24 hours of admission, at 48 hours and in day 5 of catheterization.

Findings: The rate of CAUTIs was 16.7% after 48 hours and 28% (7/25) after 5 days from insertion the indwelling catheter. *Candida* spp. was the most common cause of CAUTIs (29.4%), followed by *Escherichia coli* (23.5%), *Streptococcus* spp. and *Klebsiella* spp. (17.6%) and last *Staphylococcus* spp. (11.7%). The coronary care unit (CCU) showed the highest prevalence of CAUTIs (57.1%), followed by Oncology (42.8%), and Internal Medicine (33.3%). Females showed a significantly higher rate of acquired urinary tract infections (UTIs) compared with males ($P<.05$).

Conclusions: The risk of CAUTIs was found to be relatively high and increase by duration of catheterization. These results recommend minimally usage of catheter in medical practice in terms of both frequency and time, particularly for female patients and in CCU ward. Identification of the microbiological profile of the CAUTIs would help efficient treatment of the infected patients.

Keywords: Catheter associated urinary tract infections, Prevalence, Hospital, Microbiological profile

Background and Objectives

People who seek healthcare are unable to tolerate the additional burden of acquiring a new infection. Healthcare associated infections (HAIs) are a major concern for healthcare management and frontlines to maximize patient safety. HAI is global health problem because of their seriousness, burden and costs to healthcare system. They also impose serious problems to safety of t patients.[1] In developing countries, the prevalence and incidence of HAIs varies between 5.7 to 19.1, and 1.7 to 23.6 per 100 patients respectively.[2] Studies from European hospitals indicates that 1 in every 18 patients has HAIs.[3] In the United States 1.7 million suffer from HAIs and 100 000 dies every year as result of these infections.[4]

Urinary catheterization occurs in 15%-25% of all hospitalized patients and urinary tract infections (UTIs) caused by urinary catheter are the most common type of HAIs,[5] representing 30% to 40% of all HAIs in some regions of the world.[6-9] Over 80% of catheter associated urinary tract infections (CAUTIs) are linked to insertion of indwelling catheter.[10] The rate of these infections can be reduced through effective infection prevention and control program (ICP).[3,11] It is estimated that strict infection and prevention program in has resulted in 15%-69% reception in infection and prevention of 9000 deaths from CAUTIs.[12,13]

In Palestine, where ICP is at the beginning and starting

*Corresponding Author: Aymen Mohammed Elsous, Quality Improvement and Infection Control Office, Shifa medical complex, Ministry of Health, Gaza Strip, Palestine. Tel: +970598926886,
Email: aymenelsous65@gmail.com

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Research Article

Nurses and Physicians Attitudes toward Nurse-Physician Collaboration: A Survey from Gaza Strip, Palestine

Aymen Elsous,[1,2] **Mahmoud Radwan,**[2,3] **and Samah Mohsen**[1]

[1]*Quality Improvement and Infection Control Office, Shifa Medical Complex, Al Rimal, Gaza City, Gaza Strip, State of Palestine*
[2]*Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, International Campus, Tehran, Iran*
[3]*General Directorate of International Cooperation, Ministry of Health, Al Rimal, Gaza City, Gaza Strip, State of Palestine*

Correspondence should be addressed to Mahmoud Radwan; mradwan78@hotmail.com

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Interprofessional collaboration and teamwork between nurses and physicians is essential for improving patient outcomes and quality of health services. This study examined the attitudes of nurses and physicians toward nurse-physician collaboration. A cross-sectional study was conducted among nurses and physicians ($n = 414$) in two main referral public hospitals in the Gaza Strip using the Arabic Jefferson Scale of Attitude toward Physician-Nurse Collaboration. Descriptive statistics and difference of means, proportions, and correlations were examined using Student's t-test, one-way ANOVA, and Pearson correlation and $p < 0.05$ was considered as statistical significant. Response rate was 42.8% (75.6% for nurses and 24.4% for physicians). Nurses expressed more positives attitudes toward collaboration than physicians (M ± SD on four-point scale: 3.40 ± 0.30 and 3.01 ± 0.35, resp.) and experience duration was not proved to have an interesting influence. Teamwork approach in the professional practice should be recognized taking into consideration that the relationship between physicians and nurses is complementary and nurses are partners in patient care.

1. Introduction

The interprofessional collaboration between physicians and nurses is crucial and has been highlighted in different contexts [1, 2]. Collaboration, between physicians and nurses, means cooperation in work, sharing responsibilities for solving problems, and making decisions to formulate and carry out plans for patient care [3]. Although the provision of healthcare is becoming more complex, collaboration among healthcare workers can be a path to improve the quality of healthcare services especially in hospitals in which environment is characterized by ongoing interaction among professionals. Nurse-physician collaboration and teamwork can improve patient outcomes and lower healthcare cost [4], increase job satisfaction [5], and maintain patients' safety [6]. The communication between nurses and physicians is considered a principal part of the information flow in healthcare; meanwhile the growing evidences show that improper or poor communication can create a chronic state of conflict between nurses and physician leading to increase in the medical errors and poor outcomes [4, 7]. Furthermore, it has been shown that unsatisfactory interprofessional relationships between physicians and nurses partially contributed to shortage of nurses and enforced nurses to leave their professions [8].

Nurses and physicians extremely contribute to the patient care but often do not appreciate the role of each other [9]. In previous studies, doctors and nurses viewed collaboration differently; doctors view collaboration as following the instructions and the orders, while nurses view it as a complementary role more significantly than physicians do [10]. Bujak and Bartholomew suggest that presently "the two most important people responsible for patient care are the nurses and the physicians, but they often do not talk to each other properly, and when they do, the interchange is often dysfunctional" [11]. Traditionally, relationship between the

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A cross-sectional study to assess the patient safety culture in the Palestinian hospitals: a baseline assessment for quality improvement

Aymen Elsous[1], Ali Akbari Sari[2], Arash Rashidian[1], Yousef Aljeesh[3], Mahmoud Radwan[1] and Hatem AbuZaydeh[4]

[1]Department of Health Management and Economics, School of Public Health, International campus, Tehran University of Medical Sciences, Tehran, 14155 Box 6446, Iran
[2]School of Public Health, Tehran University of Medical Sciences, Tehran, 14155 Box 6446, Iran
[3]Dean Faculty of Nursing, Islamic University of Gaza, PO Box 108, Gaza Strip, Palestine
[4]Al Mustaqbal Research Center, Gaza Strip, Palestine
Corresponding author: Ali Akbari Sari. Email: akbarisari@tums.ac.ir

Summary

Objectives: To measure and establish a baseline assessment of the patient safety culture in the Palestinian hospitals.
Design: A cross-sectional descriptive study using the Arabic version of the Safety Attitude Questionnaire (Short Form 2006).
Participants: A total of 339 nurses and physicians returned the questionnaire out of 370 achieving a response rate of 91.6%.
Setting: Four public general hospitals in the Gaza Strip, Palestine.
Methods: Nurses and physicians were randomly selected using a proportionate random sampling. Data analysis performed using Statistical Package for the Social Sciences software version 20, and p value less than 0.05 was statistically significant.
Main outcomes measures: Current status of patient safety culture among healthcare providers and percentage of positive attitudes.
Results: Male to female ratio was 2.16:1, and mean age was 36.5 ± 9.4 years. The mean score of Arabic Safety Attitude Questionnaire across the six dimensions on 100-point scale ranged between 68.5 for Job Satisfaction and 48.5 for Working Condition. The percentage of respondents holding a positive attitude was 34.5% for Teamwork Climate, 28.4% for Safety Climate, 40.7% for Stress Recognition, 48.8% for Job Satisfaction, 11.3% for Working Conditions and 42.8% for Perception of Management. Healthcare workers holding positive attitudes had better collaboration with co-workers than those without positive attitudes.
Conclusion: Findings are useful to formulate a policy on patient safety culture and targeted a specific safety culture dimension to improve the safety of patients and improve the clinical outcomes within healthcare organisations.

Keywords

Assessment, safety culture, safety attitude questionnaire, hospitals, Palestine

Introduction

Errors are certain to happen in human life.[1] In health settings, work is complex in nature making it vulnerable to errors. The Institute of Medicine (IOM) disseminated an alarming report on practitioners' errors in which most of them were preventable.[2] It suggested that promoting safety necessitates changes in the culture of work setting toward recognising errors as a guide for improvement not for blaming employees. After the 'To Err is Human: Building a Safer Health System' of IOM, the quality of care and patient safety have received extensive attention and became a priority in any healthcare system.[3] Safety culture is a fundamental element when seeking improvement or quality in healthcare. It is defined as shared values, attitudes and perceptions of safety within an organisation toward minimising patient harm.[4] It includes the following components: (1) recognising high-risk setting as errors prone in nature, (2) free blame environment, (3) management involvement in allocating resources for safety concern and (4) collaboration among disciplines to seek solutions.[5] Organisations with positive safety culture are characterised by mutual trust communication, shared perception around safety and by confidence of effectiveness of preventive measures.[6] This is compatible with Davies and his colleagues'[7] presentation of culture 'the way we do around here'.

Employees with positive safety culture are more likely to engage into safety-related behaviours when compared to those with perceived negative safety culture.[8] In healthcare, safety culture has been associated with quality, safety performance, safe practices and clinical outcomes including workplace accidents, falls and medication errors.[8,9]

ORIGINAL ARTICLE

Oman Medical Journal [2017], Vol. 32, No. 2: 115–123

Psychometric Properties of an Arabic Safety Attitude Questionnaire (Short Form 2006)

Aymen Elsous[1]*, Ali Akbarisari[2], Arash Rashidian[1], Yousef Aljeesh[3], Mahmoud Radwan[1] and Hatem Abu Zaydeh[4]

[1]Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, International Campus, Tehran, Iran

[2]Dean School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

[3]Dean Faculty of Nursing, Islamic University of Gaza, Gaza Strip, Palestine

[4]Al Mustaqbal Research Center, Gaza Strip, Palestine

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Keywords:
Reliability and Validity; Safety; Questionnaire; Safety Culture; Gaza Strip.

ABSTRACT

Objectives: There is a widespread interest in exploring healthcare providers' attitudes and perceptions about patient safety culture. This study was done to determine the reliability and validity of the Arabic version of Safety Attitude Questionnaire (SAQ) in Palestinian hospitals. ***Methods:*** This was a methodological study and the SAQ was translated into Arabic using the forward-backward translation technique. Four Ministry of Health hospitals in the Gaza Strip were randomly selected, and proportionate systematic sampling was followed to select the participants. Questionnaires were distributed to 370 physicians and nurses. Face and content validity were tested, and the content validity index was determined using the average approach. Internal consistency was assessed with Cronbach's alpha, split-half reliability, and intercorrelation between the questionnaire scales. Construct validity was assessed through exploratory and confirmatory factor analysis. ***Results:*** A total of 339 questionnaires were received, giving a response rate of 91.6%. Questionnaire acceptability was good and relevant to the study purpose. Cronbach's alpha value was 77.7 (74.7–82.2). Goodness of fit indices from the confirmatory factor analysis showed a satisfactory model fit: comparative fit of indices (CFI = 0.797), root mean square error of approximation (RMSEA = 0.085), and standardized root square residual (SRMR = 0.074). Factor analysis with varimax rotation revealed that six factors explained 62.3% of the variance. ***Conclusions:*** The Arabic version of SAQ (short form 2006) is valid and reliable, and shows a satisfactory model of fit. This instrument shows promise to be a sound tool to assess the safety culture in Palestinian hospitals.

Worldwide, millions of patients die every year as a direct result of unsafe care.[1] The Institute of Medicine (IOM) of the United States released a groundbreaking report "To Err is human," which stated that 44 000 to 98 000 people die every year from iatrogenic medical events, 7 000 of which were from medical errors.[2]

In Palestine, adverse events are frequent and sometimes serious but can be prevented. One out of seven patients suffers harm in Palestinian hospitals.[3] Patient safety is defined as the avoidance and prevention of adverse events or injuries stemming from the processes of health care.[4] Patient safety culture is an essential component of health care quality measures, and contributes to minimizing the risk of adverse events.[5] Recently, a focus on patient safety culture and patient outcomes in healthcare organizations has attracted a lot of attention because of its importance in creating a work environment that enables the delivery of safe care.[6] Patient safety culture is defined as a subset of organizational culture that comprises values and beliefs concerning patient safety within healthcare organizations.[7] Assessment of the patient safety culture can be done either qualitatively (on site observation, interview, focus group discussion) or quantitatively (questionnaires). The most widely used approach is face-to-face interviews or self-administered questionnaires.[6]

While a variety of instruments exists to assess patient safety culture, the most widely used are the Safety Attitude Questionnaire (SAQ),[8] and the Hospital Survey on Patient Safety Culture (HSPSC).[9] The SAQ shows a positive association between obtained score and improvement in patient care delivery, and remains the most sensitive in

frontiers in Endocrinology

ORIGINAL RESEARCH
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Medications Adherence and Associated Factors among Patients with Type 2 Diabetes Mellitus in the Gaza Strip, Palestine

Aymen Elsous[1,2], Mahmoud Radwan[1,3], Hasnaa Al-Sharif[4] and Ayman Abu Mustafa[5]*

[1] *Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences – International campus, Tehran, Iran,* [2] *Quality Improvement and Infection Control Office, Shifa Medical Complex, Gaza Strip, Palestine,* [3] *Directorate General of International Cooperation, Ministry of Health, Gaza Strip, Palestine,* [4] *Director of Chronic Diseases Department, Al Rimal Martyrs Health Center, Ministry of Health, Gaza Strip, Palestine,* [5] *Department of Research, Directorate General of Human Resources Development, Ministry of Health, Gaza Strip, Palestine*

Aim: The aim of this study was to evaluate the adherence to anti-diabetic medications among patients with type 2 diabetes mellitus (DM) seeking medical care in the Gaza Strip, Palestine.

Methods: A cross-sectional study was conducted among 369 primary care patients with type 2 DM from October to December 2016. Adherence to medications was measured using the Morisky Medication Adherence Scale (MMAS-4). Socio-demographic and clinical variables, provider–patient relationship, health literacy, and health belief were examined for each patient. Univariate, binary logistic regression and multiple linear regression were applied to determine the independent factors influencing adherence to anti-diabetic medications using SPSS version 22.

Results: Of all the respondents, 214 (58%), 146 (39.5%), and nine (2.5%) had high (MMAS score = 0), medium (MMAS score = 1 + 2), and low (MMAS score ≥ 3) adherence to anti-diabetic medications, respectively. Factors that were independently associated with adherence to anti-diabetic medications were as follows: female gender [odds ratio (OR): 1.657, 95% confidence interval (CI): 1.065–2.578] and perception of disease's severity (OR: 1.510, 95% CI: 0.410–5.560). Elderly (t = 1.345) and longer duration of DM (t = 0.899) were also predictors of adherence but showed no statistical significance ($p > 0.05$).

Conclusion: The level of complete adherence to anti-diabetic medications was sub-optimal. New strategies that aim to improve patients' adherence to their therapies are necessary taking into consideration the influencing factors and the importance of having diabetes educators in the primary care centers.

Keywords: medication adherence, diabetes mellitus, factors, Palestine, cross-sectional

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Brian Godman, Karolinska Institutet, Sweden

****Correspondence:***
Mahmoud Radwan
mradwan78@hotmail.com

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INTRODUCTION

Diabetes mellitus (DM) is a serious and a rapidly growing public health problem that affects millions of people. It usually co-exists with other medical conditions, and its prevalence is increasing year by year reaching epidemic proportions. Currently, 387 million people have DM (1) and are expected to

Iran J Public Health, Vol. 46, No.5, May 2017, pp.650-658

Original Article

Psychometric Soundness of an Arabic Version of the Jefferson Scale of Attitude toward Physician and Nurse Collaboration (JSAPNC): A Preliminary Study

***Aymen ELSOUS**[1, 2], **Ali AKBARI SARI**[1], **Mahmoud RADWAN**[1], **Samah MOHSEN**[2], **Hatem ABU ZAYDEH**[3]

1. *Dept. of Health Management and Economics, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran*
2. *Quality Improvement and Infection Control Office, Shifa Medical Complex, Ministry of Health, Gaza Strip, Palestine*
3. *Al Mustaqbal Research Center, Gaza Strip, Palestine*

***Corresponding Author:** Email: aymenelsous65@gmail.com

(Received 14 Sep 2016; accepted 12 Jan 2017)

Abstract

Background: The Jefferson Scale of Attitude toward Physician-Nurse Collaboration (JSAPNC) has been used to measure the attitude regarding collaboration between nurses and physicians. The aim of this preliminary study was to test the reliability and validity of an Arabic version of the questionnaire and adapt it for use in Palestine.

Methods: Forward-backward translation of guidelines provided in the literature was followed. Content validity was examined by nine health experts and reliability was assessed with Cronbach's coefficient alpha; test-retest reliability. Construct validity was explored with exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) by means of survey among 414 physicians and nurses worked at Shifa Medical Complex in the Gaza Strip in 2015.

Results: Response rate was 65% and Cronbach's coefficient alpha was 73.2 for the entire sample. Test-retest reliability was 0.79 measured by Pearson correlation**.** Factor analysis with Varimax rotation revealed four factors explained 60.5% of the variance in the responses labeled as physician-nurse collaboration, doctor's authority, Shared education and Nursing role in-patient care. Goodness of fit indices from the CFA showed a satisfactory model of fit; Comparative Fit Index (CFI) = 0.89; Root Mean Square Error of Approximation (RMSEA) = 0.06; Standardized Root Mean Square Residual (SRMR) = 0.03; and Hoelter index = 206.

Conclusion: The Arabic version of JSAPNC is psychometrically sound tool with satisfactory measurement characteristics including validity and internal consistency reliability. Future research is required to replicate these findings with larger and representative sample. Generalization to Arab speaking countries can be considered but with caution.

Keywords: Reliability, Validity, Psychometrics, Physician-nurse collaboration, Teamwork, Inter professional collaboration

Introduction

Inter-professional collaboration is critical for patient care and outcomes. Teamwork and collaboration between physicians and nurses have seen as a rock component of professionalism because they have been found to be matched with improvement of health outcomes and quality of patient care (1) including reduction of mortality rate in inpatient settings (2), job satisfaction (3), maintaining patient safety (4) and lower health care cost (5).

The collaboration between physicians and nurses is a communicative process within the provision of patient care and is involving share of responsibility, solving common field problems, integration of patient care management and decision making through obvious and defective communication path (6). Collaboration means "collective action toward a common goal in spirit of trust and harmony" (7).

2- Danial Getacher Feleke

First Name	Last Name	Program	Level	School
Daniel Getacher	Feleke	Health Education	M.Sc.	Public Health

Published Articles:

	Title of the Article
1	DNA Sequence Polymorphism of the Lactate Dehydrogenase Genefrom Iranian Plasmodium vivax and Plasmodium falciparum Isolates

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http:// tums.ac.ir

Iran J Parasitol

Open access Journal at
http:// ijpa.tums.ac.ir

Iranian Society of Parasitology
http:// isp.tums.ac.ir

Original Article

DNA Sequence Polymorphism of the Lactate Dehydrogenase Genefrom Iranian *Plasmodium vivax* and *Plasmodium falciparum* Isolates

Daniel GETACHER FELEKE [1], *Mehdi NATEGHPOUR [1,2], Afsaneh MOTEVALLI HAGHI [1], Homa HAJJARAN [1], Leila FARIVAR [1], Mehdi MOHEBALI [1], Reza RAOOFIAN [3]

1. *Department of Medical Parasitology and Mycology, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran*
2. *Center for Research of Endemic Parasites of Iran, Tehran University of medical sciences, Tehran, Iran*
3. *Legal Medicine Research Center, Legal Medicine Organization, Tehran Iran*

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P. vivax

***Correspondence Email:**
nateghpourm@sina.tums.ac.ir

Abstract

Background: Parasite lactate dehydrogenase (*p*LDH) is extensively employed as malaria rapid diagnostic tests (RDTs). Moreover, it is a well-known drug target candidate. However, the genetic diversity of this gene might influence performance of RDT kits and its drug target candidacy. This study aimed to determine polymorphism of *p*LDH gene from Iranian isolates of *P. vivax* and *P. falciparum.*

Methods: Genomic DNA was extracted from whole blood of microscopically confirmed *P. vivax* and *P. falciparum* infected patients. *p*LDH gene of *P. falciparum* and *P. vivax* was amplified using conventional PCR from 43 symptomatic malaria patients from Sistan and Baluchistan Province, Southeast Iran from 2012 to 2013.

Results: Sequence analysis of 15 *P. vivax* LDH showed fourteen had 100% identity with *P. vivax* Sal-1 and Belem strains. Two nucleotide substitutions were detected with only one resulted in amino acid change. Analysis of *P. falciparum* LDH sequences showed six of the seven sequences had 100% homology with *P. falciparum* 3D7 and Mzr-1. Moreover, *Pf*LDH displayed three nucleotide changes that resulted in changing only one amino acid. *Pv*LDH and *Pf*LDH showed 75%-76% nucleotide and 90.4%-90.76% amino acid homology.

Conclusion: *p*LDH gene from Iranian *P. falciparum* and *P. vivax* isolates displayed 98.8-100% homology with 1-3 nucleotide substitutions. This indicated this gene was relatively conserved. Additional studies can be done weather this genetic variation can influence the performance of *p*LDH based RDTs or not.

3- Gidiglo Godwin Nutifafa

First Name	Last Name	Program	Level	School
Gidiglo Godwin	Nutifafa	Entomology	M.Sc.	Public Health

Published Articles:

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1	Knowledge, attitude and practice of healthcare workers concerning Crimean-Congo hemorrhagic fever in Western Iran

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Knowledge, attitude and practice of healthcare workers concerning Crimean-Congo hemorrhagic fever in Western Iran

Mojtaba Salimi[1,2], Abbas Aghaei Afshar[3*], Mojtaba Limoee[4], Soraya Babakhani[2], Omid Chatrabgoun[5], Ahmad Ali Hanafi-Bojd[1], Gidiglo Godwin Nutifafa[6]

[1]*Department of Medical Entomology & Vector Control, School of Public Health, Tehran University of Medical Sciences (TUMS), Tehran, Iran*

[2]*Department of Health Promotion and Network Expansion, Health Deputy, Kermanshah University of Medical Sciences, Kermanshah, Iran*

[3]*Leishmaniasis Research Center, Kerman University of Medical Sciences, Kerman, Iran*

[4]*Departments of Public Health and Health Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran*

[5]*Department of Mathematical, Statistics and Probability, Malayer University, Iran*

[6]*Department of Medical Entomology & Vector Control, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran*

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ABSTRACT

Objective: To determine the knowledge, attitude and practice of healthcare workers in Kermanshah Province about Crimean-Congo hemorrhagic fever (CCHF).

Methods: This study was conducted in 2014 on healthcare personnel in different job categories including physicians, nurses, midwives, laboratory staff and network health staff of Kermanshah Province by direct interview.

Results: A total of 367 respondents who had more than 5 years of experience in their jobs were interviewed. Among them 91% of physicians and nurses, 97% of midwives and health workers and 96% of laboratory staff stated that they had not been confronted with CCHF patients so far. Regarding knowledge, 76% of physicians, 78% of nurses, 77% of midwives and 58% of laboratory staff believed that the disease is remediable. Most of the interviewed participants stated that the disease pertains to people who are in close contact with domestic animals, but they did not consider their own occupations as one of the risk factors. More than 70% of the respondents believed that the disease may exist in the province or their work field. Generally, the knowledge about CCHF was inadequate, with nurses having the lowest level of knowledge.

Conclusions: Knowledge of Kermanshah healthcare staff about CCHF was poor, especially nurses in a high risk job category. Therefore, it is necessary to conduct specific training programs for the disease identification, transmission, prevention, and treatment as well as the use of personal protection and safety devices.

1. Introduction

Crimean-Congo hemorrhagic fever (CCHF) is an acute hemorrhagic fever caused by segmented, negative-stranded RNA virus belonging to the family Bunyaviridae, genus *Nairovirus*, which is the second most widespread of all medically important arboviruses, after dengue virus. Basically, this disease is transmitted to humans by domestic animals and bite of an infected tick or via aerosol generated from infected animals' excreta. Human to human transmission occurs following contact with an infected person's blood, tissue or fluid discharge. The vectors of this arthropod-borne disease are generally hard ticks of Ixodidae family,

*Corresponding author: Abbas Aghaei Afshar, Leishmaniasis Research Center, Kerman University of Medical Sciences, Kerman, Iran.
Tel: +98 341 3224616
E-mail: afshara2@yahoo.com

The study protocol was approved by the Ethic Committee of Kermanshah University of Medical Sciences which approved the investigations. Informed written consent was obtained from all participants in this study. Confidentiality on the content of the records was kept by the investigators and information was only utilized for the research purpose.

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4- Joseph Kimuli Balikuddembe

First Name	Last Name	Program	Level	School
Joseph Kimuli	Balikuddembe	Disaster Management and Emergency Health	PhD	Public Health

Published Articles:

	Title of the Article
1	Virtual Disaster Simulation: Lesson Learned from an International Collaboration That Can Be Leveraged for Disaster Education in Iran
2	Road traffic incidents in Uganda: A systematic review study of five years trend
3	Progress in nutrition related millennium development goals in Uganda before adoption of post-2015 development agenda: review of goals 1, 2 and 4
4	Factors affecting the exposure, vulnerability and emergency medical service capacity for victims of road traffic incidents in Kampala Metropolitan Area: a Delphi study

PLOS | CURRENTS DISASTERS

Virtual Disaster Simulation: Lesson Learned from an International Collaboration That Can Be Leveraged for Disaster Education in Iran

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Citation

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Authors

Ali Ardalan

Disaster and Emergency Health Academy, National Institute of Health Research, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran; Harvard Humanitarian Initiative, Harvard University, Cambridge, USA.

Joseph Kimuli Balikuddembe

Disaster and Emergency Health Academy, National Institute of Health Research, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.

Pier Luigi Ingrassia

Research Center in Emergency and Disaster Medicine and Computer Science applied to Medicine(CRIMEDIM); Università del Piemonte Orientale, Novara, Italy.

Luca Carenzo

Research Center in Emergency and Disaster Medicine and Computer Science applied to Medicine (CRIMEDIM), Università del Piemonte Orientale, Novara, Italy.

Francesco Della Corte

Research Center in Emergency and Disaster Medicine and Computer Science applied to Medicine (CRIMEDIM), Università del Piemonte Orientale, Novara, Italy.

Ali Akbarisari

Department of Health Care Management, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.

Original Article

Road traffic incidents in Uganda: A systematic review study of five years trend

Joseph Kimuli Balikuddembe[a, b], Ali Ardalan[a, c, d *], Davoud Khorasani-Zavareh[e, f, g], Amir Nejati[h] Kasiima Stephen Munanura[i]

[a] Department of Disaster Public Health, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.
[b] Tehran University of Medical Sciences – International Campus, Tehran, Iran
[c] National Institute of Health Research, Tehran University of Medical Sciences, Tehran, Iran.
[d] Harvard Humanitarian Initiative, Harvard University, Cambridge, USA.
[e] Safety Promotion and Injury Prevention Research Center, Shahid Beheshti University of Medical Sciences, Tehran- Iran.
[f] Department of Health in Disaster and Emergency, School of Health Safety and Environment, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[g] Department of Clinical Science and Education, Karolinska Institute, Stockholm, Sweden.
[h] Emergency Medicine Research Center, Department of Emergency Medicine, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran.
[i] Directorate of Road Traffic and Road Safety, Uganda Police Force, Kampala – Uganda.

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Abstract:

Background: Over the years, Uganda has been one of low and middle-income countries bearing the heaviest burden of road traffic incidents (RTI). Since the proclamation of the United Nations Decade of Action for Road Safety 2011 – 2020, a number of measures have been taken to reduce the burden. However, they ought to be premised on existing evidence-based research which the present review ventures to undertake by reporting about the most recent five years trend of RTI in Uganda.

Methods: Based on Preferred Reporting Items for Systematic Reviews and Meta-Data Analysis (PRISMA) guidelines a systematic review was employed. Using a thematic analysis, articles were grouped into: trauma etiology, trauma care, mortality, cost, trauma registry and communication, intervention and treatment for final analysis.

Results: Of the nineteen articles that were identified to be relevant to the study, the etiology of RTI was inevitably observed to be an important cause of injuries in Uganda. The risk factors cut-across: the crash type, injury physiology, cause, victims, setting, age, economic status, and gender. All studies that were reviewed advanced varying recommendations aimed at responding to the trend of RTIs in Uganda, of which some are in tandem with the five pillars of the United Nations Decade of Action for Road Safety 2011 – 2020.

Conclusion: Peripheral measures to the burden of RTIs in Uganda were undertaken within the five year's timeframe (2011 - 2015) of implementing the United Nations Decade of Action for Road Safety. The measures however, ought to be scaled-up on robust evidence based research available from all the concerned stakeholders beyond Kampala/ or central region to other parts of Uganda.

* ***Corresponding Author at:***
Ali Ardalan: *Department of Disaster Public Health, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.* Tel: +98-912-305019, Fax: +98-21- 88991108, Email: aardalan@tums.ac.ir (***Ardalan A.***).

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PROGRESS IN NUTRITION RELATED MILLENNIUM DEVELOPMENT GOALS IN UGANDA BEFORE ADOPTION OF POST-2015 DEVELOPMENT AGENDA: REVIEW OF GOALS 1, 2 AND 4

Balikuddembe KJ[1&2*], Hosseinzadeh-Attar MJ[3] and A Ardalan[4]

Corresponding author email: jbalikuddembe.k@gmail.com

[1]East African Center for Disaster Health and Humanitarian Research, Kampala, Uganda

[2]Department of Disaster Public Health, School of Public Health - Tehran University of Medical Sciences, Tehran Iran; Tehran University of Medical Sciences - International Campus, Tehran Iran

[3]Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics - Tehran University of Medical Science, Tehran, Iran

[4]Department of Disaster Public Health, School of Public Health -Tehran University of Medical Sciences, Tehran, Iran; National Institute of Health Research, Tehran University of Medical Sciences, Tehran, Iran; Harvard Humanitarian Initiative, Harvard University, Cambridge, USA

ABSTRACT

Promulgation of Millennium Development Goals (MDG) in year 2000 gave hope to the world that common interests and challenges such as poverty and hunger, education, gender equality nd women empowerment, child mortality and maternal health, diseases such as, HIV/AIDS, malaria, environmental sustainability, as well as global partnerships that were affecting the world could, respectively, be prioritized and responded to within a timeframe of the year 2001 to 2015. In this case, the developing countries like Uganda were accorded great attention. Nutrition has been at the forefront of the MDG implementation as one of the daunting challenges affecting developing countries. This paper is based on a narrative review of quantitative and qualitative data aimed at establishing the progress Uganda made towards achieving the three nutrition related MDG (1, 2 and 4). A timeframe of 2001 when the goals were officially launched up to the deadline of 31st December 2015 and the adoption of the Post-2015 Development Agenda was considered.

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RESEARCH ARTICLE Open Access

Factors affecting the exposure, vulnerability and emergency medical service capacity for victims of road traffic incidents in Kampala Metropolitan Area: a Delphi study

Joseph Kimuli Balikuddembe[1,2], Ali Ardalan[1,3,4*], Davoud Khorasani Zavareh[5,6,7], Amir Nejati[1,8] and Stephen Kasiima[9]

Abstract

Background: The Kampala Metropolitan Area (KMA) is the fastest developing region in Uganda. Over recent years, this has placed exponential demand on the road sector, which consequently has contributed to rapid growth in motorized vehicles which, predisposes the region to a high risk of road traffic incidents (RTIs). A number of concerted road safety and post-crash management measures to respond to RTIs in the KMA in particular and Uganda as a whole have been undertaken. However, there is a need to greatly improve the measures by better identifying the factors influencing the exposure, vulnerability and emergency medical service (EMS) capacity for RTI victims. The present study seeks to investigate and reveal these factors.

Methods: A Delphi technique employing a questionnaire and involving a multidisciplinary panel of experts was used in three rounds.

Results: The ten (10) most important factors affecting the exposure, vulnerability and EMS capacity for victims of RTIs in the KMA were identified. Socio-cultural, infrastructure and road safety aspects were the factors most identified as affecting the exposure and vulnerability. The absence of a national EMS policy and post-crash care system, as well as the fact that many victims lack health insurance, were noted to be the factors adversely affecting the EMS capacity.

Conclusions: There exists is a real need to substantially reduce the burden of RTIs in KMA, with ultimate goal of saving lives that are being lost needlessly and reducing the impact of injuries and trauma and the economic losses associated with it. This study offers insights into the causes of RTIs and the most appropriate ways of responding to them especially with the establishment and empowerment of predefined and structured EMS systems.

Keywords: Road traffic incidents, Exposure, Vulnerability, Emergency medical services, Kampala, Uganda

Background

In recent years, the Kampala Metropolitan Area (KMA) in particular and Uganda as a whole have been registering exponential progress in the road sector. Some roads have been fully or substantially completed; some are under construction and some are due for construction as soon as it becomes possible [1]. This crucial progress in the road sector has helped to spearhead the modest economic growth and development in Uganda. However, at the same time it has resulted, in an upsurge of road traffic incidents (RTIs) which contribute to mortality, injury, morbidity, trauma and disability [2–4]. RTIs also cost the governments, especially in the low and middle income countries (LMICs) such as Uganda, approximately 3% of their annual Gross Domestic Product (GDP) [5].

The KMA is the fastest developing region in Uganda. It has close proximity to Kampala, the capital city of Uganda, which is the political epicenter and economic hub accounting for 80% of all of Uganda's industrial and commercial activities [6]. Most of the developed roads in good condition and Emergency Medical Service (EMS)

* Correspondence: aardalan@tums.ac.ir
[1]Department of Disaster Public Health, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[3]National Institute of Health Research, Tehran University of Medical Sciences, Tehran, Iran
Full list of author information is available at the end of the article

5- Luche Tadesse Ejeta

First Name	Last Name	Program	Level	School
Luche Tadesse	Ejeta	Disaster Management and Emergency Health	PhD	Public Health

Published Articles:

	Title of the Article
1	Health Sector Initiatives for Disaster Risk Management in Ethiopia: A Narrative Review
2	Application of Behavioral Theories to Disaster and Emergency Health Preparedness: A Systematic Review
3	Predictors of community preparedness for flood in Dire-Dawa town, Eastern Ethiopia: Applying adapted version of Health Belief Model

PLOS | CURRENTS DISASTERS

Health Sector Initiatives for Disaster Risk Management in Ethiopia: A Narrative Review

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Authors

Luche Tadesse

Department of Disaster Public Health, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran; Private Consultant, Addis Ababa, Ethiopia.

Ali Ardalan

Department of Disaster & Emergency Health, Iran's National Institute of Health Research; Department of Disaster Public Health, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran; Harvard Humanitarian Initiative, Harvard University.

Abstract

Background: Natural and man-made disasters are prevailing in Ethiopia mainly due to drought, floods, landslides, earthquake, volcanic eruptions, and disease epidemics. Few studies so far have critically reviewed about medical responses to disasters and little information exists pertaining to the initiatives being undertaken by health sector from the perspective of basic disaster management cycle. This article aimed to review emergency health responses to disasters and other related interventions which have been undertaken in the health sector.

Methods: Relevant documents were identified by searches in the websites of different sectors in Ethiopian and international non-governmental organizations and United Nations agencies. Using selected keywords, articles were also searched in the data bases of Medline, CINAHL, Scopus, and Google Scholar. In addition, pertinent articles from non-indexed journals were referred to.

Results: Disaster management system in Ethiopia focused on response, recovery, and rehabilitation from 1974 to 1988; while the period between 1988 and 1993 marked the transition phase towards a more comprehensive approach. Theoretically, from 1993 onwards, the disaster management system has fully integrated the mitigation, prevention, and preparedness phases into already existing response and recovery approach, particularly for drought. This policy has changed the emergency response practices and the health sector has taken some initiatives in the area of emergency health care. Hence, drought early warning system, therapeutic feeding program in hospitals, health centers and posts in drought prone areas to manage promptly acute malnutrition cases have all been put in place. In addition, public health disease emergencies have been responded to at all levels of health care system.

PLOS | CURRENTS DISASTERS

Application of Behavioral Theories to Disaster and Emergency Health Preparedness: A Systematic Review

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Authors

Luche Tadesse Ejeta

Department of Disaster & Emergency Health, School of Public Health, Tehran University of Medical Sciences-International Campus, Tehran, Iran; Private Consultant, Addis Ababa, Ethiopia.

Ali Ardalan

Department of Disaster Public Health, School of Public Health, Tehran University of Medical Science, Tehran, Iran; Department of Disaster and Emergency Health, National Institute of Health Research, Tehran University of Medical Science, Tehran, Iran; Harvard Humanitarian Initiative, Harvard University, Cambridge, USA.

Douglas Paton

School of Psychological and Clinical Sciences, Charles Darwin University, Darwin, Northern Territory, Australia.

Abstract

Background: Preparedness for disasters and emergencies at individual, community and organizational levels could be more effective tools in mitigating (the growing incidence) of disaster risk and ameliorating their impacts. That is, to play more significant roles in disaster risk reduction (DRR). Preparedness efforts focus on changing human behaviors in ways that reduce people's risk and increase their ability to cope with hazard consequences. While preparedness initiatives have used behavioral theories to facilitate DRR, many theories have been used and little is known about which behavioral theories are more commonly used, where they have been used, and why they have been preferred over alternative behavioral theories. Given that theories differ with respect to the variables used and the relationship between them, a systematic analysis is an essential first step to answering questions about the relative utility of theories and providing a more robust evidence base for preparedness components of DRR strategies. The goal of this systematic review was to search and summarize evidence by assessing the application of behavioral theories to disaster and emergency health preparedness across the world.

Methods: The protocol was prepared in which the study objectives, questions, inclusion and exclusion criteria, and sensitive search strategies were developed and pilot-tested at the beginning of the study. Using selected keywords, articles were searched mainly in PubMed, Scopus, Mosby's Index (Nursing Index) and Safetylit

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Predictors of community preparedness for flood in Dire-Dawa town, Eastern Ethiopia: Applying adapted version of Health Belief Model

Luche Tadesse Ejeta[a,b,**], Ali Ardalan[c,d,e,*], Douglas Paton[f], Mehdi Yaseri[g]

[a] Department of Disaster and Emergency Health, School of Public Health, Tehran University of Medical Sciences-International Campus, No. 6-Hajatdost Alley-South Felestin Street, After Keshavarz Blvd., P.O. BOX: 1416683511, Tehran, Iran
[b] Private Consultant, Addis Ababa, Ethiopia
[c] Department of Disaster Public Health, School of Public Health, Tehran University of Medical Science, No. 78, Italia Ave. 1417755331, Tehran, Iran
[d] Department of Disaster and Emergency Health, National Institute of Health Research, Tehran University of Medical Science, Tehran, Iran
[e] Harvard Humanitarian Initiative, Harvard University, Cambridge, USA
[f] School of Psychological and Clinical Sciences, Charles Darwin University, Ellengowan Drive, Casuarina, Darwin, Northern Territory 0909, Australia
[g] Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

A cross-sectional study was conducted in June and July 2015, aiming at investigating the cross cultural utility of adapted version of Health Belief Model (HBM) in predicting disaster preparedness for flood hazards at household levels in Dire Dawa town, Ethiopia. To accommodate the fact that this work was undertaken in a collectivistic culture in which social processes play more prominent roles in interpretation and action selection, a structured questionnaire was developed by adding community participation to the prominent constructs of HBM and modifying self-efficacy to collective-efficacy. Households (660) were selected by stratified systematic random sampling technique. From each household, an individual aged 18 or above was selected by random and participated in the study. Structural Equation Modeling (SEM) and Generalized Structural Equation Modeling (GSEM) analyses were done using STATA version-13.0. SEM analysis showed that the total effects of perceived threat (path coefficient (β)=−0.002, 95% Confidence Interval (CI): [−0.003, −0.001]), perceived benefits minus perceived barriers (β=−0.048, 95% CI: [−0.080, −0.015]), and cues to actions (β=−0.18, 95% CI: [−0.25, −0.11]) on preparedness were significant. The total effects of collective efficacy (β=0.011, 95% CI: [−0.027, 0.049]), perceived susceptibility (β=−0.0007, 95% CI: [−0.003, 0.002]), perceived severity (β=−0.002, 95% CI: [−0.007, 0.004]), and community participation (β=−0.0001, 95% CI: [−0.0003, 0.0001]) on preparedness were non-significant. In GSEM factor analysis, ethnicity, religion and residential duration were significantly associated with preparedness. Intervention is needed on barriers and perceived threat to enhance collective efficacy and preparedness.

1. Introduction

The adverse impacts of natural hazards remain high. For example, in 2014, 324 natural hazard events were registered worldwide and these caused 7823 deaths. Of the events that contributed to these deaths, hazards of hydrological and meteorological origins were the most frequently occurring [1]. Losses from hydrological and meteorological phenomenon will increase in the future as a result of global climatic changes [2–5]. Given the current and anticipated future impact of such events, it becomes important to consider how to facilitate people's readiness or preparedness to deal with hydrological and meteorological hazard event consequences. This view is consistent with the intention advocated by the "Hyogo Framework for Action (HFA) 2005–2015", developed under the leadership of United Nations International Strategy for Disaster Reduction (UNISDR) and through the collaboration of representatives of nations and partner organizations [6].

One of the five priority areas of HFA was strengthening "disaster preparedness for effective response at all levels" and the final expected outcome of HFA was "substantial reduction of disaster losses, in lives and in the social, economic and environmental assets of communities and countries" [6]. UNISDR is reporting that "progress has been

* Corresponding author at: Department of Disaster Public Health, School of Public Health, Tehran University of Medical Science, No. 78, Italia Ave. 1417755331, Tehran, Iran.
** Corresponding author at: Private Consultant, Addis Ababa, Ethiopia.
E-mail addresses: tadesse.ejeta@gmail.com (L.T. Ejeta), aardalan@gmail.com, aardalan@tums.ac.ir (A. Ardalan), Douglas.Paton@cdu.edu.au (D. Paton), m.yaseri@gmail.com (M. Yaseri).

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6- Kabir Magaji Hamid

First Name	Last Name	Program	Level	School
Kabir Magaji	Hamid	Immunology	PhD	Public Health

Published Articles:

	Title of the Article
1	The Role of Death Domains Superfamily in Multiple Sclerosis Pathogenesis
2	Role of apoptosis in common variable immunodeficiency and selective immunoglobulin A deficiency
3	Quantitative Evaluation of BAFF, HMGB1, TLR 4 and TLR 7 Expression in Patients with Relapsing Remitting Multiple Sclerosis
4	EBV and vitamin D status in relapsing‐remitting multiple sclerosis patients with a unique cytokine signature
5	Autoantibodies Profile in Vitiligo
6	Role of Proangiogenic Factors in Immuno-pathogenesis of Multiple Sclerosis:A Systemic Review

The Role of Death Domains Superfamily in Multiple Sclerosis Pathogenesis

Kabir M. Hamid[1], Abbas Mirshafiey[2*]

[1]Department of Immunology, School of Public Health, Tehran University of Medical Sciences—International Campus (TUMS-IC), Tehran, Iran
[2]Department of Immunology, School of Public Health, Tehran University of Medical Sciences (TUMS), Tehran, Iran
Email: kabiru20@yahoo.com, [*]mirshafiey@tums.ac.ir

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Abstract

Multiple sclerosis (MS) and its animal model, experimental autoimmune encephalomyelitis (EAE), are inflammatory diseases of the central nervous system (CNS), mediated by several immune cells. Oligodendrocytes are responsible for the formation and maintenance of myelin around multiple axons. In MS oligodendrocytes are the targets of inflammatory and immune attacks. Thus, the destruction of a single oligodendrocyte, possibly by apoptosis, results in the loss of myelin around several axons and the loss of many oligodendrocytes limiting the ability to repair or regenerate demyelinated areas. Apoptosis is mediated by an aggregation of various protein components, specifically death domains (DD) superfamily. This superfamily is composed of the death domain (DD), the death effector domain (DED), the caspase recruitment domain (CARD) and the pyrin domain (PYD) subfamilies. Within each subfamily, members form homotypic interactions and facilitate the assembly of oligomeric signaling complexes. Members of the death domain superfamily are critical components of apoptotic and inflammatory signaling. We summarize the structure and functions of the DD superfamily, and describe the role of the DD proteins in oligodendrocytes death and proinflammatory activation in MS pathogenesis.

Keywords

Multiple Sclerosis, Death Domain, Oligodendrocytes, Inflammation, Apoptosis

Subject Areas: **Immunology, Neurology, Pathology**

1. Introduction

Multiple sclerosis (MS) and its animal model, experimental autoimmune encephalomyelitis (EAE), are inflam-

[*]Corresponding author.

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Review

Role of apoptosis in common variable immunodeficiency and selective immunoglobulin A deficiency

Reza Yazdani[a,b], Maryam Fatholahi[c], Mazdak Ganjalikhani-Hakemi[a], Hassan Abolhassani[b,d], Gholamreza Azizi[e], Kabir Magaji Hamid[f,g], Nima Rezaei[h], Asghar Aghamohammadi[b,*]

[a] Department of Immunology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
[b] Research Center for Immunodeficiencies, Pediatrics Center of Excellence, Children's Medical Center, Tehran University of Medical Science, Tehran, Iran
[c] Department of Biology, Faculty of Science, University of Isfahan, Isfahan, Iran
[d] Division of Clinical Immunology, Department of Laboratory Medicine, Karolinska Institutet at the Karolinska University Hospital Huddinge, Stockholm, Sweden
[e] Imam Hassan Mojtaba Hospital, Alborz University of Medical Sciences, Karaj, Iran
[f] Immunology Department, School of Public Health, Tehran University of Medical Sciences-International Campus (TUMS-IC), Tehran, Iran
[g] Immunology Department, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria
[h] Department of Immunology, School of Medicine, Tehran University of Medical Science, Tehran, Iran

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ABSTRACT

Common variable immunodeficiency (CVID) and selective IgA deficiency (SIgAD) are the most common primary immunodeficiencies in human. Both diseases share clinical manifestation and molecular defects. Increased apoptosis may be one of the mechanisms involved in the pathogenesis of CVID and SIgAD. Elevated apoptosis in this disorder leads to defective long-term survival of B-cells, reduced antibody production, decreased lymphocyte proliferation and defective cytokine secretion. For the first time, we reviewed the role of apoptosis in CVID and SIgAD.

1. Introduction

Common variable immunodeficiency (CVID) is the most common symptomatic primary immunodeficiency characterized by defective antibody production and an increased incidence of recurrent bacterial infections, inflammatory and autoimmune disorders, malignancies and granuloma (Cunningham-Rundles and Bodian, 1999; Aghamohammadi et al., 2005; Chapel and Cunningham-Rundles, 2009; Aghamohammadi et al., 2010). CVID has prevalence rate of about 1:50,000 to 1:25,000 (Cunningham-Rundles, 2010; Jolles, 2013). The diagnostic criteria for CVID includes marked reduction of serum IgG, IgA, and/or IgM levels, defective specific antibody responses to protein and polysaccharide antigens and also increased susceptibility to recurrent bacterial infections as well as no evidence of profound T-cell deficiency in patients older than 4 years (Aghamohammadi et al., 2005; Chapel et al., 2008). CVID has a complex genetic basis and may arise from a number of different gene defects involved in B-cell activation and differentiation, for instance *inducible T-cell costimulator* (*ICOS*) (Grimbacher et al., 2003), *transmembrane activator and CALM interactor* (*TACI*) (Salzer et al., 2005), *B-cell activating factor-receptor* (*BAFF-R*) (Warnatz et al., 2009), *CD19, CD21, CD81* (van Zelm et al., 2006; van Zelm et al., 2010; Thiel et al., 2012; Yazdani et al., 2014), *CD20* (Kuijpers et al., 2010), *Lipopolysaccharide-responsive and beige-like anchor protein* (*LRBA*) (Lopez-Herrera et al., 2012) and *Phospholipase Cγ2* (*PLCγ2*) (Ombrello et al., 2012) genes. In spite of the results obtained from recent years, many underlying defects are not yet known (Eibel et al., 2010).

Selective IgA deficiency (SIgAD) is the most common primary antibody deficiencydescribed as serum IgA level of less than 7 mg/dl, in the presence of normal IgG subclasses and IgM as well as normal specific antibody response in individuals older than 4 years and exclusion of other causes of hypogammaglobulinaemia (Aghamohammadi et al., 2009; Wang and Hammarström, 2012). Prevalence of SIgAD differs among racial groups, ranging from lowest frequency in Asian and oriental populations to the highest frequency in Caucasians and western countries (Yel, 2010; Modell et al., 2014; Yazdani et al., 2015). Individuals with SIgAD usually are asymptomatic, however abnormality of immunoglob-

* Corresponding author at: Children's Medical Center Hospital, 62 Qarib St., Keshavarz Blvd., Tehran 14194, Iran. Fax: +98 21 6692 3054.
E-mail address: aghamohammadi@sina.tums.ac.ir (A. Aghamohammadi).

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BRIEF COMMUNICATION
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Quantitative Evaluation of BAFF, HMGB1, TLR 4 and TLR 7 Expression in Patients with Relapsing Remitting Multiple Sclerosis

Kabir Magaji Hamid[1,2], Ahmad Nejati[3], Zabihollah Shoja[4], Yaghoub Mollaei-Kandelousd[5], Rozita Doosti[6], Abbas Mirshafiey[7], Abbas Tafakhori[8], Mohammad Ali Sahraian[6], and Sayed Mahdi Marashi[3]

[1] *Department of Pathobiology, Immunology division, School of Public Health, Tehran University of Medical Sciences-International Campus (TUMS-IC), Tehran, Iran*
[2] *Department of Immunology, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria*
[3] *Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*
[4] *Department of Virology, Pasteur Institute of Iran, Tehran, Iran*
[5] *Immunology Department, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran*
[6] *MS Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran*
[7] *Department of Pathobiology, Immunology Division, SPH, Tehran University of Medical Sciences, Tehran, Iran*
[8] *Iranian Center of Neurological Research, Department of Neurology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

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ABSTRACT

Multiple sclerosis is a chronic inflammatory disease of the central nervous system characterized by a complex immune response. Because of the complex nature of MS pathogenesis, a panel of biomarkers derived from different platforms will be required to reflect disease-related alterations.

Monitoring and evaluation of molecules associated with the pathogenesis of the disease would provide useful information on disease progression and therapeutic assessment. In view of this, we evaluated the mRNA expression levels of B-cell activating factor (BAFF), high mobility group box 1 (HMGB-1), Toll like receptor (TLR) 4 and TLR7 in MS. These molecules are implicated in the pathogenesis of MS; however, they have received little attention. PBMCs were isolated from whole blood of 84 relapsing remitting multiple sclerosis patients and 70 healthy controls. Relative quantitative RT-PCR was applied to quantify the transcriptional levels of the immune markers.

The mRNA expression levels of TLR7 were significantly elevated in RRMS patients than healthy controls. TLR4 expression was found to be significantly lower in the patients than control group. We found no difference analyzing the mRNA levels of BAFF and HMGB1. Our data highlights the immune marker correlates in RRMS patients.

However, further in-depth studies are warranted to check the role and the relevance of these immune markers in autoimmune diseases such as MS.

Keywords: Biomarkers, Cytokines, HMGB proteins, Inflammation, Multiple Sclerosis, RNA messenger

Corresponding Author: Sayed Mahdi Marashi, PhD; Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. P.O.BOX: 14155- 6446, Tel/Fax: (+98 21) 8896 2343, E-mail: m-marashi@tums.ac.ir

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ORIGINAL INVESTIGATION

EBV and vitamin D status in relapsing-remitting multiple sclerosis patients with a unique cytokine signature

Ahmad Nejati[1] · Zabihollah Shoja[2] · Shohreh Shahmahmoodi[1] · Abbas Tafakhori[3] · Yaghoub Mollaei-Kandelous[4] · Farhad Rezaei[1] · Kabir Magaji Hamid[5] · Abbas Mirshafiey[8] · Rozita Doosti[6] · Mohammad Ali Sahraian[6] · Mahmood Mahmoudi[7] · Fazel Shokri[8] · Vince Emery[9] · Sayed Mahdi Marashi[1,5]

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Abstract Multiple sclerosis, a debilitating autoimmune and inflammatory disease of the central nervous system, is associated with both infectious and non-infectious factors. We investigated the role of EBV infection, vitamin D level, and cytokine signature in MS patients. Molecular and serological assays were used to investigate immune biomarkers, vitamin D level, and EBV status in 83 patients with relapsing-remitting multiple sclerosis and 62 healthy controls. In total, 98.8 % of MS patients showed a history of EBV exposure compared to 88.6 % in the healthy group ($p = 0.005$). EBV DNA load was significantly higher in MS patients than healthy subjects ($p < 0.0001$). Using a panel of biomarkers, we found a distinct transcriptional signature in MS patients compared to the healthy group with mRNA levels of CD73, IL-6, IL-23, IFN-γ, TNF-α, IL-15, IL-28, and IL-17 significantly elevated in MS patients ($p < 0.0001$). In contrast, the mRNA levels for TGF-β, IDO, S1PR1, IL-10, and CCL-3 were significantly lower in MS patients compared to healthy controls ($p < 0.0001$). No significant differences were found with the mRNA levels of IL-13, CCL-5, and FOXP3. Interestingly, in MS patients we found an inverse correlation between vitamin D concentration and EBV load, but not EBNA-1 IgG antibody levels. Our data highlight biomarker correlates in MS patients together with a complex interplay between EBV replication and vitamin D levels.

Keywords Epstein–Barr virus · Relapsing-remitting multiple sclerosis · Vitamin D · Immune biomarker signature

Abbreviations

EBV	Epstein–Barr virus
RRMS	Relapsing-remitting multiple sclerosis
PRMS	Primary remitting multiple sclerosis
EDSS	Expanded Disability Status Scale
EBNA-1	EBV nuclear antigen 1
EBNA-2	EBV nuclear antigen 2
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase
IDO	Indoleamine 2,3-dioxygenase
S1PR1	Sphingosine-1-phosphate receptor 1
CNS	Central nervous system

Ahmad Nejati and Zabihollah Shoja have contributed to this work equally.

✉ Sayed Mahdi Marashi
m-marashi@tums.ac.ir

1 Virology Department, School of Public Health (SPH), Tehran University of Medical Sciences (TUMS), Tehran 14155-6446, Iran

2 Virology Department, Pasteur Institute of Iran, Tehran, Iran

3 Iranian Centre of Neurological Research, Department of Neurology, School of Medicine, Tehran University of Medical Sciences (TUMS), Tehran, Iran

4 Immunology Department, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran

5 Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran

6 MS Research Center, Neuroscience Institute, Tehran University of Medical Sciences (TUMS), Tehran, Iran

7 Department of Epidemiology and Biostatistics, School of Public Health (SPH), Tehran University of Medical Sciences (TUMS), Tehran, Iran

8 Immunology Department, School of Public Health (SPH), Tehran University of Medical Sciences (TUMS), Tehran, Iran

9 Department of Microbial and Cellular Sciences, University of Surrey, Guildford, Surrey GU2 7XH, UK

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Review Article Hybrid Open Access

Autoantibodies Profile in Vitiligo

Kabir Magaji Hamid[1,2]*, Zelalem Kiros Bitsue[2] and Abbas Mirshafie [3]

[1]Department of Immunology, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University Sokoto, P.M.B 2346, Nigeria
[2]Department of Immunology, School of Public Health, Tehran University of Medical Sciences-International Campus (TUMS-IC) Tehran-14155, Box: 6446, Iran
[3]Department of Immunology, School of Public Health, Tehran University of Medical Sciences, (TUMS) Tehran-14155, Box: 6446, Iran

Abstract

Vitiligo is one of the disease which is yet to understand its pathogenesis, however many studies associate this disease as an autoimmune. Detection of autoimmune cells in the serum, lesional and perilesional area of vitiligo patients gives more insight on the disease mechanism. Presence of autoantibodies against melanocytes antigens in vitiligo patients indicates an autoimmune involvement in the aetiology of the disease. Identification and characterization of vitiligo autoantibodies would pave the way for developing new laboratory test for diagnosis. Studying the autoantibodies profile can give an impression on the disease condition of vitiligo patients. We realized the need of research emphasis in this area as more is yet to be discovered. In this review we give an account on different autoantibodies and their associated autoantigens in vitiligo as another effort of providing an updated data for detail analysis.

Keywords: Antibodies; Autoimmunity; Melanocytes; Pigmentation; Vitiligo

Introduction

Vitiligo is an acquired depigmenting disorder in which melanocytes are destroyed, resulting in patchy depigmentation on skin and mucosal surfaces [1,2]. The worldwide prevalence is range from 0.5–2% [3]. Clinically, vitiligo presents as round or oval white, hypopigmented macules with regular or raised red borders [4]. The disease was classified based on distribution patterns of vitiliginous lesions into focal vitiligo (isolated lesion), segmental vitiligo (unilateral macular lesions which generally cover a dermatome), non-segmental (generalized) vitiligo (most common form, disseminated macules of variable size, usually with a symmetric distribution and a certain predilection for extensor surfaces) [5,6] and universalis vitiligo (severe form that affects more than 80% of the body surface) [4].

The pathogenesis of vitiligo is unclear. although both genetic [7] and environmental factors are the ones implicated as the major cause [8], however, there are other several factors proposed in the pathogenesis of the disease (Figure 1), these include the following, physical trauma [9,10], psychological stress [11], infections [12], neural factors [11,13,14], biochemical factors [15-17], melanocytes growth factors [18], melanocortin hormones [19] and autoimmunity [20].

Most authorities favored the autoimmune causes due to the strong associations of vitiligo with multiple autoimmune diseases; the presence of autoantibodies [21,22] (Table 1), so that autoreactive T lymphocytes against pigment cells supports the theory that there is an autoimmune involvement in the aetiology of the disease [23]. However, even if the specific antibodies to pigment cells or secondary antibodies are not pathogenic, the identification and characterization of their target antigens could be a landmark for uncovering the pathogenic mechanism, formation of autoantibodies [24] and development of biomarkers. In this review we describe some autoantibodies and their associated autoantigens as potential biomarkers for laboratory diagnosis, treatment, monitoring and assessment of vitiligo.

Anti-Melanocytes

Melanocytes originate from neural crest and are responsible for the synthesis of melanin in melanosomes, membrane-bound organelles [25,26]. They are able to secrete a wide range of signal molecules, including cytokines, Pro-opiomelanocortin (POMC) peptides, catecholamines, and NO in response to UV irradiation and other stimuli, for the regulation of variety of skin cells [27]. In active non-segmental vitiligo, melanocyte cytotoxicity is associated with increase in serum levels of immunoglobulin G (IgG) anti-melanocyte/ vitiligo antibodies (V-IgG) and immunologic markers [28]. IgG anti-melanocyte antibodies were reported to induce melanocyte damage in vitro by a complement-mediated mechanism and antibody-dependent cellular cytotoxicity [29,30]. The melanocytotoxicity could be due to wrong presentation of vitiligo antigens to destructive cytotoxic T cells; this result from abnormal expressions of HLA-DR and increase expression of intercellular adhesion molecule-1 (ICAM-1) on melanocytes by IgG anti-melanocyte antibodies [29,31]. Antibodies to melanocytes occur at a significantly increased frequency in the sera of vitiligo patients when compared with healthy individuals [32]. Interestingly, correlations can also exist between the incidence and level of melanocyte antibodies and both the activity and extent of vitiligo [33]. Identification of anti-melanocyte or vitiligo antibodies against target antigens is useful in developing new diagnostic tests and serves as biomarkers for assessing the progress of the disease [23].

Anti-thyroid peroxidase (anti-TPO)

Anti-TPO antibodies are specific for the autoantigen TPO; found in active phase of chronic autoimmune thyroiditis; can be used in monitoring the disease progress in patients with these antibodies [34]. Most of the anti-TPO antibodies are produced by thyroid infiltrating lymphocytes and partly from lymph nodes and bone marrow [35]. In the past decades, many research teams reported the associations between vitiligo and other autoimmune diseases such as thyroid disease and anti-thyroid antibodies [36]. A previous study by Dave et al. reported 31.4% prevalence of thyroid-specific autoantibodies in patients with vitiligo [37]. A more recent study reported a mean prevalence of 20.8% in patients with vitiligo [38]. Again, Kasumagic-Halilovic et al. found higher frequency of anti-TPO in vitiligo patients than control group [39]. Considering these findings vitiligo shows strong association with thyroid autoimmunity, therefore anti-TPO

***Corresponding author:** Kabir Magaji Hamid, Department of Immunology, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University Sokoto, P.M.B 2346, Nigeria, Tel: +989102159812; E-mail:kmhamid@hotmail.co.uk

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REVIEW ARTICLE
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Role of Proangiogenic Factors in Immunopathogenesis of Multiple Sclerosis: A Systemic Review

Kabir Magaji Hamid[1, 2] and Abbas Mirshafiey[3]

[1] *Department of Immunology, School of Public Health, Tehran University of Medical Sciences-InternationalCampus, Tehran, Iran*
[2] *Department of Immunology, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria*
[3] *Department of Immunology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*

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ABSTRACT

Angiogenesis is a complex and balanced process in which new blood vessels form from preexisting ones by sprouting, splitting, growth and remodeling. This phenomenon plays a vital role in many physiological and pathological processes.

However, the disturbance in physiological process can play a role in pathogenesis of some chronic inflammatory diseases, including multiple sclerosis (MS) in human and its animal model. Although the relation between abnormal blood vessels and MS lesions was established in previous studies, but the role of pathological angiogenesis remains unclear.

In this study, the link between proangiogenic factors and multiple sclerosis pathogenesis was examined by conducting a systemic review. Thus we searched the English medical literature via PubMed, ISI web of knowledge, Medline and virtual health library (VHL) databases. In this review, we describe direct and indirect roles of some proangiogenic factors in MS pathogenesis and report the association of these factors with pathological and inflammatory angiogenesis.

Keywords: Angiogenesis Inducing Agent; Blood-Brain Barrier; Encephalomyelitis, Autoimmune, Experimental; Endothelial Cells; Extracellular Matrix; Matrix Metalloproteinase; Multiple Sclerosis; Vascular Endothelial Growth Factor A.

INTRODUCTION

Angiogenesis is a complex and finely balanced process that consists of the formation of new blood vessels from the pre-existing ones such as capillaries and post-capillary venules. Angiogenesis plays a pivotal role during embryonic development and later; in adult life; in several physiological and pathological conditions.[1]

Under physiological conditions, angiogenesis depends on the tight balance of pro-angiogenic and anti-angiogenic factors.[2] Moreover, in normal tissues, vascular inactivity is maintained by the dominant influence of endogenous anti-angiogenic over pro-angiogenic stimuli.[3] However, disturbance of the

Corresponding Author: Abbas Mirshafiey, PhD;
Department of Immunology, School of Public Health, Tehran University of Medical Sciences, Tehran-14155, Box: 6446, Iran. Tel/ Fax: (+98 21) 6646 2267, E-mail: mirshafiey@tums.ac.ir

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7- Alhassan Hussaini Mohammed

First Name	Last Name	Program	Level	School
Alhassan	Hussaini Mohammed	Immunology	PhD by Research.	Public Health

Published Articles:

	Title of the Article
1	Immunoregulation of Inflammatory and Inhibitory Cytokines by Vitamin D3 in Patients with Inflammatory Bowel Diseases
2	Immunomodulatory and Immunosuppressive Roles of 1a,25(OH)2D3 in Autoimmune Diseases

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Immunoregulation of Inflammatory and Inhibitory Cytokines by Vitamin D3 in Patients with Inflammatory Bowel Diseases

H. Alhassan Mohammed*,† , A. Mirshafiey*, H. Vahedi‡, G. Hemmasi§, A. Moussavi Nasl Khameneh¶, K. Parastouei¶ & A. A. Saboor-Yaraghi*

*Department of Immunology, School of Public Health, Tehran University of Medical Sciences, International Campus, TUMS-IC, Tehran, Iran; †Department of Immunology, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria; ‡Digestive Disease Research Institute (DDRI), Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran; §Department of Internal Medicine and Gastroenterology, Iran University of Medical Sciences, Tehran, Iran; and ¶Department of Cellular and Molecular Nutrition, School of Nutritional Sciences and Dietetics, International Campus, TUMS-IC, Tehran, Iran

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Correspondence to: Dr A. A. Saboor-Yaraghi, Department of Pathobiology/Immunology, Tehran University of Mediical Sciences, International Campus, P.O. Box 14155-6446, TUMS-IC, Tehran, Iran. E-mail: asaboor@tums.ac.ir

Abstract

Inflammatory bowel disease (IBD) is a group of idiopathic, chronic and relapsing inflammatory conditions of the gastrointestinal tract, caused by an aberrant and exaggerated immunological response in the gut. Supplementation of vitamin D3 in patients with IBD exerts both direct and indirect regulatory roles on the naïve T cells, thereby maintaining a balance between *inflammatory and inhibitory cytokines*. The direct actions of vitamin D3 on naïve T cells result in the proliferation of more regulatory T cells and inhibitory cytokines such as IL-4, IL-10 and IL-5. The binding of vitamin D to dendritic cells (DCs) through vitamin D receptors inhibits the action of IL-12 on DCs, resulting in the downregulation of Th1 and Th17. On the other hand, this interaction favours Th2 and Treg upregulation and facilitates the maintenance of immune homoeostasis between *inflammatory and inhibitory cytokines* which is essentially significant in the management of patients with IBD. The aim of this review was to explore the current and mounting scientific evidence on the roles of vitamin D3 in *immunoregulation of inflammatory and inhibitory cytokines* in patients with IBDs. An extensive literature search was conducted using keywords such as Vitamin D3*, IBD*, inflammatory cytokines*, inhibitory cytokines*, naïve-T-cells* and antigen presenting cells* through PubMed, SCOPUS and MEDLINE search engines. The results of the accumulated bodies of research that have been conducted demonstrate that vitamin D3 plays a major role not only in the immunoregulation of cytokines involved in the pathogenesis of IBDs but also in many other inflammatory disorders.

Introduction

Inflammatory bowel disease (IBD) is a group of idiopathic, chronic and relapsing inflammatory conditions of the gastrointestinal tract caused by an aberrant immunological response in the gut [1]. IBD is characterized by severe inflammation of the small bowel and/or colon leading to recurrent abdominal pain and diarrhoea. It is classified into two main subtypes: Crohn's disease (CD) and ulcerative colitis (UC) [1]. These two conditions can be differentiated based on the site of the inflammation and the nature of histological alterations in the intestinal wall. Crohn's disease can affect the entire gastrointestinal tract, from mouth to anus, although it affects mainly the terminal ileum and colon. It is usually transmural and often discontinuous causing patchy inflammatory lesions in the GI tract. On the other hand, UC is mostly restricted to the rectum, colon and caecum. It affects only the intestinal mucosa in a continuous pattern [1]. Immunological investigations have shown that CD is a predominately Th1- and Th17-mediated process which is in contrast to UC which appears to be predominately mediated by Th2 and NK T cells [1].

Vitamin D3 (1, 25-dihydroxyvitamin-D3), otherwise known as calcitriol, is a fat-soluble vitamin. It has been associated with the regulation of bone, calcium and phosphorus metabolism [2], but recent advances in scientific research have revealed the involvement of vitamin D3 in the regulation and modulation of the immune system especially in patients with IBD and other autoimmune disorders [3]. Moreover, vitamin D3 deficiency is presently considered as a predisposing risk factor for the development of multiple sclerosis (MS), rheumatoid arthritis, type 1 diabetes mellitus, IBD and many other inflammatory

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Immunomodulatory and Immunosuppressive Roles of 1α,25(OH)2D3 in Autoimmune Diseases

H. Alhassan Mohammed*, A. A. Saboor-Yaraghi*, A. Mirshafiey*, H. Vahedi†, M. R. Shiri-Shahsavar‡ & A. Mousavi Nasl Khameneh‡

*Department of Pathobiology/Immunology, School of Public Health, Tehran University of Medical Sciences, International Campus, TUMS-IC, Tehran, Iran; †Digestive Disease Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran; and ‡Department of Cellular and Molecular Nutrition, School of Nutritional Sciences and Dietetics, International Campus. TUMS-IC, Tehran, Iran

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Correspondence to: H. Alhassan Mohammed, Department of Pathobiology/Immunology, School of Public Health, Tehran University of Medical Sciences, International Campus, P.O.BOX 14155-6446 TUMS-IC, Tehran, Iran. GSM.NO: +989354407684 E-mail:halhassanmohd@gmail.com.

Co-Correspondance to: Dr. A.A. Saboor-Yaraghi. Department of Pathobiology/Immunology, Tehran University of Mediical Sciences, International Campus, P.O.Box 14155-6446,TUMS-IC, Tehran, Iran. GSM.NO. +989122372737, Email: asaboor@tums.ac.ir

Abstract

Autoimmune diseases are pathological conditions characterized by abnormal responses, accompanied by autoantibodies to self-molecules. The role of vitamin D in autoimmune diseases has increased significantly in the recent past from its functions in calcium and phosphate homoeostasis, and it is now involved in the regulations and proliferations of Th1 and Th17 lymphocyte. 1α,25(OH)2D3 is very important in ameliorations of inflammatory disorders arising from autoimmune diseases, but the mechanism by which this is performed is still a bone of contentions. This review aimed to highlight the existing facts about the roles of Vitamin D in the treatment and management of autoimmune diseases. An extensive online literature search was conducted using PubMed, MEDLINE and Scopus. Accumulated bodies of research evidence are available which demonstrates that Vitamin D has a very important part to play in the regulation of immune responses in autoimmune diseases. Some of the authors suggested that Vitamin D3 carry-out its immunosuppressive and immune modulatory action, through its actions on antigen-presenting cells and activated T and B cells with the help of Vitamin D receptors present on the each of these cells. Vitamin D supplementation assists in autoimmune disorders by making qualitative and quantitative changes in the immune system (downregulation of Th1 and upregulations of Th2 cells). This resulted in the body to be more tolerant of self and less likely to mount autoimmune responses.

Introduction

Autoimmune disease is a condition which is triggered by the immune system initiating an attack on self-molecules due to the deterioration of immunologic tolerance to autoreactive immune cells [1]. Smith and Germolec state that 'autoimmune disorders affect approximately 3% of the North American and European populations, >75% of those affected being women'. Number of studies has suggested that the initiation of attacks against the body's self-molecules in autoimmune diseases is strongly associated with factors such as genetics, infections and/or environment [1]. Autoimmune diseases are pathological conditions identified by abnormal autoimmune responses and characterized by autoantibodies and T cell responses to self-molecules by immune system reactivity [1].

Autoimmune diseases are the third leading cause of morbidity and mortality in the industrialized world; this is surpassed only by cancer and cardiovascular diseases [1], and despite this relatively high morbidity and mortality, the aetiological origin of most autoimmune diseases remains elusive. One of the most recent agents found to be associated with autoimmunity is 1, 25(OH) 2D3. 1, 25 (OH) 2D3 has multiple immunomodulatory, anti-inflammatory and immunosuppressant properties.

Supplementation of 1,25(OH)2D3 was shown to be therapeutically effective in various animal models such as type 1 diabetes mellitus [2], inflammatory bowel disease [3] and systemic lupus erythematous (SLE) [4].

1,25(OH)2D3 seems to interact with the immune system through its actions on the regulation and differentiation of cells such as lymphocytes, macrophages and natural killer cells (NK), besides interfering in the in vivo

SCANDINAVIAN JOURNAL OF Immunology AN INTERNATIONAL MONTHLY JOURNAL

8- Abraham Assan

First Name	Last Name	Program	Level	School
Abraham	Assan	Public Health	MPH	Public Health

Published Articles:

	Title of the Article
1	Assessing the Knowledge, Attitudes, and Practices of Students Regarding Ebola Virus Disease Outbreak

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Original Article

Assessing the Knowledge, Attitudes, and Practices of Students Regarding Ebola Virus Disease Outbreak

Kourosh HOLAKOUIE-NAIENI [1], Alireza AHMADVAND [1], Owais RAZA [2], Abraham ASSAN [3], Adel Hussein ELDUMA [2], Alieu JAMMEH [3], Aram Salih Mohammed Amin KAMALI [3], Ahang Abdullah KAREEM [3], Fatima Mahmud MUHAMMAD [3], Hasnain SA-BAHAT [3], Kabir Ozigi ABDULLAHI [3], Raeed Ahmad SAEED [3], Sami Najmaddin SAEED [3]

1. *Dept. of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*
2. *Dept. of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences – International Campus, Tehran, Iran*
3. *School of Public Health, Tehran University of Medical Sciences – International Campus, Tehran, Iran*

***Corresponding Author:** Email: holakoik@hotmail.com

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Abstract

Background: The emergence and spread of Ebola outbreak is a growing problem worldwide, which represents a significant threat to public health. Evidence has shown that the level of knowledge, attitude, and practice of people in the society play major roles in controlling the spread of Ebola virus disease. This study was designed to determine knowledge, attitude and practice of students at School of Public Health, Tehran University of Medical Sciences towards Ebola.

Methods: A cross-sectional survey was performed in Tehran, Iran in 2014 using a pretested self-administered questionnaire on a stratified sample of 400 students. Descriptive and multivariate analyses were used for statistical analysis.

Results: All-in-all, 385 students returned the completed questionnaires making a response rate of 96.3%., 239 (62.2%) were females and 145 (37.8%) were males. The mean age of female and males were 28.44 and 30.3 years respectively. Of the 385students, 83 (21.7%) were studying at PhD level, 210 (55.0%) at Masters Level (including MPH) and 89 (23.3%) at Bachelors level. knowledge of the students regarding EVD transmission was lowest among students of Department of Occupational Health (50.0%), followed by Health Education and Promotion Department (33.3%). Virology Department recorded the highest percentage of students who had selected correct answers regarding EVD prevention (100.0%)

Conclusion: These findings will aid in the assessment of the adequacy of current students' educational curriculum. Also, it will provide further insight in designing future multifaceted interventions to promote specific messages to change attitude and improve practice.

Keywords: Ebola, Outbreak, Tehran, Iran, Knowledge, Attitude, Practice, Students

Introduction

As stated by Center of Disease Control and Prevention (CDC – US), current Ebola epidemic is the largest epidemic since the first outbreak in Sudan and Zaire, 1976 (1). The Ebola virus (EBOV) belongs to RNA virus family of *Filoviridea* and is the most pathogenic strain. It was

9- Mahmoud Radwan

First Name	Last Name	Program	Level	School
Mahmoud	Radwan	Health Services Management	PhD	Public Health

Published Articles:

	Title of the Article
1	Appraising the methodological quality of the clinical practice guideline for diabetes mellitus using the AGREE II instrument: a methodological evaluation

Research article

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Appraising the methodological quality of the clinical practice guideline for diabetes mellitus using the AGREE II instrument: a methodological evaluation

Mahmoud Radwan[1], **Ali Akbari Sari**[2], **Arash Rashidian**[2], **Amirhossein Takian**[1], **Sanaa Abou-Dagga**[3] **and Aymen Elsous**[1]

[1]Department of Health Management and Economics, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[2]School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[3]Department of Research Affairs and Graduates Studies, Islamic University of Gaza, Gaza Strip, Palestine
Corresponding author: Ali Akbari Sari. Email: akbarisari@tums.ac.ir

Summary

Objectives: To evaluate the methodological quality of the Palestinian Clinical Practice Guideline for Diabetes Mellitus using the Translated Arabic Version of the AGREE II.
Design: Methodological evaluation. A cross-cultural adaptation framework was followed to translate and develop a standardised Translated Arabic Version of the AGREE II.
Setting: Palestinian Primary Healthcare Centres.
Participants: Sixteen appraisers independently evaluated the Clinical Practice Guideline for Diabetes Mellitus using the Translated Arabic Version of the AGREE II.
Main outcome measures: Methodological quality of diabetic guideline.
Results: The Translated Arabic Version of the AGREE II showed an acceptable reliability and validity. Internal consistency ranged between 0.67 and 0.88 (Cronbach's α). Intraclass coefficient among appraisers ranged between 0.56 and 0.88. The quality of this guideline is low. Both domains 'Scope and Purpose' and 'Clarity of Presentation' had the highest quality scores (66.7% and 61.5%, respectively), whereas the scores for 'Applicability', 'Stakeholder Involvement', 'Rigour of Development' and 'Editorial Independence' were the lowest (27%, 35%, 36.5%, and 40%, respectively).
Conclusions: The findings suggest that the quality of this Clinical Practice Guideline is disappointingly low. To improve the quality of current and future guidelines, the AGREE II instrument is extremely recommended to be incorporated as a gold standard for developing, evaluating or updating the Palestinian Clinical Practice Guidelines. Future guidelines can be improved by setting specific strategies to overcome implementation barriers with respect to economic considerations, engaging of all relevant end-users and patients, ensuring a rigorous methodology for searching, selecting and synthesising the evidences and recommendations, and addressing potential conflict of interests within the development group.

Keywords

AGREE II, Clinical Practice Guideline, diabetes mellitus, psychometric properties, methodological quality

Introduction

Diabetes mellitus (DM) is a rapidly growing public health problem. It is a metabolic disease characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. 'Long-term complications of diabetes include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations and high incidence of cerebrovascular disease and hypertension'.[1] The World Health Organization estimates that about 347 million people globally have diabetes and projects that diabetes will be the seventh leading cause of death in 2030.[2] Most diabetes deaths (more than 80%) occur in low- and middle-income countries.[2] In Palestine, the prevalence rate was 10.5% in the West Bank and 11.8% in the Gaza Strip among the registered Palestinian refugees aged 40 years and older.[3] Abu-Rmeileh et al.[4] estimated the prevalence of DM in Palestine at 20.8% and 23.4% in 2020 and 2030, respectively.[4] The Palestinian Clinical Practice Guideline (CPG) for DM was developed to promote evidence-based medicine in screening, diagnosis, and treatment and to standardise the care provided for diabetic patients type 1 and 2. The Palestinian CPG was adapted from international guidelines with extensive participation of local experts to ensure the acceptance in, applicability to and consistency with the Palestinian local context.[5]

CPGs are defined as 'systematically developed statements to assist practitioners and patient decisions about appropriate healthcare for specific circumstances'.[6] It has been shown that CPGs are effective in promoting the quality of healthcare services and improving patients' outcomes.[7] The large numbers of the published CPGs have raised many inquiries about their quality,[8] and the method of developing CPGs has been exposed to extensive

10- Assadullah Rasooli

First Name	Last Name	Program	Level	School
Assadullah	Rasooli	Public Health	MPH	Public Health

Published Articles:

	Title of the Article
1	Knowledge and Attitude toward Tuberculosis among Tuberculosis Patients Seeking Help in Diagnostic and Treatment Centers,Kabul Province in Afghanistan

Iran J Public Health, Vol. 44, No.5, May 2015, pp.711-713

Letter to the Editor

Knowledge and Attitude toward Tuberculosis among Tuberculosis Patients Seeking Help in Diagnostic and Treatment Centers, Kabul Province in Afghanistan

Assadullah RASOOLI [1], ***Elham AHMADNEZHAD*** [2], ***Keramt NOURI JELYANI*** [3], ****Kourosh HOLAKOUIE-NAIENI*** [3]

1. *School of Public Health, International Campus (TUMS-IC), Tehran University of Medical Sciences, Tehran, Iran*
2. *National Institute of Health Research, Tehran University of Medical Sciences, Tehran, Iran*
3. *Dept. of Epidemiology and Biostatistics, School of Public Health, , Tehran University of Medical Sciences, Tehran, Iran*

***Corresponding Author:** Email: holakoik@hotmail.com

(Received 14 Nov 2014; accepted 20 Jan 2015)

Dear Editor-in-Chief

Afghanistan is one of the 22 high TB burden countries and TB is a major public health problem. Current estimates show that the incidence of active TB cases is 278/100,000, mortality mounts to 15,000 cases/year (1) .Correct knowledge and positive perception of the patients towards TB, and its management is pillars of success in TB control programme in any TB burden countries. Several factors influence TB outcome that the treatment well management is the one of most important. Knowledge about general management of tuberculosis has well been recognized as an important factor influencing compliance with tuberculosis treatment. A low knowledge on tuberculosis is a likely cause of the delay in seeking treatment.

Studies of the knowledge and attitude of tuberculosis patients about various aspects of TB in Afghanistan are lacking though TB is a major public health problem there. Our findings should enable the TB authorities to design and implement an intervention to the perception of TB in the community.

This cross sectional study was conducted in DOTS implementer health facilities. The study was conducted among all the 285 patients aged +15 years currently under treatment for Pulmonary Tuberculosis, Kabul Province, Afghanistan. Patients were interviewed at the centers. Each interview was conducted at a time when patient came to receive anti tuberculosis treatment from the center. A questionnaire containing socio-demographic variables, knowledge and attitude of patients about the different event of tuberculosis was developed. Each interview lasted for about 30 minutes. The collected data was entered in $SPSS_{20}$ statistical package. Pearson Chi-square test was applied for testing associations between variables that, the distribution of knowledge and attitude was compared between categories of each socio-demographic variables, and general frequency of different variables, and descriptive analysis was done.

The research has been approved by Ethical Committee of Tehran University of Medical Sciences.

A total of 285 patients (+15) years suffering from pulmonary tuberculosis were interviewed. The minimum, maximum and mean score of knowledge was 1, 13, 9.47± 0.175, satisfaction was, 38, 63, 52.65±0.305 and attitude was, 2, 8, 4.96±0.066.

11- Saeed Shojaei

First Name	Last Name	Program	Level	School
Saeed	Shojaei	Health Care Management	PhD	Public Health

Published Articles:

	Title of the Article
1	Evaluation of International Standards of Management of Communication and Information Technology (MCIT) in Khorasan Razavi Hospitals from the Perspective of Managers
2	An Investigation on the Status of Implementation of Communications and Information Management System (MCI) in Khorasan Razavi Hospitals

Health, 2015, 7, 920-926
Published Online August 2015 in SciRes. http://www.scirp.org/journal/health
http://dx.doi.org/10.4236/health.2015.78109

Evaluation of International Standards of Management of Communication and Information Technology (MCIT) in Khorasan Razavi Hospitals from the Perspective of Managers

Saeed Shojaei[1], Fereshteh Farzianpour[2*], Mohammad Arab[2], Abbas Rahimi Foroushani[3], Esmaeil Hosseinzadeh Roknabadi[2]

[1]Department of Health Management and Economic, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[2]Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[3]Department of Epidemiology and Biostatistics, Tehran University of Medical Sciences, Tehran, Iran
Email: s.shojaei2011@gmail.com, [*]farzianp@sina.tums.ac.ir, arabmoha@tums.ac.ir, rahimifo@tums.ac.ir

Received 1 July 2015; accepted 2 August 2015; published 5 August 2015

Abstract

The general goal of the management of communication and information technology (MCIT) in the health sector, is to accelerate collecting, achieving and supporting the health system processes, and effective decision-making for managing this system; because preparing and providing health care services for society is very complex, and highly dependent on the information system. The aim of this investigation is to determine the mean scores of the possibility of implementing the MCIT standards in Khorasan Razavi hospitals, from the perspective of managers. This was a cross sectional descriptive-analytic study conducted in two steps in all hospitals. In the first step, the applicability of the standards in hospitals was studied. In the second step, the current status of hospitals was compared with international standards MCIT. In order to determine the validity of the questionnaires, opinions of professors and experts were acquired. Regarding the reliability, the SPSS V. 12 calculated the value of Cronbach's to be 0.95 for the first questionnaire and 0.86 for the second questionnaire. Data were analyzed using statistic tests of one way ANOVA and t-test. The level of significance was fixed at 0.5. In the 16 hospitals studied, the mean and standard deviation of MCIT were (57.25 ± 13.74). The MCIT standards are applicable in hospitals of Khorasan

[*]Corresponding author.

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An Investigation on the Status of Implementation of Communications and Information Management System (MCI) in Khorasan Razavi Hospitals

Saeed Shojaei[1], Fereshteh Farzianpour[2], Mohammad Arab[2] & Abbas Rahimi Foroushani[3]

[1] Department of Health Management and Economic, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran

[2] Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

[3] Departments of Epidemiology and Biostatistics, Tehran University of Medical Sciences, Tehran, Iran

Correspondence: Fereshteh Farzianpour, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. E-mail: farzianp@sina.tums.ac.ir

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Abstract

Background and Objectives: The aim of this investigation is to determine the mean scores of the possibility of implementing the MCI standards in Khorasan Razavi hospitals, from the perspective of Managers, in order to provide a suitable model for evaluating and promoting the system.

Methods: This was a Research and method (R&D) and Survey Research method, which is of the type of Cross-Sectional, descriptive-analytic Studies conducted in two steps in hospitals of Khorasan Razavi from July to December 2014. This study was approved by the Ethical Committee of Tehran University of Medical Sciences (TUMS) in 2013/6/10. About the nature and purpose of the study was explained to the participants. Were used to apply functional assessment, based on Accreditation Model. In order to collect data, two questionnaires were used, all of which were taken from the standards of MCI. The reliability and validity of the questionnaires were approved by experts.Cronbach's alphas for the questionnaires were obtained to be (0.95, 0.86), respectively. In order to analyze information, statistical analyses, including one way ANOVA, and Independent sample t-test were used.

Results: The mean scores of the possibility of implementing the MCI standards in Khorasan Razavi hospitals, were (51.6 and 12.27), respectively.

Conclusions: According to half (43.8%) of managers, the MCI standards are applicable in hospitals of Khorasan Razavi; however, their application requires greater efforts by the hospitals.

Keywords: Communications and Information Management System (MCI), Khorasan Razavi, Hospitals

1. Background

Providing care for patients, is a complex effort, which to a large extent, depends on the transfer of information. This transfer of information is done in relation to the community and their families, and other health care specialists (Ajami et al., 2006). Failing to inform, is one of the most common root causes of safety incidents (Rahnavard et al., 2003).

To provide coordinated and integrated services, health care organization cites information about the knowledge of each patient's care, provided care, care outcomes, and their performance. With regard to cases, such as human resources, materials and financial resources, information is a resource that leaders should effectively and efficiently manage (Srafi Zadeh et al., 2005; Iran Nejad Parizi et al., 2007). Every organization seeks to acquire, manage and use information, to promote the patients' efficiencies, as well as individual and overall performance of the organization. Over time, the organization becomes competent in the following areas.

1). Identifying information needs;

2). Information Management System Design;

12- Abedin Saghafipour

First Name	Last Name	Program	Level	School
Abedin	Saghafipour	Entomology	PhD	Public Health

Published Articles:

	Title of the Article
1	Assessing the Fauna of Aquatic Insects for Possible Use for Malaria Vector Control in Large River, Central Iran

Assessing the Fauna of Aquatic Insects for Possible Use for Malaria Vector Control in Large River, Central Iran

Mansoureh Shayeghi[1], Jalil Nejati[1], Leila Shirani-Bidabadi[1], Mona Koosha[1], Mehdi Badakhshan[1], Mulood Mohammadi Bavani[1], Kourosh Arzamani[1], Nayyereh Choubdar[1], Fatemeh Bagheri[1], Abedin Saghafipour[2], Arshad Veysi[1], Fateh Karimian[1], Amir Ahamd Akhavan[1], and Hassan Vatandoost[1]

[1] *Department of Medical Entomology and Vector Control, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*

[2] *Department of Medical Entomology and Vector Control, School of Public Health, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran*

Received: 27 Jul. 2014; Accepted: 24 Dec. 2014

Abstract- Insects with over 30,000 aquatic species are known as very successful arthropods in freshwater habitats. Some of them are applied as biological indicators for water quality control, as well as the main food supply for fishes and amphibians. The faunistic studies are the basic step in entomological researches; the current study was carried out emphasizing on the fauna of aquatic insects in Karaj River, northern Iran. A field study was carried out in six various sampling site of Karaj River during spring 2013. The aquatic insects were collected using several methods such as D-frame nets, dipping and direct search on river floor stones. Specimens were collected and preserved in Ethanol and identified by standard identification keys. Totally, 211 samples were collected belonging to three orders; Plecoptera, Trichoptera and Ephemeroptera. Seven genuses (Perla, Isoperla, Hydropsyche, Cheumatopsyche, Baetis, Heptagenia and Maccafferium) from five families (Perlidae, Perlodidae, Hydropsychidae, Batidae, Heptagenidae) were identified. The most predominant order was Plecoptera followed by Trichoptera. Karaj River is a main and important river, which provides almost all of water of Karaj dam. So, identification of aquatic species which exist in this river is vital and further studies about systematic and ecological investigations should be performed. Also, monitoring of aquatic biota by trained health personnel can be a critical step to describe water quality in this river. Understanding the fauna of aquatic insects will provide a clue for possible biological control of medically important aquatic insects such as Anopheles as the malaria vectors.

Acta Med Iran 2015;53(9):523-532.

Keywords: Aquatic insects; Faunistic; Karaj River; Iran

Introduction

Insects are known as very successful arthropods in freshwater and brackish water habitats. The success of aquatic insects to exploit of these habitats can be confirmed by their diversity and abundance in most types of freshwater resources. Over 30,000 aquatic insect species have been identified that exist in freshwater; in contrast, only several hundred are marine (1).

The larval stage of mayflies (Ephemeroptera), dragonflies and damselflies (Odonata), stoneflies (Plecoptera), alderflies (Megaloptera), lacewings (Neuroptera), flies (Diptera), caddiesflies (Trichoptera), moths (Lepidoptera) and wasps (Hymenoptera) are known as residents of freshwater, although the adults are terrestrial. Also, some species of beetles (Coleoptera) and bugs (Hemiptera) are aquatic but which their larval, nymphal and adult stages exist in the water which called fully aquatic (2).

Some orders such as Ephemeroptera, Plecoptera and Trichoptera (EPT), are known as an environmental condition indicator in water resources. In the United States, the number of EPT species is often applied as a "biological indicator" of water quality (3).

One of the environmental topics that the world faces today is the water crisis (4). Industrial activities and urbanization have raised pollution in rivers, streams, and

Corresponding Author: H. Vatandoost
Department of Medical Entomology and Vector Control, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 21 88951393, Fax: +98 21 88951393, E-mail address: vatando@tums.ac.ir

13- Adel Mazloumi

First Name	Last Name	Program	Level	School
Adel	Mazloumi	Occupational Health	PhD	Public Health

Published Articles:

	Title of the Article
1	Determination the Levels of Subjective and Observer Rating of Drowsiness and Their Associations with Facial Dynamic Changes

Iran J Public Health, Vol. 46, No.1, Jan 2017, pp.93-102

Original Article

Determination the Levels of Subjective and Observer Rating of Drowsiness and Their Associations with Facial Dynamic Changes

Mohsen POURSADEGHIYAN [1], ***Adel MAZLOUMI*** [2], ****Gebraeil NASL SARAJI*** [2], ***Ali NIKNEZHAD*** [3], ***Arash AKBARZADEH*** [4], ***Mohammad Hossein EBRAHIMI*** [5]

1. *Research Center in Emergency and Disaster Health, University of Social Welfare and Rehabilitation, Tehran, Iran*
2. *Dept. of Occupational Health, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran*
3. *Dept. of Mechatronics, Faculty of Engineering, Islamic Azad University South Tehran Branch, Tehran, Iran*
4. *Dept. of Biostatistics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*
5. *Occupational and Environmental Health Research Center, Shahroud University of Medical Sciences, Shahroud, Iran*

***Corresponding Author:** Email: jnsaraji@sina.tums.ac.ir

(Received 23 Mar 2016; accepted 12 Jul 2016)

Abstract

Background: We determined the levels of subjective and observer drowsiness and facial dynamics changes.

Methods: This experimental study was done in the virtual reality laboratory of Khaje-Nasir Toosi University of Technology in 2015. Facial dynamics changes like changes in eyes, mouth and eyebrows were surveyed on twenty-five drivers in 2015byKSS (Karolinska Sleepiness Scale) and ORD (Observer Rating of Drowsiness). ANOVA Repeated Measure and MANOVA Repeated Measure tests were used for data analysis. Also, neural network and Viola-Jones were used to detect facial characteristics. PERCLOS (Percentage of Eye Closure), blink frequency and blink duration were inspected for eyes parameters. The size of open mouth during drowsiness was inspected for mouth parameter. During the inspection of eyebrow, the number 50 denoted eyebrow in normal position. For eyebrows above the normal position, a range of 50 to 55 was specified; in addition, 45-50 was found as the specified range for eyebrows under normal position.

Results: Descriptive statistics of the dynamic changes in mouth and eyes illustrated that during the driving process, the level of sleepiness increased as well as changes of eyes and mouth. However, statistical findings during car driving revealed that dynamic changes in eyebrows had clear expression with a constant trend. Similar studies on data obtained from KSS and ORD showed that both of these parameters simultaneously increased as well as the level of drowsiness. In addition, a significant relationship existed between facial expression and drowsiness.

Conclusion: This research would be an effective and efficient tool for timely alarming and detecting the drowsiness quickly and precisely.

Keywords: Driver drowsiness, Facial dynamic changes, ORD, KSS

Introduction

Detecting drowsiness can aid the reduction of a number of fatal road accidents. Studies have shown that more than 1.3 million and 20 to 50 million people are killed and injured in road accidents, respectively (1). Statistics issued by theUS National Highway Traffic Safe Administration (NHTSA) have indicated that 100000 car crashes happen every year which is only caused by driver sleepiness. Road accidents cost over 12.5 billion

14- Aioub Sofizadeh

First Name	Last Name	Program	Level	School
Aioub	Sofizadeh	Entomology	PhD	Public Health

Published Articles:

	Title of the Article
1	Spatial Analyses of the Relation between Rodent's Active Burrows and Incidence of Zoonotic Cutaneous Leishmaniasis in Golestan Province, Northeastern of Iran

Original Article

Spatial Analyses of the Relation between Rodent□s Active Burrows and Incidence of Zoonotic Cutaneous Leishmaniasis in Golestan Province, Northeastern of Iran

Aioub Sofizadeh [1], *Hassan Vatandoost [2], *Yavar Rassi [2], Ahmad Ali Hanafi-Bojd [2], Sayena Rafizadeh [3]

[1]Department of Medical Entomology and Vector Control, School of Public Health,Tehran University of Medical Sciences, International Campus (TUMS- IC), Tehran, Iran
[2]Department of Medical Entomology and Vector Control, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[3]Ministry of Health and Medical Education, Tehran, Iran

(Received 24 Nov 2□14 □acce□ted 19 Aug 2015)

Abstract

Background: Zoonotic cutaneous leishmaniasis (ZCL) is one of the most important vector-borne diseases in Iran. Wild Rodents play as a reservoir. The main aim of this study was to determine spatial analyses of the relationship between rodent's active burrows and Incidence of ZCL in Golestan Province, north east of Iran**.**

Methods: The cross-sectional study was conducted in 59 rural districts in Golestan Province. Spatial distribution of rodent's active burrows, human cases of ZCL and Incidence of disease were collected, using Geographical Information Systems (GIS). The relationship of them were analyzed by Sperman test, SPSS software version No.13.

Results: The most number of rodents' active burrows, human positive cases (100 persons) and high Incidence of disease (35/1000) were observed in Korand rural district of Gonbad-e Kavoos County. There was significant correlation between the number of rodents active burrows with Incidence rate of disease (0.470, P< 0.001) as well as the number of cases in each districts (0.465, P< 0.001), There is high correlation between higher Incidence rate and human positive cases in districts with number of rodents' active burrows.

Conclusion: Vicinity of wild rodents' burrows to villages plays an important role in transmission of ZCL to humans.

Keywords: Cutaneous leishmaniasis, Rodent burrows, Spatial analysis, Golestan, Iran

Introduction

The World Health Organization considers leishmaniasis as one of the most neglected tropical diseases which has received little attention and resources despite its serious impacts on both the economic developments and quality of life (WHO 2012). Leishmaniasis is one of the most important vector-borne disease and public health problem in Iran that transmitted by sandflies to human and other animals. Iran is facing both form of leishmaniasis: cutaneous and visceral. The main visceral foci are located in Ardabil (Northwest) and Fars (Southwest). There are also foci with low endemicity in other parts of the country. Cutaneous leishmaniasis is the main vector-borne disease in the country with an average of more than 22,000 cases in the last decade (Karimi et al. 2014), about 80% of them are zoonotic cutaneous leishmaniasis (ZCL), the endemic foci of this type are in rural areas of 17 out of 31 province (Yaghoobi-Ershadi 2012, Karimi et al. 2014). ZCL is a disease that primarily uses animals such as rodents as reservoir hosts (Mirzaei et al. 2011). Humans are an accidental host that can be involved in the transmission cycle of Leishmania parasites (Rouhani et al. 2014). Geographically, ZCL is widely distributed in Af-

***Corresponding author:** Dr Hassan Vatandoost, E-mail: hvatandoost1@yahoo.com, vatando@tums.ac.ir, Dr Yavar Rassi, E-mail: rassiy@tums.ac.ir

http://jad.tums.ac.ir
Published Online: October 04, 2016

15- Soheila Asgari

First Name	Last Name	Program	Level	School
Soheila	Asgari	Epidemiology		Public Health

Published Articles:

	Title of the Article
1	Effect of Anterior Chamber Depth on the Choice of Intraocular Lens Calculation Formula in Patients with Normal Axial Length

Eye (2015) 29, 926–931

www.nature.com/eye

CLINICAL STUDY

Matched optical quality comparison of 3-year results of PRK–MMC and phakic IOL implantation in the correction of high myopia

M Miraftab[1], H Hashemi[1] and S Asgari[2]

Abstract

Aims **To compare 3-year results of PRK–MMC and phakic intraocular lens (PIOL) implantation in patients with >8.0 diopters (D) of myopia.**

Methods **This study was conducted as a non-randomized clinical trial on 23 eyes treated with PIOL (Artiflex; group A) and 23 eyes treated with PRK–MMC (group B). This report compares 3-year treatment results in these two groups.**

Results **At 3 years after surgery, uncorrected visual acuity was 0.02 ± 0.06 LogMAR in group A and 0.04 ± 0.07 LogMAR in group B ($P = 0.639$). Mean best corrected visual acuity in group A (0.004 ± 0.02) was better than group B (0.03 ± 0.07 LogMAR) ($P = 0.035$). Mean manifest refraction spherical equivalent was -0.16 ± 0.21 and -0.09 ± 0.20D ($P = 0.190$), respectively. Mesopic contrast sensitivity (CS) in the spatial frequency of three cycle/degree (CS3) significantly decreased in both groups, but the reduction was significantly higher in group B ($P = 0.024$). CS6 decreased significantly only in group B ($P = 0.019$). Changes in CS12 and CS18 showed no significant inter-group difference. In group A, the increase in C6 trefoil ($0.16 \pm 0.18\,\mu$m, $P = 0.003$) and reduction in spherical aberration (SA; $0.16 \pm 0.08\,\mu$m, $P < 0.001$) were statistically significant. In group B, the reduction in vertical coma ($P = 0.052$), and increases in horizontal coma ($P = 0.044$), coma ($P < 0.001$), SA ($P < 0.001$), and total higher order aberrations ($P < 0.001$) were significant after surgery.**

Conclusion **Based on 3-year results, PIOL implantation is a better choice than PRK–MMC for treating patients with >8.0D myopia. However, for patients with an inadequate aqueous depth, PRK–MMC can be an acceptable treatment option with a potential for decreased quality of vision.**

Eye (2015) **29,** 926–931; doi:10.1038/eye.2015.71; published online 15 May 2015

Introduction

Treatment options for the correction of high myopia include refractive surgeries such as photorefractive keratectomy (PRK), laser *in situ* keratomileusis (LASIK), and intraocular refractive procedures. Clinicians have different opinions on the applications of these methods. Some prefer PRK because of the risk of post-LASIK ectasia, and some prefer phakic intraocular lens (PIOL) implantation due to the risk of corneal haze after PRK.[1–3]

We designed a matched comparative study of patients with >8.0 diopters (D) of myopia and compared results of treatment with PRK and PIOL in these two groups. Our 1-year results[4] indicated that surface ablation and PIOL implantation correct uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), refraction, and astigmatism similarly, and they do not impact mesopic contrast sensitivity (CS). Almost all higher order aberrations (HOAs) increased after PRK–MMC, but PIOL implantation was only associated with increased C6 (trefoil) and total HOA, whereas spherical aberration (SA) decreased.

As assessment of treatment results requires longer follow-up times, here we present 3-year results with these two methods, to report visual function changes in this period.

[1]Noor Ophthalmology Research Center, Noor Eye Hospital, Tehran, Iran

[2]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran

Correspondence:
H Hashemi, Noor Ophthalmology Research Center, Noor Eye Hospital, No. 96 Esfandiar Blvd., Vali'asr Ave, Tehran 19686-53111, Iran
Tel: +98 21 88651515;
Fax: +98 21 886514.
E-mail: hhashemi@norc.ac.ir

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16- Hossein Mohsenipouya

First Name	Last Name	Program	Level	School
Hossein	Mohsenipouya	Health Education	PhD	Public Health

Published Articles:

	Title of the Article
1	Predictors of Health-Promoting Behaviors in Coronary Artery Bypass Surgery Patients: An Application of Pender's Health Promotion Model

Iran Red Crescent Med J. 2016 September; 18(9):e38871. doi: 10.5812/ircmj.38871.

Published online 2016 July 18. **Research Article**

Predictors of Health-Promoting Behaviors in Coronary Artery Bypass Surgery Patients: An Application of Pender's Health Promotion Model

Hossein Mohsenipoua,[1] Fereshteh Majlessi,[2] Davood Shojaeizadeh,[2,*] Abbas Rahimiforooshani,[3] Rahman Ghafari,[4] and Valiollah Habibi[4]

[1]Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, International Campus (TUMS- IC), Tehran, IR Iran
[2]Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran
[3]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran
[4]Department of Cardiac Surgery, School of Medicine, Mazandaran University of Medical Sciences, Sari, IR Iran

[*]*Corresponding author*: Davood Shojaeizadeh, Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran. Fax: +98-2188896696, E-mail: shojae5@yahoo.com

Received 2016 April 30; **Revised** 2016 May 19; **Accepted** 2016 June 18.

Abstract

Background: Advances in coronary artery surgery have reduced patient morbidity and mortality. Nevertheless, patients still have to face physical, psychological, and social problems after discharge from hospital.
Objectives: The objective of this study was to determine the efficacy of Pender's health promotion model in predicting cardiac surgery patients' lifestyles in Iran.
Methods: This cross-sectional study comprised 220 patients who had undergone coronary artery bypass graft (CABG) surgery in Mazandaran province (Iran) in 2015. The subjects were selected using a simple random sampling method. The data were collected via (1) the health-promoting lifestyle profile II (HPLP II) and (2) a self-designed questionnaire that included two main sections: demographic characteristics and questions based on the health-promoting model constructs.
Results: Spiritual growth (28.77 $\pm$ 5.03) and physical activity (15.79 $\pm$ 5.08) had the highest and lowest scores in the HPLP II dimensions, respectively. All the health promotion model variables were significant predictors of health-promoting behaviors and explained 69% of the variance in health-promoting behaviors. Three significant predictors were estimated using regression coefficients: behavioral feelings ($\beta = 0.390$, $P < 0.001$), perceived benefits ($\beta = 0.209$, $P < 0.001$), and commitment to a plan of action ($\beta = 0.347$, $P < 0.001$).
Conclusions: According to the results of the study, health-promoting model-based self-care behaviors can help identify and predict cardiac surgery patients' lifestyles in Iran. This pattern can be used as a framework for discharge planning and the implementation of educational interventions to improve the lifestyles of CABG patients.

Keywords: Self-Care Behavior, Health Promotion Model, Coronary Artery Bypass, Healthy Lifestyle

1. Background

According to a world health organization (WHO) report in 2011, cardiovascular disease causes 45% of deaths among Iranian people (1). Coronary artery bypass graft surgery (CABG), as the most comprehensive treatment of coronary heart disease, has stood the test of time, having been in use for nearly 50 years (2). In the United States, 400,000 such surgeries are performed annually (3). CABG is carried out on 60% of patients suffering from coronary artery ischemic diseases (CHD) (4). Due to the inherent progression of CHD and the development of vein graft atherosclerosis, patients treated with CABG are at risk of subsequent ischemic events during the months and years following the procedure (2). Even though CABG has improved in terms of its success rate, patients still have to deal with a number of physical, psychological, and social problems in the period following discharge from hospital (5). The side effects reported by patients after CABG include a variety of problems such as postoperative pain, insomnia, changes in appetite or taste, chest pain, respiratory difficulties, arrhythmia, palpitations, numbness of the arms, abdominal distention, weight loss, anxiety related to the treatment and their ability to adhere to the recommended physical activity schedule, weakness, headache, vertigo, depression, nausea, and vomiting (6). Patients undergoing cardiac surgery must be well-informed of the potential problems, activity enhancements, nutrition, and medication beforehand since the success of the surgery is highly dependent on the patients' understanding of the disease

17- Javad Vatani

First Name	Last Name	Program	Level	School
Javed	Vatani	Occupational Health	PhD	Public Health

Published Articles:

	Title of the Article
1	The Relative Costs of Accidents Following the Establishment of the Health, Safety and Environment Management System (HSE-MS) for the Construction Industry in Tehran

Iran Red Crescent Med J. 2016 December; 18(12):e27140. doi: 10.5812/ircmj.27140.

Published online 2016 August 20. **Research Article**

The Relative Costs of Accidents Following the Establishment of the Health, Safety and Environment Management System (HSE-MS) for the Construction Industry in Tehran

Javad Vatani,[1] Gebraeil Nasl Saraji,[1,*] Abolghasem Pourreza,[2] Mahmood Salesi,[3] Iraj Mohammad Fam,[4] and Seyed Abolfazl Zakerian[1]

[1]Department of Occupational Health, School of Public Health, International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, IR Iran
[2]Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran
[3]Truma Research Center, Baqiyatallah University of Medical Sciences, Tehran, IR Iran
[4]Department of Occupational Health, School of Public Health, Hamedan University of Medical Sciences, Tehran, IR Iran

[*]*Corresponding author*: Gebraeil Nasl Saraji, Department of Occupational Health, School of Public Health, International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, IR Iran. Tel: +98-9121182069, Fax: +98-2188951390, E-mail: jnsaraji@sina.tums.ac.ir

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Abstract

Background: Accidents in the construction industry are a significant problem in many countries around the world. Occupational accidents result in reduced working hours, loss of life, and other related costs. These accidents result in socio-economic losses such as disability support costs, loss of working time, and increased medical care needs. They also create a lot of waste for communities and labor organizations.
Objectives: Despite extensive studies calculating the cost of accidents, our understanding of these costs is still not clear or practically applicable; consequently, the ultimate aim of the present study is to provide a new framework for the calculation of the (direct and indirect) costs of construction accidents.
Methods: In this paper, using a new and structured seven-step approach, the costs of construction accidents were calculated. In order to calculate the total cost of construction accidents in the city of Tehran for 2013 - 2014, the severity of accident results were first classified into five groups: 1, short-term absences from work; 2, long-term absences; 3, partial disability; 4, total disability; and 5, death. The types of costs resulting from accidents were also categorized: 1, production disturbance costs; 2, human capital costs; 3, medical costs; 4, administrative costs; 5, transfer costs; and 6, other costs. These costs were classified according to the direct or indirect costs resulting from the incident and the imposition of costs on workers, employers and society. Finally, the calculated amount of investment in HSE-MS was analyzed using statistical tests.
Results: The present study indicates that before and after the establishment of HSE-MS that the maximum calculated cost was related to the production disturbance cost (before: $568,000; after: $80,500) and the lowest cost was related to transfer costs (before: $15,000; after: $3,000) and other costs (before: $98,000; after: $28,500). Statistical analyses indicates that there is a significant difference (P = 0.007) between the direct and indirect costs of accidents for before and after the establishment of HSE-MS. In other words, the direct and indirect costs had multiple, significant differences. The present study indicates that the indirect cost is four times greater than the direct costs.
Conclusions: Accidents resulting in death, total disability and partial disability impose huge costs that are borne by society, and employers bear relatively low costs due to the health, treatment and welfare systems provided by society for the treatment and rehabilitation of injured workers and their families. Also, the results of this study show that investment in the HSE-MS is effective and associated with reduced accidents.

Keywords: Accidents, Indirect Costs, Direct Costs, HSE-MS, Construction Industry

1. Background

1.1. Definition of an Accident

1, An unfortunate incident that happens unexpectedly and unintentionally, typically resulting in damage or injury (1).

2, A sudden event (such as a crash) that is not planned or intended and that causes damage or injury (2).

3, An event that is not planned or intended: an event that occurs by chance (2).

The construction industry plays an important role in the economy of many countries; for example, in the UK it represents 10 percent of GDP and more than 1.5 million (3), and there are a large number of occupational accidents in this industry. The most important parts of the costs of occupational accidents are the human costs that result in reduced working years, the loss of life, and other related losses (4, 5). Every year, millions of occupational accidents occur worldwide; some of these accidents are fatal, and others leads to temporary or permanent disability (6). Human contemporary history has recorded multiple disasters with multi-billion dollar financial losses and numerous human casualties including the explosion of the space shuttle Challenger (1986), the nuclear reactor explosion at Chernobyl (1986), the San Juanico accident in Mexico (1984), and the Bhopal plant accident in India (1984) (7). Each year, there are approximately 120 million occupational accidents worldwide, and more than 200 thousand deaths are caused by these accidents (6). In India, annually 7.7 million occupational accidents are reported, which represent an average loss of 3.25 working days per accident occurrence (8). In the year 2007, across 15 European countries the number of occupational accidents with more than three days' absence from work in manufacturing companies was about 942,000 (9). In the US, occupational accidents in the construction industry resulted in

18- Mohammad Reza Jalilnavaz

First Name	Last Name	Program	Level	School
Mohammad Reza	Jalilnavaz	Entomology	PhD	Public Health

Published Articles:

	Title of the Article
1	Application of Flumethrin Pour-On on Reservoir Dogs and Its Efficacy against Sand Flies in Endemic Focus of Visceral Leishmaniasis, Meshkinshahr, Iran

Original Article

Application of Flumethrin Pour-On on Reservoir Dogs and Its Efficacy against Sand Flies in Endemic Focus of Visceral Leishmaniasis, Meshkinshahr, Iran

Mohammad Reza Jalilnavaz [1], Mohammad Reza Abai [2], *Hassan Vatandoost [2, 3], Mehdi Mohebali [4], Amir Ahmad Akhavan [2], Zabihollah Zarei [5], Sayena Rafizadeh [6], Hassan Bakhshi [2], *Yaver Rassi [2]

[1]Tehran University of Medical Sciences, International Campus (TUMS- IC), Tehran, Iran
[2]Department of Medical Entomology and Vector Control, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[3]Institue for Environmental Research, Tehran University of Medical Sciences, Tehran, Iran
[4]Department of Medical Parasitology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[5]Public Health Research of Meshginshahr, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[6]Ministry of Health and Medical Education, Tehran, Iran

(Received 13 Aug 2014; accepted 24 Aug 2014)

Abstract

Background: Visceral leishmaniasis (VL) is one of the most important parasitic zoonotic diseases in the world. Domestic dogs are the main domestic reservoirs of VL in endemic foci of Iran. Various methods, including vaccination, treatment of dogs, detection and removal of infected dogs have different results around the world. General policy on control of canine visceral leishmaniasis is protection of them from sand fly bites. The aim of this study was evaluation of pour-on application of flumethrin on dogs against blood-feeding and mortality of field-caught sand flies.

Methods: Once every 20 days from May untill September 2013, the treated and control dogs were exposed with field caught sandflies for 2 hours under bed net traps. After the exposure time, both alive and dead sand flies were transferred in netted cups to the laboratory. The mortality rate of them was assessed after 24 hours. The blood-fed or unfed conditions were determined 2 hours after exposure to the dogs under stereomicroscope.

Results: The blood feeding index was varied from 12.0 to 25.0 % and 53.0 to 58.0 % for treated and control dogs respectively (P< 0.0001). The blood feeding inhibition was 75.0–87.0 % and 41.0–46.0 % for the control and treated dogs (P< 0.0001), respectively.The total mortality rate was 94.0–100 % and 19.0–58.0 % respectively for the treated and control groups (P< 0.001).

Conclusion: Application of pour-on flumethrin on dogs caused 90–100 % mortality until 2.5 month and inhibited the blood-feeding of sand flies.

Keywords: Visceral leishmaniasis, Flumethrin pour-on, Sand fly, Control, Iran

Introduction

Visceral leishmaniasis (VL) is the vector-borne disease and has great importance in public health due to the fatality among children. Although there is an increasing interest to VL but there is not enough approach for control measures. There are various epidemiological features of VL which indicating the needs for defining different control measures (WHO 1990). Kala-azar is a Mediterranean-form in Iran which the *Leishmania infantum* isolated from VL patients (Mohebali et al. 2005), the sand flies species from subgenera *Larroussius* and *Paraphlebotomus* acts as vectors (Azizi et al. 2006) and the dogs and wild canids are considered as principal reservoirs (Edrissian et al. 1993, Mohebali et al. 2002). Asymptomic infected dogs are suspected as the main reservoir host for sand

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19- Mohsen Karchani

First Name	Last Name	Program	Level	School
Mohsen	Karchani	Occupational Health	PhD	Public Health

Published Articles:

	Title of the Article
1	Association of Subjective and Interpretive Drowsiness with Facial Dynamic Changes In Simulator Driving
2	Presenting a model for dynamic facial expression changes in detecting drivers' drowsiness

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Presenting a model for dynamic facial expression changes in detecting drivers' drowsiness

Mohsen Karchani[1], Adel Mazloumi[2], Gebraeil Nasl Saraji[3] ,Faramarz Gharagozlou[4], Ali Nahvi[5], Khosro Sadeghniiat Haghighi[6], Bahador Makki Abadi[7], Abbas Rahimi Foroshani[8]

[1] Ph.D. Student of Department of Occupational Health, School of Public Health, International Campus, Tehran University of Medical Sciences (TUMS.IC), Tehran, Iran
[2] Assistant Professor, Department of Occupational health, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[3] Professor, Department of Occupational Health, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[4] Ph.D., Department of Occupational Health Engineering, Health College, Kermanshah University of Medical Sciences and Health Services, Kermanshah, Iran
[5] Associate Professor, Department of Mechatronics, Faculty of Mechanical Engineering of Khaje Nasir Toosi University, Tehran .Iran
[6] Associate Professor, Department of Occupational Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[7] Assistant Professor, Department of Medical Engineering, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[8] Associate Professor, Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Type of article: Brief report

Abstract
Drowsiness while driving is a major cause of accidents. A driver fatigue detection system that is designed to sound an alarm, when appropriate, can prevent many accidents that sometime leads to the loss of life and property. In this paper, we classify drowsiness detection sensors and their strong and weak points. A compound model is proposed that uses image processing techniques to study the dynamic changes of the face to recognize drowsiness during driving.
Keywords: Automobile driving, Drowsiness, Facial expression, Image processing

One of the problems of modern society is road safety and security, and sleepy drivers are a major cause of accidents on roads around the world (1). Fatigue and the monotony of driving are two important factors that can lead to a decrease in a driver's alertness level (2). In a report released by the National Highway Traffic Safety Administration (NHTSA) in 1994, Knipling and Wang determined that, from 1989 through 1993, an average of 100,000 crashes occurred annually due to drivers' fatigue and drowsiness. In these crashes, 1,550 people were killed and 40,000 others had various injuries (3). From an economic perspective, America's sleepy drivers cost the economy about $12.4 billion annually (4, 5). In Britain, driver fatigue is one of the main contributors to 20% of the accidents that occur (6). In addition, driver fatigue is the main contributor in 18% of fatal accidents in Australia (7). Research that was conducted in Japan (8, 9) and France (10) indicated that drowsiness is the main cause of fatalities in vehicles. There are no exact studies or statistics that address this issue in other countries (11). Generally, driver fatigue is a

Corresponding author:
Dr. Gebraeil Nasl Saraji, Department of Occupational Health, School of Public Health, International Campus (TUMS.IC), Tehran University of Medical Sciences, Tehran, Iran.
Tel: +98.2188951390, Fax: +98.2188954781, E-mail: jnsaraji@sina.tums.ac.ir
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Original Article

Association of Subjective and Interpretive Drowsiness with Facial Dynamic Changes In Simulator Driving

Mohsen Karchani (PhD)[a], Adel Mazloumi (PhD)[b], Gebraeil NaslSaraji (PhD)[a], Arash Akbarzadeh (MSc)[c], Ali Niknezhad (MSc)[d], Mohammad Hossien Ebrahimi (MD)[e], Mehdi Raei (MSc)[f,g], and Mohammad Khandan (MSc)[h*]

[a] Department of Occupational Health, School of Public Health, International Campus Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Occupational Health, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[d] Department of Mechatronics, Faculty of Engineering, Islamic Azad University South Tehran Branch, Tehran, Iran
[e] Department of Occupational Health, School of Public Health, Shahroud University of Medical Sciences, Shahroud, Iran
[f] Department of Biostatistics, School of Health, Kermanshah University of Medical Sciences, Kermanshah, Iran
[g] Department of Biostatistics, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran
[h] Department of Ergonomics, Faculty of Health, Work Health Research Centre, Qom University of Medical Sciences- Qom, Iran

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Observer Rating of Drowsiness
Simulator driving

*** Correspondence**
Mohammad Khandan (MSc)
Tel: +98 25 37842226
Fax: +98 25 37833361
E-mail: mkhandan@muq.ac.ir

ABSTRACT

Background: Major injuries and death in accidents have roots in drowsiness. Sleepiness is a main result of insufficient sleep. It is vital to explore drowsiness and its level. There are various sorts of methods in the forms of subjective and objective approaches. The goal of this study was to detect the association of subjective and interpretive drowsiness with facial dynamic changes.

Methods: This experimental study was conducted in the Virtual Reality Lab, in Khaje-Nasir Toosi University of Technology, Tehran Iran on 40 drivers in 2015. Facial Dynamic changes (eyes, mouth and eyebrows), Karolinska Sleepiness Scale (KSS) and Observer Rating of Drowsiness (ORD) were applied. The neural network and Viola-Jones were utilized for facial characteristics detection. Statistical analyses were conducted using SPSS version 21.

Result: Thirty-four drivers got drowsy during the test. They were selected randomly among suburban drivers at the age in a range of 26 to 60 yr old. Descriptive statistics of the dynamic changes in eyebrows, mouth and eyes showed that these features were of meaningful changes with respect to the level of drowsiness during driving. A relationship between the dynamic changes of facial features and ORD was recognized. Moreover, there was a significant relationship between facial expression and drowsiness *(P<0.05)*.

Conclusions: Results of KSS and ORD illustrated that there were dynamic changes in eyes and mouth and eyebrow parameters while driver felt sleepy. This research is helpful in a way that specific changes in elements of face could be effective to provide tools to predict drowsiness.

Citation: Karchani M, Mazloumi A, NaslSaraji G, Akbarzadeh A, Niknezhad A, Ebrahimi MH, Raei M, Khandan M. Association of Subjective and Interpretive Drowsiness with Facial Dynamic Changes In Simulator Driving. J Res Health Sci. 2015; 15(4): 250-255.

Introduction

In the whole world, in 2009, more than 1.3 million and 20-50 million people were killed and injured in crashes, respectively[1]. Statistics issued by US National Highway Traffic Safe Administration (NHTSA) indicates that 100,000 car crashes happen annually and drivers' drowsiness is one of the main reasons of car accidents. Cost of road accidents is over 12.5 billion dollar per year[2]. Major injuries and death in accidents have roots in drowsiness[3]. Sleepiness is a main result of insufficient sleep[4]. Drowsiness among drivers was considered as one of the main factors in crashes and can result in serious consequences such as harsh physical injuries, deaths and consequently large amount of economic losses[5].There are various methods to monitor sleepiness status such as movement of the steering wheel, pressure on the acceleration pedal, yawning, eye closure, eye blinking, position of head and physiological signals like EEG, ECG, and EMG. Other than these, subjective ratings of sleepiness, easily applied and unobtrusive, are an alternative, some tools in Likert-type, for example Karolinska Sleepiness Scale (KSS)[4,6]. Levels of drowsiness have been related to the risk of accidents in driving through simulators[7].

Despite the fact that instruments have the appearance of reactivity in response to differentiations in the level of alertness, they have some problems with some special assessments like large inter-individual differences[8]. In addition, they are defenselessness against effects of other factors that are not related to sleepiness[8]. Researchers dealing with high numbers of drivers in the field, use observer ratings approach through in-car video recordings to express the quantity of drowsiness among drivers[9]. Facial expression, movements of the body, changes in body position and eyelid closures duration are of criteria to make decision about sleepiness[10]. Undoubtedly, methods like observer rated

20- Amjad Mirani

First Name	Last Name	Program	Level	School
Amjad	Mirani	Public Health	MPH	Public Health

Published Articles:

	Title of the Article
1	Knowledge, attitude, and practices about polio vaccination of the guardian in super high-risk areas of Gadap town, Karachi, Pakistan

Iran J Public Health, Vol. 46, No.5, May 2017, pp.715-716

Letter to the Editor

Knowledge, Attitude, and Practices about Polio Vaccination of the Guardian in Super High-risk Areas of Gadap Town, Karachi, Pakistan

Amjad MIRANI [1], ***Kourosh HOLAKOUIE-NAIENI** [2], **Reza MAJDZADEH** [2], **Shahrzad NEMATOLLAHI** [2], **Saima BAIG** [3]

1. *International Campus, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*
2. *Dept. of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*
3. *Dept. of Media Studies Social Sciences, Sindh Madressatul Islam University, Karachi, Pakistan*

***Corresponding Author:** Email: holakoik@hotmail.com

(Received 10 Nov 2016; accepted 05 Dec 2016)

Dear Editor-in-Chief

Over 90% of Polio cases in Pakistan have been reported from four major transmission zones in Fata, Khyber-Pakhtunkhwa (K-P), Baluchistan, central Punjab and Sindh

Despite comprehensive governmental efforts since 1994 to eradicate polio (1), Pakistan is still facing substantial challenges such as inadequate program management, parental refusal and opposition of vaccination from the local groups (2). Media, religious leaders, community leaders and health care providers had vital role for dissemination of key messages about Polio.

Therefore, this study aimed to determine Knowledge, Attitude and Practice (KAP) of guardians about Polio vaccination and related factors in Super High-risk Areas of Gadap Town and put recommendation in form of a preventive action plan.

We assessed the KAP of guardians towards Polio vaccination. Totally, 554 guardians with children less than 5 yr of age were drawn from three Super High-risk Areas of Gadap Town in Karachi in 2016, using cluster sampling technique. A KAP questionnaire was administered. The results were further used to develop an action plan in order to increase KAP of guardians regarding Polio vaccination.

This cross-sectional descriptive study was approved by Ethical Committee of School of Public Health, Tehran University of Medical Sciences (TUMS), Tehran, Iran. Verbal informed consent prior to questionnaire completion was sought from the study subjects.

The mean age of study respondents was 34 (± 9.62) yr. Sixty percent of the guardians had private job, 40% of them had piped tank toilet, and 37% did not use treated water. Most of the guardians had knowledge about Polio as a health problem, clinical symptoms, a cause of permanent disability; while 58.16% were used to keep child`s vaccination card. Main sources of information about polio were healthcare providers, media, and local leaders. Totally, 86% of the guardians had positive attitude regarding polio vaccination including no fear of side effects, accessibility of health care facility, and promotion of local and religious leaders through education. 73.1% of guardians agreed that vaccination in form of EPI (i.e. Expanded Program on Immunization) could be an effective tool to protect children from Polio disease, while 91.2% agreed that proper hygiene & care could protect children from contracting Polio. In the current study, majority of the guardians had good know-

21- Elham Ashrafi

First Name	Last Name	Program	Level	School
Elham	Ashrafi	Epidemiology	PhD	Public Health

Published Articles:

	Title of the Article
1	National and Sub-national Burden of Visual Impairment in Iran 1990–2013; Study Protocol

Study Protocol

National and Sub-national Burden of Visual Impairment in Iran 1990–2013; Study Protocol

Elham Ashrafi MSc PhD Candidate[1,2,3], Seyed-Farzad Mohammadi MD MPH•[3,4], Akbar Fotouhi MD PhD[2], Alireza Lashay MD[3], Mohsen Asadi-lari MD MPH PhD[6], Alireza Mahdavi MD MPH[4], Mahmoud Jabbarvand MD[3], Sahar Sobhani MD[5], Farshad Farzadfar MD MPH DSc•[5,7]

Abstract

Background: Although Visual Impairment (VI) and its prevention is a public health issue, sub-optimal information about its magnitude in national level and its distribution is one of the impediments for visual health advocacy. In this article, we are detailing the approaches which will be taken to estimate the magnitude (prevalence, incidence, and burden), distribution, and trend (1990 to 2013) of low vision and blindness in Iran. Besides that, an attempt will be made to describe inequalities and their determinants.

Methods: After finalizing the list of diseases, a systematic search will be started using confirmed search terms and all published and unpublished data will be extracted. Other data sources, including data from hospital records will be added to the data extraction sheet. Using distinct statistical models including spatio-temporal model and multilevel autoregressive model, we will estimate rate of burden measures of eye disease and their uncertainty interval by sex, age, year, and province as well as social determinants of visual impairment inequality.

The results are to be reported in separated analyses of meta-analysis, trend, risk factors and diseases burden, inequality, Bayesian prediction modeling, and map for visualizing the results.

Conclusion: The results of the current study will address gaps in different regions and have implication for evidence-based policy making in Iran.

Keywords: Blindness, burden, DALY, eye diseases, visual impairment, social determinants of health

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Introduction

Visual Impairment (VI) is a global public health concern. The estimation of people suffering from VI all over the world is 259 million from which 42 million are blind and 217 million have low vision.[1] Eye diseases are responsible for 27.7 million Disability-adjusted life year (DALY), which constitutes 1.8% of total DALY of the world population. Eye diseases are placed in rank 14th in the world and 11th among developing countries. This position is estimated to shift up to rank 8th in 2020 (a proportion of about 2.7% DALY).[2]

Authors' affiliations: [1]Tehran University of Medical Sciences, International Campus (TUMS- IC), Tehran, Iran. [2]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. [3]Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran. [4]Center for Non-Communicable Diseases Control, Ministry of Health and Medical Education, Tehran, Iran. [5]Non-communicable Diseases Research Center, Endocrinology and Metabolism Population Science Institute, Tehran University of Medical Sciences, Tehran, Iran. [6]Department of Epidemiology and Biostatistics, School of Public Health, Iran University of Medical Sciences, Tehran, Iran. [7]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran.

•Corresponding authors and reprints: Seyed-Farzad Mohammadi MD MPH, Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran. Address: First floor, Eye Research Center, Farabi Eye Hospital, Qazvin Square, Tehran 1336616351, Iran. Telefax: 98-21-55421002; E-mail: sfmohamm@razi.tuma.ac.ir. Farshad Farzadfar MD MPH DSc, Non-communicable Diseases Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran. Address: No. 4, 4th Floor, Ostad Nejatollahi St., Enqelab Ave., Tehran 1599666615, Iran, Telefax: 98-21-88913543; E-mail: f-farzadfar@tums.ac.ir.

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It has been shown that the prevalence of blindness in developing countries is higher than that of the developed countries and it is noteworthy that close to three quarters of the world's blindness is either curable or preventable.[3] The estimation of VI in Eastern Mediterranean Region is 24 million (blind: 5 million; low vision: 19 million).[4] The prevalence of blindness and low vision in Iran has been reported variably from 0.39% to 6.9%.[5–8]

It should be mentioned that these estimates are conservative; monocular blindness is not included in the definition of blindness but it has physical and psychological morbidities. Refractive error and presbyopia are difficult to be quantified. They are underrepresented in health condition and disease burden estimates despites being the most common health condition in the whole medicine.

Blindness and its accompanying disability could be devastating; in a child, it means a major life-long physical handicap and it ruins early childhood development,[9] and is a frequent element in the poverty syndemy.[10] Finally, in the aging population, it causes major psychological impacts like depression[11] and physically imposes risk of fractures and falls. VI is a prototype non-communicable disease especially in the aging population and a constant feature of 'epidemiologic transition'. Visual health is gaining an ever-increasing importance in the sight-intensive life of the third millennium overwhelmed with smartphones, digital media, etc. Dry eye is a new pandemy, increasingly being recognized and treated but not reflected in burden studies.[2] Last but not least, the connection between survival and visual health is now more than established; VI has been shown to be associated with poor survival in older persons and others reported improved survival following cataract surgery.[12–15] Modern statistical approaches, e.g., Bayesian

22- Fataneh Bakhshi

First Name	Last Name	Program	Level	School
Fataneh	Bakhshi	Health Education	Ph.D	Public Health

Published Articles:

	Title of the Article
1	The relationship between individual empowerment and health-promoting lifestyle among women NGOs in northern Iran

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The relationship between individual empowerment and health-promoting lifestyle among women NGOs in northern Iran

Fataneh Bakhshi[1], Davoud Shojaeizadeh[2], Roya Sadeghi[3], Mohammad Hossein Taghdisi[4], Saharnaz Nedjat[5]

[1] Ph.D. Candidate of Health Education and Promotion, Department of Health Education and Promotion, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[2] Ph.D. of Health Education and Promotion, Professor, Department of Health Education and Promotion, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[3] Ph.D. of Health Education and Promotion, Associate Professor, Department of Health Education and Promotion, school of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[4] Ph.D. of Health Education and Promotion, Professor, Department of Health Education and Promotion, School of Public Health, Iran University of Medical Sciences, Tehran, Iran
[5] Ph.D. of Epidemiology and Biostatistics, Professor, Department of Epidemiology and Biostatistics, School of Public Health, Knowledge Utilization Research Center, Tehran University of Medical Sciences, Tehran, Iran

Type of article: Original

Abstract

Introduction: According to the health-promoting approach, people should be empowered such that they take responsibility for their health and follow a healthy lifestyle. Empowerment is a process in which people confront problems and tasks in their lives in order to better control them. This study was conducted to specify the relationship between individual empowerment and health-promoting lifestyle among women NGOs of northern Iran.

Methods: In this cross-sectional study, 290 women NGOs of Guilan Province were selected randomly using multistage cluster sampling, and were examined using the questionnaire of health-promoting lifestyle profile II and individual empowerment inventory scale. Data were analyzed using STATA 11 software via one-way ANOVA, Pearson correlation coefficient and multivariate linear regression.

Results: Both variables of individual empowerment and health-promoting lifestyle were of favorable status among the population under study. The highest score in individual empowerment belonged to the domain of social support and the highest score in lifestyle belonged to spiritual growth. A significant relationship was found between individual empowerment and health-promoting lifestyle ($p<0.001$). The highest correlation between individual empowerment and dimensions of health-promoting lifestyle was related to interpersonal relationships. In addition, it was specified that 21% of lifestyle variance could be explained by individual empowerment.

Conclusion: There is a relation between individual empowerment and health-promoting lifestyle. Individual empowerment is a predictive variable to have a health-promoting lifestyle. Therefore, by increasing individuals' empowerment, their healthy lifestyle can be promoted.

Keywords: Empowerment; Life style; NGOs

1. Introduction

Today, lifestyle is an important and significant strategy in which to prevent non-communicable diseases (NCDs) (1). Worldwide, over one third of mortality rate occurs due to an unhealthy lifestyle, and is the leading cause of prevalence of coronary diseases, hypertension, type II diabetes, tooth decay, stroke and a number of cancers (2). In Iran, diseases caused by an unhealthy lifestyle are the most common cause of morbidity and mortality (3). The

Corresponding author:
Dr. Roya Sadeghi, Department of Health Education and Promotion, School of Public Health, International campus, Tehran University of Medical Sciences, Tehran, Iran.
Tel: +98.2188955888, Fax: +98.2188989128, Email: sadeghir@tums.ac.ir
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23- Mahboubeh Bayat

First Name	Last Name	Program	Level	School
Mahboubeh	Bayat	Health Management	Ph.D	Public Health

Published Articles:

	Title of the Article
1	Affecting Factors on the Performance of Community Health Workers in Iran's Rural Areas: A Review Article

Iran J Public Health, Vol. 45, No.11, Nov 2016, pp.1399-1410

Review Article

Affecting Factors on the Performance of Community Health Workers in Iran's Rural Areas: A Review Article

Gholamhossein SALEHI ZALANI [1], ****Mahboubeh BAYAT*** [2], ***Azad SHOKRI*** [3], ***S. Elmira MIRBAHAEDDIN*** [4], ***Vahid RASI*** [5], ***Samira ALIREZAEI*** [5], ***Fatemeh MANAFI*** [6]

1. *Center for Health Human Resources Research & Studies, Ministry of Health and Medical Education, Tehran, Iran*
2. *Dept. of Health Management and Economics, School of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran*
3. *Health Services Management of Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran*
4. *Center for Human Resources Research & Studies, Ministry of Health and Medical Education, Tehran, Iran*
5. *Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, Iran*
6. *Dept. of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*

***Corresponding Author:** Email: h.bayat57@gmail.com

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Abstract

Background: This study aimed to use a mixed-method approach to investigate affecting factors on the performance of Community Health Workers (CHW) in Iran's villages.

Methods: This study was conducted during 2014-2015 with a mixed method in three phases of literature review, Delphi technique and developing a rich picture. Overall, in order to finalize the affecting factors and their relationships between qualitative content analysis, Delphi technique, AHP technique and Focus Group Discussion were used, respectively.

Results: Affecting factors on CHW performance were divided into four main categories, 10 sub-themes and 35 contents. Increase in the level of people's awareness, disease patterns, demographic structure and lifestyle were placed in four priorities respectively on the basis of importance.

Conclusion: To the most extent CHW cannot face current needs of rural communities. It challenges equitable access to healthcare services and also conflicts with the primary philosophy of CHW presence in rural areas. CHW can be used in two forms; either as an assistant to rural family physicians or with the same previous functions.

Keywords: Affecting factors, CHW, Performance, Rural areas, Iran

Introduction

The primary objective of health system is to improve the accessibility of underserved groups and to reduce rural and urban inequalities in benefiting health care outcomes (1). Hence, after the Islamic Revolution in Iran, the government increased its focus on rural areas and established primary health care system. Iran's Primary Health Care (PHC) System was developed for the provision of health services in rural centers and health houses in which CHW performs in the most basic level (2). CHW is currently the most vital health service delivery agent in Iran's health system. Significant results in the society's health status are the achievements of high effectiveness in CHW performance (3), especially improvement in the health of mothers and children and in most health indicators during the last 40 yr (2). However, in the best circumstances, if a structure designed according to the existing needs remains unchanged, it gradually loses its responsiveness to the needs in course of changing conditions (4-7). Currently, primary health care networks in rural

24- Hossein. Mohsenipouya

First Name	Last Name	Program	Level	School
Hossein	Mohsenipouya	Health Education	Ph.D	Public Health

Published Articles:

	Title of the Article
1	Health-related variables and predictors of Health-promoting Lifestyle in cardiovascular disease patients
2	Predictors of Health-Promoting Behaviors in Coronary Artery Bypass Surgery Patients: An Application of Pender's Health Promotion Model

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Health-related variables and predictors of Health-promoting Lifestyle in cardiovascular disease patients

Hossein Mohsenipouya[1], Fereshteh Majlessi[2], Davood Shojaeizadeh[3], Abbas Rahimi Foroushani[4], Rahman Ghafari[5], Vali Habibi[5], Azam Seyfi Makrani[6]

[1] Ph.D. Candidate, Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, International Campus (TUMS- IC), Tehran, Iran
[2] MD, Professor, Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[3] Ph.D., Professor, Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[4] Ph.D., Professor, Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[5] MD, Assistant Professor, Department of Cardiac Surgery, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
[6] B.Sc. in Nursing, Fatemehzahra Hospital, Mazandaran University of Medical Sciences, Sari, Iran

Type of article: Original

Abstract

Introduction: The principal cause for death in the world is cardiovascular disease. Poor lifestyle is a contributing element in this regard. The objective of this study was to estimate the effects of health-related variables and lifestyle variables on the results of exercise stress tests in patients with cardiovascular disease in Iran.

Methods: The study population in this case-control study was 220 patients who were candidates for exercise stress tests in Mazandaran Province (Iran) in 2015. The patients were divided randomly into two groups based on the results of their exercise stress tests, i.e., positive (110 patients) and negative (110 patients). The data collection tool was a standard questionnaire entitled "Health promotion lifestyle profile-II." The data were analyzed using mean, standard deviation, the chi-squared test, and logistic regression by SPSS version 22 software.

Results: The risk of a positive exercise stress test increases with age. The age group above 65 was 1.049 times more at risk of a positive exercise stress test than the age group of less than 45. The people with dyslipidemia had 1.635 times greater risk of positive exercise stress tests than the group without dyslipidemia. In addition, patients with hypertension had 1.579 times greater risk of positive exercise stress tests than the group without hypertension. The lack of individual health responsibility (Odds ratio (OR): 1.622), stress management (OR: 1.592), and physical activity (OR: 1.245) contributed more to positive exercise tests than the other risk factors.

Conclusion: Educational interventions can improve the responsibility for health, physical activity, and stress management among people with the risk of cardiovascular disease.

Keywords: cardiovascular disease; exercise stress test; health-promoting lifestyle

1. Introduction

One-fifth of deaths are cause by cardiovascular disease, and coronary heart disease is one of the major causes of death among people around the world. The elements that contribute to cardiovascular disease include family history, dyslipidemia, hypertension, diabetes, and smoking (1). It has been estimated that eighty-four billion U.S. dollars have been spent on cardiac disease, stroke, and diabetes in 23 developing countries from 2006 to 2015. These three diseases account for 80% of the total deaths caused by chronic diseases. Twenty-four million deaths in low- and

Corresponding author:
MD, Fereshteh Majlessi, Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98.2188989134, Email: dr_f_majlessi@yahoo.com
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Predictors of Health-Promoting Behaviors in Coronary Artery Bypass Surgery Patients: An Application of Pender's Health Promotion Model

Hossein Mohsenipoua,[1] Fereshteh Majlessi,[2] Davood Shojaeizadeh,[2,*] Abbas Rahimiforooshani,[3] Rahman Ghafari,[4] and Valiollah Habibi[4]

[1]Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, International Campus (TUMS- IC), Tehran, IR Iran
[2]Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran
[3]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran
[4]Department of Cardiac Surgery, School of Medicine, Mazandaran University of Medical Sciences, Sari, IR Iran

[*]*Corresponding author*: Davood Shojaeizadeh, Department of Health Education and Promotion, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran. Fax: +98-2188896696, E-mail: shojae5@yahoo.com

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Abstract

Background: Advances in coronary artery surgery have reduced patient morbidity and mortality. Nevertheless, patients still have to face physical, psychological, and social problems after discharge from hospital.
Objectives: The objective of this study was to determine the efficacy of Pender's health promotion model in predicting cardiac surgery patients' lifestyles in Iran.
Methods: This cross-sectional study comprised 220 patients who had undergone coronary artery bypass graft (CABG) surgery in Mazandaran province (Iran) in 2015. The subjects were selected using a simple random sampling method. The data were collected via (1) the health-promoting lifestyle profile II (HPLP II) and (2) a self-designed questionnaire that included two main sections: demographic characteristics and questions based on the health-promoting model constructs.
Results: Spiritual growth (28.77 $\pm$ 5.03) and physical activity (15.79 $\pm$ 5.08) had the highest and lowest scores in the HPLP II dimensions, respectively. All the health promotion model variables were significant predictors of health-promoting behaviors and explained 69% of the variance in health-promoting behaviors. Three significant predictors were estimated using regression coefficients: behavioral feelings ($\beta = 0.390$, $P < 0.001$), perceived benefits ($\beta = 0.209$, $P < 0.001$), and commitment to a plan of action ($\beta = 0.347$, $P < 0.001$).
Conclusions: According to the results of the study, health-promoting model-based self-care behaviors can help identify and predict cardiac surgery patients' lifestyles in Iran. This pattern can be used as a framework for discharge planning and the implementation of educational interventions to improve the lifestyles of CABG patients.

Keywords: Self-Care Behavior, Health Promotion Model, Coronary Artery Bypass, Healthy Lifestyle

1. Background

According to a world health organization (WHO) report in 2011, cardiovascular disease causes 45% of deaths among Iranian people (1). Coronary artery bypass graft surgery (CABG), as the most comprehensive treatment of coronary heart disease, has stood the test of time, having been in use for nearly 50 years (2). In the United States, 400,000 such surgeries are performed annually (3). CABG is carried out on 60% of patients suffering from coronary artery ischemic diseases (CHD) (4). Due to the inherent progression of CHD and the development of vein graft atherosclerosis, patients treated with CABG are at risk of subsequent ischemic events during the months and years following the procedure (2). Even though CABG has improved in terms of its success rate, patients still have to deal with a number of physical, psychological, and social problems in the period following discharge from hospital (5). The side effects reported by patients after CABG include a variety of problems such as postoperative pain, insomnia, changes in appetite or taste, chest pain, respiratory difficulties, arrhythmia, palpitations, numbness of the arms, abdominal distention, weight loss, anxiety related to the treatment and their ability to adhere to the recommended physical activity schedule, weakness, headache, vertigo, depression, nausea, and vomiting (6). Patients undergoing cardiac surgery must be well-informed of the potential problems, activity enhancements, nutrition, and medication beforehand since the success of the surgery is highly dependent on the patients' understanding of the disease

Chapter Three

Pharmaceutical Sciences Research Center

1- Faheem Maqbool

First Name	Last Name	Program	Level	School
Faheem	Maqbool	Pharmacology and Toxicology	PhD	Pharmaceutical Sciences Research Center

Published Articles:

	Title of the Article
1	Discovery Approaches for Novel Dyslipidemia Drugs
2	Exposure to mercury from dental amalgams: a threat to society
3	Science for the benefits of all: The way from idea to product
4	Targeting the TLR4 signaling pathway by polyphenols: A novel therapeutic strategy for neuroinflammation
5	Review of endocrine disorders associated with environmental toxicants and possible involved mechanisms
6	Effects of methyl mercury on the activity and gene expression of mouse Langerhans islets and glucose metabolism
7	Protective effects of cerium oxide and yttrium oxide nanoparticles on reduction of oxidative stress induced by sub-acute exposure to diazinon in the rat pancreas
8	Immunotoxicity of mercury: Pathological and toxicological effects

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Discovery Approaches for Novel Dyslipidemia Drugs

Faheem Maqbool[1,2], Malihe Safavi[4], Haji Bahadar[1,2], Mahban Rahimifard[2], Kamal Niaz[1,2] and Mohammad Abdollahi[1,2,3,*]

[1]*International Campus, Tehran University of Medical Sciences, Tehran, Iran;* [2]*Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran;* [3]*Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical, Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran;* [4]*Department of Biotechnology, Iranian Research Organization for Science and Technology, Tehran, Iran*

Mohammad Abdollahi

Abstract: *Introduction*: Dyslipidemia is increased fasting level of total cholesterol (TC), LDL cholesterol (LDL-C), and triglycerides (TG), along with decreased levels of HDL cholesterol (HDL-C). Owing to effect on the cardiovascular system and increased chances of metabolic diseases, it is needed to review novel under development drugs and new approaches in drug discovery for dyslipidemia. *Areas Covered*: This article reviews all phases I to IV clinical trials and preclinical trials with results associated with novel treatment of dyslipidemia. Drug discovery for dyslipidemia, toward newer targets has been addressed. *Findings*: Statins are, currently available, best choice of drugs for treating dyslipidemia and coronary diseases. In addition to this, lipid lowering drugs support treatment to a great extent, either as monotherapy or in combinations with other groups. Pravastatin used in combination with cholesteryl ester, transfers protein inhibitors (CETP) to produce efficient results. Peroxisome proliferator-activated receptor agonists (PPAR) like muraglitazar, aleglitazar and tesaglitazar are PPAR α/γ receptor agonist, dual in action performs better in phase 3 clinical study and reduces renal and cardiovascular events. By targeting both receptors, a better treatment for cardiovascular and diabetic problems can be achieved. Proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors like humanized monoclonal antibodies, are newly discovered inhibitors that reduce the risk of cardiovascular diseases. During the past few years, nucleic acid–based therapies targeting lipid and lipoprotein metabolism, such as microsomal TG transfer protein (MTP) may be a promising therapeutic approach to treat vascular diseases. Gene regulating transcription factors involved in bile acids and cholesterol metabolism can be controlled by FXR agonists in dyslipidemia. To overcome these drawbacks, many thyroid hormone analogues have been developed to lower down cholesterol level by targeting specifically thyroid hormone β receptors abundantly present in the liver without severe side effects. Virtual screening, an important tool in screening databases of the lead compounds, provides a good platform to access new compounds. In this review, examples of novel FXR modulators, thyromimetic agents, cholesterol absorption inhibitors and other new anti hyperlipidemia scaffolds have been addressed.

Keywords: Cardiovascular disease, diabetes mellitus, dyslipidemia, FXR modulators, PCSK9 inhibitors, statins, synthetic drugs, virtual screening.

1. INTRODUCTION

Since the very beginning of the nineteen century, there has been a great concern about infectious diseases responsible for the high mortality rate [1]. The development of vaccines and antibiotics helped in the management of such diseases and decreased mortality rate. However, in the recent years, mortality rate from metabolic and cardiovascular diseases has reached to alarming level [2, 3]. Dyslipidemia has been reported as the main cause for metabolic and cardiovascular diseases causing increase in death rate. Dyslipidemia is described usually by raised fasting levels of TC, low density lipoproteins-cholesterol (LDL-C), and TG, along

*Address correspondence to this author at the Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran, University of Medical Sciences, Tehran, Iran; Tel/Fax: +98-21-66959104;
E-mail: Mohammad.Abdollahi@UToronto.Ca

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Viewpoint

Exposure to mercury from dental amalgams: a threat to society

Faheem Maqbool, Haji Bahadar, and Mohammad Abdollahi

Pharmaceutical Sciences Research Center, and Faculty of Pharmacy, Tehran University of Medical Sciences, International Campus, Tehran, Iran

The intention of this article is to call the reader's attention to the underestimated, yet very serious issue of chronic exposure to elemental mercury from dental amalgams.

Dental amalgam is an alloy used for tooth fillings that contains about 50 % of elemental mercury and has been used in hundreds of millions of patients for the last 160 years throughout the world (1). According to the 2001-2004 statistics, 181.1 million people in the US have 1.46 billion restored teeth, mostly with dental amalgam (2). As its use continues in dentistry, it is quite likely that the rate of exposure to mercury keeps increasing. Additionally, mercury is used as a preservative or antiseptic in pharmaceutical and cosmetic products and is present in the human food chain, especially in fish.

With each chewing and brushing of the teeth, dental amalgam releases low levels of elemental mercury, but due to its properties it goes undetected by the exposed person. It is generally considered safe for adults and children above six years of age by regulatory bodies such as the US Food and Drug Administration (US FDA). However, more and more evidence suggests that mercury-containing dental materials could be a source of chronic exposure to mercury (3). It is estimated that 30 μg of mercury particles per cm^2 of dental amalgam is released every day (4). The risk of exposure is greater in persons having more than one filling, and mercury toxicity is greater than that of lead. According to the World Health Organization (WHO) (5) no level of mercury exposure can be considered harmless. Furthermore, the WHO believes that dental amalgam accounts for 84 % of daily exposure to mercury.

Mercury release from dental amalgam has become a major risk factor for a number of diseases. It has been evidenced to produce neurological and renal impairments (6-8). It binds to the sulphhydryl groups of enzymes and may have toxic effects on the cardiovascular, gastrointestinal, respiratory, and reproductive system (7, 9). Epidemiological studies also suggest that mercury from amalgams may be harmful for humans and responsible for several chronic diseases (10). A cohort study in Swedish women established a link between mercury release and myocardial infarction, stroke, diabetes, and cancer (11). A study in humans conducted by Sandborugh-Englund et al. (12) found high mercury concentrations in biological fluids such as plasma, blood, and urine of a population with dental amalgams.

Harmful effects of mercury from dental amalgams are in fact unavoidable. Its release is enhanced by chewing, brushing, and changes in the pH of saliva (13). In a study by Pizzichini et al. (14) mercury in the saliva lowered total antioxidant activity (TAA) and caused a number of diseases. A number of studies have proved that mercury released from dental amalgam reacts with many other metals to yield different bonds that generate reactive oxygen species and increase oxidative stress (14-16).

The effects of mercury after release from dental amalgam or other sources may affect human life very badly (17), and every action is called for to minimize human exposure (18).

Unfortunately, in general medical practice, no physician seeks to rule out mercury poisoning when they are trying to establish the cause of a chronic disease or other diagnosis. This is of course the case

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REVIEW ARTICLE

Science for the benefits of all: The way from idea to product

Faheem Maqbool [a,b], Haji Bahadar [a,b], Mohammad Abdollahi [b,*]

[a] International Campus, Tehran University of Medical Sciences, Iran
[b] Pharmaceutical Sciences Research Center and Faculty of Pharmacy, Tehran University of Medical Sciences, Iran

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Abstract Science is a knowledge based on hypotheses, observations, and experiments. From its very beginning science has served the humanity and will continue to do so until the needs of human being are fulfilled. History is rich of many scientists who have contributed to different fields of science free of politics, religion, cast, and region. Every human being must have the right to use science and technology for beneficial purposes. Mutual coordination between academia and industries is extremely important for the growth of science. The spread of ideas is only possible with publication and distribution of information to all in the world. Unpublished new ideas will remain hidden. With no doubt, many of publications and products get the spirit from the very first ideas. It is necessary that all scientists share their ideas, opening new opportunities for others to work in the various aspects. We are of the view that, to find a solution to our problems or satisfy human needs, it is important to ponder new ways in science, generate new ideas and share with others, so the concept of "science for the benefits of all" remain alive forever.

Contents

* Corresponding author. Address: Department of Toxicology and Pharmacology, Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran. Tel./Fax: 00 98 21 66959104.
E-mail addresses: Mohammad.Abdollahi@UToronto.Ca, Mohammad@TUMS.Ac.Ir (M. Abdollahi).

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Targeting the TLR4 signaling pathway by polyphenols: A novel therapeutic strategy for neuroinflammation

Mahban Rahimifard[a,1], Faheem Maqbool[a,b,c,1], Shermineh Moeini-Nodeh[a], Kamal Niaz[a,b,c], Mohammad Abdollahi[a,b,c,**], Nady Braidy[d], Seyed Mohammad Nabavi[e,*], Seyed Fazel Nabavi[e]

[a] Toxicology and Disease Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[c] International Campus, Tehran University of Medical Sciences, (IC-TUMS), Tehran, Iran
[d] Centre for Healthy Brain Ageing, School of Psychiatry, University of New South Wales, Australia
[e] Applied Biotechnology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

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ABSTRACT

A wide array of cell signaling mediators and their interactions play vital roles in neuroinflammation associated with ischemia, brain trauma, developmental disorders and age-related neurodegeneration. Along with neurons, microglia and astrocytes are also affected by the inflammatory cascade by releasing pro-inflammatory cytokines, chemokines and reactive oxygen species. The release of pro-inflammatory mediators in response to neural dysfunction may be helpful, neutral or even deleterious to normal cellular survival. Moreover, the important role of NF-κB factors in the central nervous system (CNS) through toll-like receptor (TLR) activation has been well established. This review demonstrates recent findings regarding therapeutic aspects of polyphenolic compounds for the treatment of neuroinflammation, with the aim of regulating TLR4. Polyphenols including flavonoids, phenolic acids, phenolic alcohols, stilbenes and lignans, can target TLR4 signaling pathways in multiple ways. Toll interacting protein expression could be modulated by epigallocatechin-3-gallate. Resveratrol may also exert neuroprotective effects via the TLR4/NF-κB/STAT signaling cascade. Its role in activation of cascade via interfering with TLR4 oligomerization upon receptor stimulation has also been reported. Curcumin, another polyphenol, can suppress overexpression of inflammatory mediators via inhibiting the TLR4-MAPK/NF-κB pathway. It can also reduce neuronal apoptosis via a mechanism concerning the TLR4/MyD88/NF-κB signaling pathway in microglia/macrophages. Despite a symphony of *in vivo* and *in vitro* studies, many molecular and pharmacological aspects of neuroinflammation remain unclear. It is proposed that natural compounds targeting TLR4 may serve as important pharmacophores for the development of potent drugs for the treatment of neurological disorders.

Contents

* Corresponding author at: Applied Biotechnology Research Center, Baqiyatallah University of Medical Sciences, Tehran, P.O. Box 19395-5487, Iran.
** Corresponding author at: Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.
E-mail addresses: Mohammad.Abdollahi@UToronto.Ca, Mohammad@TUMS.Ac.Ir (M. Abdollahi), Nabavi208@gmail.com (S.M. Nabavi).
[1] Equally contributed.

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Review of endocrine disorders associated with environmental toxicants and possible involved mechanisms

Faheem Maqbool [a,b], Sara Mostafalou [c], Haji Bahadar [a], Mohammad Abdollahi [a,d,*]

[a] Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, International Campus (TUMS–IC), Tehran 1417614411, Iran
[b] Faculty of Pharmaceutical Sciences, Government College University Faisalabad, Faisalabad 38000, Pakistan
[c] School of Pharmacy, Ardebil University of Medical Sciences, Ardebil, Iran
[d] Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Endocrine disrupting chemicals (EDC) are released into environment from different sources. They are mainly used in packaging industries, pesticides and food constituents. Clinical evidence, experimental models, and epidemiological studies suggest that EDC have major risks for human by targeting different organs and systems in the body. Multiple mechanisms are involved in targeting the normal system, through estrogen receptors, nuclear receptors and steroidal receptors activation. In this review, different methods by which xenobiotics stimulate signaling pathways and genetic mutation or DNA methylation have been discussed. These methods help to understand the results of xenobiotic action on the endocrine system. Endocrine disturbances in the human body result in breast cancer, ovarian problems, thyroid eruptions, testicular carcinoma, Alzheimer disease, schizophrenia, nerve damage and obesity. EDC characterize a wide class of compounds such as organochlorinated pesticides, industrial wastes, plastics and plasticizers, fuels and numerous other elements that exist in the environment or are in high use during daily life. The interactions and mechanism of toxicity in relation to human general health problems, especially endocrine disturbances with particular reference to reproductive problems, diabetes, and breast, testicular and ovarian cancers should be deeply investigated. There should also be a focus on public awareness of these EDC risks and their use in routine life. Therefore, the aim of this review is to summarize all evidence regarding different physiological disruptions in the body and possible involved mechanisms, to prove the association between endocrine disruptions and human diseases.

1. Introduction

Endocrine system is a group of various glands that secrete hormones to control metabolism, growth and development in tissue, sexual and reproductive functions as well as sleep, and mood among other physiological changes. The use of synthetic chemicals by human has been increased extensively since the introduction of these chemicals. Endocrine-disrupting chemicals (EDC) are structurally diverse class of synthetic and natural compounds that possess the ability to alter various mechanisms of the endocrine system and potentially induce adverse health effects in exposed individuals and populations [1]. According to the latest report, about 800 chemicals that are being used in daily life possess endocrine disrupting properties [2]. Out of available EDC, only some of them have been examined. These chemicals are involved in many chronic diseases like cardiovascular problems, diabetes, obesity, reproductive abnormalities, thyroid problems, neoplasm and many homeostatic imbalances [3].

2. Search strategy

Data was obtained from different scientific databases such as PubMed, Google Scholar, ClinicalTrials.gov and ToxNet. The search terms were "various types of EDC" "endocrine disrupting chemicals and health effects", "reproductive system and EDC", "thyroid system and endocrine disruption", "EDC and cardiac system", "nuclear receptors and mechanism of EDC", "EDC and oxidative stress", "nervous system and endocrine toxicants", and "carcinogenicity and danger of EDC". The reference studies of animal models were also analyzed for further research and their applicability for studying different effects related to environment, food and occupational settings exposed to EDC. Effects of EDC in relation to different system, organs and sources of exposure have been explained in Table 1. Table shows different epidemiological studies conducted in different time periods with specific protocols and different doses of EDC. Full understanding of this review article will give us new direction to the future and guidance in endocrinology related toxicology.

* Corresponding author at: Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.
E-mail addresses: Mohammad.Abdollahi@UToronto.Ca, Mohammad@TUMS.Ac.Ir (M. Abdollahi).

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Effects of methyl mercury on the activity and gene expression of mouse Langerhans islets and glucose metabolism

Faheem Maqbool [a, b, c], Haji Bahadar [d], Kamal Niaz [a, b, c], Maryam Baeeri [b], Mahban Rahimifard [b], Mona Navaei-Nigjeh [b], Seyedeh Farnaz Ghasemi-Niri [b], Mohammad Abdollahi [a, b, c, *]

[a] International Campus, Tehran University of Medical Sciences (TUMS-IC), Tehran, Iran
[b] Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, 1417614411, Iran
[d] Department of Pharmacy, Kohat University of Science and Technology, Kohat, 26000, Pakistan

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Gene expression

ABSTRACT

Mercury (Hg) is a well-known heavy metal and causes various toxic effects. It is abundantly present in fish in the form of methyl mercury (MeHg). Also, various other forms of mercury can enter human body either from environment like inhalation or through dental amalgams. The present study was designed to assess MeHg induced toxicity in mouse plasma and pancreatic islets with respect to insulin secretion, oxidative balance, glucose tolerance, gene expression, caspases 3 and 9 activities. MeHg was dissolved in tap water and administered at doses 2.5, 5 and 10 mg/kg/day, for 4 weeks. In mice, MeHg significantly caused increase in plasma insulin as well as C-peptides. Glucose intolerance, insulin resistance and hyperglycemia are main consequences of our study that correlate with the gene expression changes of glucose homeostasis as well. MeHg caused increase lipid peroxidation in a dose-dependent manner in plasma as well as pancreatic islets. In addition, total thiol molecules and ferrous reducing antioxidant power in MeHg treated group was decreased in plasma as well as pancreatic islets. Caspases 3 and 9 activities of pancreatic islets were upregulated in MeHg exposed animals. Reactive oxygen species were extremely high in pancreatic islets of MeHg treated groups. MeHg disrupted gluconeogenesis/glycogenolysis pathways and insulin secretory functions of islets by targeting GDH, GLUT2 and GCK genes of pancreatic islets. In conclusion, the current study revealed that insulin pathways, oxidative balance and glucose metabolism encoded genetic makeup are susceptible to MeHg toxicity and the subsequent oxidative stress and alternations in gene expression could lead toward functional abnormalities in other organs.

1. Introduction

Mercury (Hg) is a heavy metal and abundantly present in the environment, owing to its release from various industrial sources, it is considered a major environmental toxicant (Karlsson et al., 2010; Ratcliffe et al., 1996). It has three forms available like elemental, inorganic and organic mercury, with different toxicity profiles. Mercury causes endocrine, immune, and neurotoxic effects (Iavicoli et al., 2009; Michalke et al., 2009). MeHg induced irreversible neurotoxicity in humans has also been reported previously (Ishitobi et al., 2010). Lipophilic nature of MeHg, makes it more toxic and it is one of the most toxic forms of mercury that comes in contact with humans through different routes of exposures, that is why it is considered as serious health threat (Maqbool et al., 2014). Among humans, the main source of exposure to MeHg is through the use of different types of fish (Clarkson et al., 2003). The release of MeHg from industrial waste into river of Japan and Minamata Bay resulted accumulation of mercury in fish and consumption of such intoxicated fish led to the death of 14 patients with this disease (Clarkson et al., 2003; Takeuchi et al., 1962). Regarding toxic effects, it has been reported that MeHg induces irreversible neurotoxicity in

* Corresponding author. Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, 1417614411, Iran.
E-mail addresses: Mohammad.Abdollahi@UToronto.Ca, Mohammad@TUMS.Ac.Ir (M. Abdollahi).

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Protective effects of cerium oxide and yttrium oxide nanoparticles on reduction of oxidative stress induced by sub-acute exposure to diazinon in the rat pancreas

Mohammad Reza Khaksar[a,1], Mahban Rahimifard[b,1], Maryam Baeeri[b], Faheem Maqbool[b,c], Mona Navaei-Nigjeh[b,d], Shokoufeh Hassani[b], Shermineh Moeini-Nodeh[b], Abbas Kebriaeezadeh[b], Mohammad Abdollahi[b,c,d,*]

[a] Department of Occupational Health, Faculty of Health, Qom University of Medical Sciences, Qom, Iran
[b] Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran
[c] Tehran University of Medical Sciences, International Campus, (TUMS-IC), Tehran 1417614411, Iran
[d] Department of Tissue Engineering, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Diazinon is a kind of organophosphorus (OP) compound that is broadly used against different species of insects and pests. Oxidative stress can occur at very early stages of diazinon exposure and the pancreas is one of the main target organs for toxicity by diazinon. The aim of this study was to evaluate the protective effects of cerium oxide nanoparticles (CeO_2 NPs) and yttrium oxide nanoparticles (Y_2O_3 NPs) against the pancreatic damage from sub-acute exposure of diazinon. Diazinon at a dose of 70 mg/kg/day was given through gavage to rats once a day. Along with diazinon, trace amounts of CeO_2 NPs and Y_2O_3 NPs (35 mg/kg and 45 mg/kg per day, respectively) were administered by intraperitoneal injection once a day for 2 weeks. Animals weight and blood glucose were measured during the treatment, and oxidative stress biomarkers, diabetes physiology, function and viability of cells were investigated at the end of the treatment in serum and pancreas tissues. Apoptosis of islets was examined by the flow cytometry. The high blood glucose level and significant weight loss resulting from diazinon were modified as a result of the application of the NPs. A significant recovery in oxidative stress markers, pro-insulin, insulin, C-peptide, adenosine diphosphate/adenosine triphosphate (ATP/ADP) ratio, caspase-3 and -9 activities and apoptosis–necrosis in the islets was observed. In conclusion, administration of CeO_2 NPs or Y_2O_3 NPs only or their combination with suitable and defined dose will help to overcome the consequences from oxidant agents.

1. Introduction

Between organophosphate pesticides, diazinon has the widespread application to control plant pests in agriculture and health [1,2]. Utilization of these synthetic compounds has been a growing process compared to the other pesticides like organochlorines, due to their low toxic effects on mammals [3,4]. Meanwhile, liver and pancreas are the major target organs for pesticides, their main effects start with hematological and biochemical alteration that lead to systemic effects [5,6]. In addition, diazinon inhibits the enzyme acetyl cholinesterase (AChE) irreversibly and, in turn, causes abnormal accumulation of AChE in the nervous system. Therefore, AChE inhibition and the related consequences are characteristic biomarkers of exposure to Ops [7–9]. Other main mechanisms of OPs toxicity, including diazinon, are their abilities to induce organ damage and change the cellular anti-oxidative capacity and disturb glucose balance, which have been majorly considered in the previous studies [10–12]. It has been reported that oxidative stress has a basic role in the damage of Langerhans islets during exposure to oxidative agents [13,14]. When oxidative damage is induced in islets, antioxidant capacity is essentially low [15]. Therefore, there is a high possibility of diabetes occurrence after any damages to pancreatic ß-cells [7,16,17]. Activity of several enzymes protects our body and other organism

* Corresponding author at: Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.
E-mail addresses: Mohammad@TUMS.Ac.Ir, Mohammad.Abdollahi@UToronto.Ca (M. Abdollahi).
[1] Equally contributed.

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Immunotoxicity of mercury: Pathological and toxicological effects

Faheem Maqbool[a,b], Kamal Niaz[a,b], Fatima Ismail Hassan[a,b], Fazlullah Khan[a,b], and Mohammad Abdollahi[a,b,c,d]

[a]International Campus, Tehran University of Medical Sciences, Tehran, Iran; [b]Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran; [c]Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran; [d]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

Mercury (Hg) is toxic and hazardous metal that causes natural disasters in the earth's crust. Exposure to Hg occurs via various routes; like oral (fish), inhalation, dental amalgams, and skin from cosmetics. In this review, we have discussed the sources of Hg and its potential for causing toxicity in humans. In addition, we also review its bio-chemical cycling in the environment; its systemic, immunotoxic, genotoxic/carcinogenic, and teratogenic health effects; and the dietary influences; as well as the important considerations in risk assessment and management of Hg poisoning have been discussed in detail. Many harmful outcomes have been reported, which will provide more awareness.

KEYWORD

Human; immunotoxicity; mercury; metal; pathology

Introduction

Mercury (Hg) is a naturally occurring element in the earth's crust. Its use has been well-documented in daily routine products, such as disinfectants, preservatives, diuretics, antiseptics, and many others. It has been observed as a main cause of many dangerous health problems, such as different systems and organs of human body.[1, 3] All three forms of Hg (inorganic, organic, and elemental) have shown versatile toxicity profiles. Exposure to humans can be via ingestion or inhalation, thus ultimately causing problems in different organs and tissues.[4] Skin, nails, hair, and kidneys have been victim of extremely high levels of Hg toxicity in humans.[5] A recent publication showed evidence of how methyl mercury (MeHg) toxicities effect glucose metabolism and pancreatic functions.[6] Earth's crest, oceans, and burning of remnants are big sources for releasing elemental Hg into the atmosphere. Inorganic Hg and mercuric salts are preservatives and disinfectants in medicinal compounds.

CONTACT Mohammad Abdollahi Mohammad.Abdollahi@UToronto.Ca; Mohammad@TUMS.Ac.Ir Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.

Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/lesc.

2- Fazlullah Khan

First Name	Last Name	Program	Level	School
Fazlullah	Khan	Pharmacology and Toxicology	PhD	Pharmaceutical Sciences Research Center

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1	An evidence‐based review of the genotoxic and reproductive effects of sulfur mustard
2	Molecular Targets Underlying the Anticancer Effects of Quercetin: An Update
3	Environmental toxicants, incidence of degenerative diseases, and therapies from the epigenetic point of view
4	Epigenetic mechanisms underlying the toxic effects associated with arsenic exposure and the development of diabetes

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REVIEW ARTICLE

Environmental toxicants, incidence of degenerative diseases, and therapies from the epigenetic point of view

Mahshid Hodjat[1,4] · Soheila Rahmani[1] · Fazlullah Khan[1,2,3] · Kamal Niaz[1,2,3] · Mona Navaei–Nigjeh[1,5] · Solmaz Mohammadi Nejad[1] · Mohammad Abdollahi[1,3]

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Abstract Epigenotoxicology is an emerging field of study that investigates the non-genotoxic epigenetic effects of environmental toxicants resulting in alteration of normal gene expression and disruption of cell function. Recent findings on the role of toxicant-induced epigenetic modifications in the development of degenerative diseases have opened up a promising research direction to explore epigenetic therapy approaches and related prognostic biomarkers. In this review, we presented comprehensive data on epigenetic alterations identified in various diseases, including cancer, autoimmune disorders, pulmonary conditions as well as cardiovascular, gastrointestinal and bone disease. Although data on abnormalities of DNA methylation and their role in the development of diseases are abundant, less is known about the impact of histone modifications and microRNA expressions. Further, we discussed the effects of selected common environmental toxicants on epigenetic modifications and their association with particular abnormalities. A number of different environmental toxicants have been identified for their role in aberrant DNA methylation, histone modifications, and microRNA expression. Such epigenetic effects were shown to be tissue-type specific and highly associated with the level and duration of exposure. Finally, we described present and future therapeutic strategies, including medicines and dietary compounds for combating the toxicant-induced epigenetic alterations. There are currently seven histone deacetylase inhibitors and two DNA methyltransferase inhibitors approved for clinical use and many other promising candidates are in preclinical and clinical testing. Dietary compounds are thought to be the effective and safe strategies for treating and prevention of epigenetic pathophysiological conditions. Still more concentrated epigenetic researches are required for evaluation of chemical toxicity and identifying the causal association between key epigenetic alteration and disease.

Keywords Epigentic changes · Environmental exposures · Epigenetic machinery · Histone modification · Therapy · Nutrition

✉ Mohammad Abdollahi
mohammad@tums.ac.ir

1 Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran

2 International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran

3 Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

4 Dental Research Center, Tehran University of Medical Sciences, Tehran, Iran

5 Department of Tissue Engineering and Applied Cell Sciences, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

Introduction

Evaluating and monitoring the potentially hazardous effects of environmental toxicants on human health are important issues of the present industrial era. Ubiquitous exposure to the vast number of known and unknown synthetic toxicants has become an inevitable part of the modern life that could be responsible for the imbalance of normal physiological status and the cause of serious diseases and abnormalities in individuals (Hodjat et al. 2016; Khan et al. 2016; Koopaei and Abdollahi 2017; Niaz et al. 2017). Therapeutic approaches to intervene the toxicant-induced

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Review

Epigenetic mechanisms underlying the toxic effects associated with arsenic exposure and the development of diabetes

Fazlullah Khan [a, b, c], Saeideh Momtaz [d, c], Kamal Niaz [a, b, c], Fatima Ismail Hassan [a, b, c], Mohammad Abdollahi [a, b, c, *]

[a] International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran
[b] Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[d] Department of Pharmacology and Applied Medicine, Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran

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ABSTRACT

Background: Exposure to inorganic arsenic (iAs) is a major threat to the human health worldwide. The consumption of arsenic in drinking water and other food products is associated with the risk of development of type-2 diabetes mellitus (T2DM). The available experimental evidence indicates that epigenetic alterations may play an important role in the development of diseases that are linked with exposure to environmental toxicants. iAs seems to be associated with the epigenetic modifications such as alterations in DNA methylation, histone modifications, and micro RNA (miRNA) abundance.
Objective: This article reviewed epigenetic mechanisms underlying the toxic effects associated with arsenic exposure and the development of diabetes.
Method: Electronic databases such as PubMed, Scopus and Google scholar were searched for published literature from 1980 to 2017. Searched MESH terms were “Arsenic”, “Epigenetic mechanism”, “DNA methylation”, “Histone modifications” and “Diabetes”.
Results: There are various factors involved in the pathogenesis of T2DM but it is assumed that arsenic consumption causes the epigenetic alterations both at the gene-specific level and generalized genome level.
Conclusion: The research indicates that exposure from low to moderate concentrations of iAs is linked with the epigenetic effects. In addition, it is evident that, arsenic can change the components of the epigenome and hence induces diabetes through epigenetic mechanisms, such as alterations in glucose transport and/or metabolism and insulin expression/secretion.

Contents

* Corresponding author. Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.
E-mail addresses: Mohammad.Abdollahi@UToronto.Ca, Mohammad@TUMS.Ac.Ir (M. Abdollahi).

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REVIEW ARTICLE

An evidence-based review of the genotoxic and reproductive effects of sulfur mustard

Fazlullah Khan[1,2,3] · **Kamal Niaz**[1,2,3] · **Fatima Ismail Hassan**[1,2,3] · **Mohammad Abdollahi**[1,2,3]

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Abstract Sulfur mustard (SM) is a chemical warfare agent which is cytotoxic in nature, and at the molecular level, SM acts as DNA alkylating agent leading to genotoxic and reproductive effects. Mostly, the exposed areas of the body are the main targets for SM; however, it also adversely affects various tissues of the body and ultimately exhibits long-term complications including genotoxic and reproductive effects, even in the next generations. The effect of SM on reproductive system is the reason behind male infertility. The chronic genotoxic and reproductive complications of SM have been observed in the next generation, such as reproductive hormones disturbances, testicular atrophy, deficiency of sperm cells, retarded growth of sperm and male infertility. SM exerts toxic effects through various mechanisms causing reproductive dysfunction. The key mechanisms include DNA alkylation, production of reactive oxygen species (ROS) and nicotinamide adenine dinucleotide (NAD) depletion. However, the exact molecular mechanism of such long-term effects of SM is still unclear. In general, DNA damage, cell death and defects in the cell membrane are frequently observed in SM-exposed individuals. SM can activate various cellular and molecular mechanisms related to oxidative stress (OS) and inflammatory responses throughout the reproductive system, which can cause decreased spermatogenesis and impaired sperm quality via damage to tissue function and structure. Moreover, the toxic effects of SM on the reproductive system as well as the occurrence of male infertility among exposed war troopers in the late exposure phase is still uncertain. The chronic effects of SM exposure in parents can cause congenital defects in their children. In this review, we aimed to investigate chronic genotoxic and reproductive effects of SM and their molecular mechanisms in the next generations.

Keywords Sulfur mustard (SM) · Genotoxicity · Infertility

Introduction

SM is a chemical warfare agent showing both acute and chronic pathological effects in humans upon exposure. There are various body organs affected by SM, which mainly includes skin, eyes and lungs (Ghabili et al. 2011). During the Iraq–Iran war (1983–1988), this agent was used many times by Iraqi military forces against both Iranian soldiers and Iraqi Kurdish residence. It has been reported that during this war, almost 100,000 Iranians suffered from the deleterious effects of SM (Emad and Rezaian 1997). Due to the SM attack, many death cases were reported in the Iranian population. The victims of such attacks were intensively investigated by Iranian researchers. They observed several complications among the victims of SM attacks. Respiratory, dermatological, hematological and endocrine complications were most commonly observed among SM victims. These chronic complications adversely affected the quality of life of exposed patients (Mansour Razavi et al. 2012). The use of SM, as a chemical warfare

✉ Mohammad Abdollahi
Mohammad.Abdollahi@UToronto.Ca; Mohammad@TUMS.Ac.Ir

[1] International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran

[2] Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran

[3] Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran

nutrients

MDPI

Review

Molecular Targets Underlying the Anticancer Effects of Quercetin: An Update

Fazlullah Khan [1,2], Kamal Niaz [1,2], Faheem Maqbool [1,2], Fatima Ismail Hassan [1,2], Mohammad Abdollahi [1,2,*], Kalyan C. Nagulapalli Venkata [3], Seyed Mohammad Nabavi [4] and Anupam Bishayee [3,*]

1 Pharmaceutical Sciences Research Center, International Campus, Tehran University of Medical Sciences, Tehran 1417614411, Iran; fazlullahdr@gmail.com (F.K.); kamalniaz1989@gmail.com (K.N.); faheemthepharmacist@gmail.com (F.M.) pharm.fatee@yahoo.com (F.I.H.)

2 Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran 1417614411, Iran

3 Department of Pharmaceutical Sciences, College of Pharmacy, Larkin Health Sciences Institute, Miami, FL 33169, USA; kvenkata@Ularkin.org

4 Applied Biotechnology Research Center, Baqiyatallah University of Medical Sciences, Tehran 1435916471, Iran; nabavi208@gmail.com

* Correspondence: Mohammad.Abdollahi@UToronto.Ca or Mohammad@TUMS.Ac.Ir (M.A.); abishayee@Ularkin.org or abishayee@gmail.com (A.B.); Tel.: +98-216-959-104 (M.A.); +1-305-760-7511 (A.B.)

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Abstract: Quercetin, a medicinally important member of the flavonoid family, is one of the most prominent dietary antioxidants. It is present in a variety of foods—including fruits, vegetables, tea, wine, as well as other dietary supplements—and is responsible for various health benefits. Numerous pharmacological effects of quercetin include protection against diseases, such as osteoporosis, certain forms of malignant tumors, and pulmonary and cardiovascular disorders. Quercetin has the special ability of scavenging highly reactive species, such as hydrogen peroxide, superoxide anion, and hydroxyl radicals. These oxygen radicals are called reactive oxygen species, which can cause oxidative damage to cellular components, such as proteins, lipids, and deoxyribonucleic acid. Various oxygen radicals play important roles in pathophysiological and degenerative processes, such as aging. Subsequently, several studies have been performed to evaluate possible advantageous health effects of quercetin and to collect scientific evidence for these beneficial health claims. These studies also gather data in order to evaluate the exact mechanism(s) of action and toxicological effects of quercetin. The purpose of this review is to present and critically analyze molecular pathways underlying the anticancer effects of quercetin. Current limitations and future directions of research on this bioactive dietary polyphenol are also critically discussed.

Keywords: quercetin; cancer prevention; diet; bioavailability; DNA damage; polyphenols

1. Introduction

During the last decade, the proportion of scientific studies based on non-nutritive components of diet has increased. Such components are present in diet and have the ability to protect the body from the harmful effects of degenerative diseases, cancer, and cardiovascular ailments. Carotenoids and flavonoids, two distinct groups of phytochemicals, represent valuable constituents of food. Other dietary agents—such as phytoalexins, phenolic acids, indole-3-carbinol, and organosulfur compounds—are also important phytochemicals with interesting biological activities [1,2]. Phytochemicals are generally present in a variety of foods, fruits, vegetables, beverages, and many other food products and medicinally important herbal preparations. The important point that brings the attention of the scientists towards the naturally occurring compounds for the

3- Haji Bahadar

First Name	Last Name	Program	Level	School
Haji	Bahadar	Pharmacology and Toxicology	PhD	Pharmaceutical Sciences Research Center

Published Articles:

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1	Toxicity of Nanoparticles and an Overview of Current Experimental Models
2	The molecular mechanisms of liver and islets of Langerhans toxicity by benzene and its metabolite hydroquinone in vivo and in vitro
3	Assessment of benzene induced oxidative impairment in rat isolated pancreatic islets and effect on insulin secretion
4	Molecular mechanisms involved in lead induced disruption of hepatic and pancreatic glucose metabolism
5	Growing burden of diabetes in Pakistan and the possible role of arsenic and pesticides

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Toxicity of Nanoparticles and an Overview of Current Experimental Models

Haji Bahadar[1], Faheem Maqbool[1], Kamal Niaz[1] and Mohammad Abdollahi[*1,2,3]

[1]Dept. of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, International Campus, Tehran University of Medical Sciences, Tehran, Iran; [2]Endocrinology and Metabolism Research Center, Institute of Clinical Endocrine Sciences, Tehran University of Medical Sciences, Tehran, Iran; [3]Toxicology and Poisoning Research Center, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Nanotechnology is a rapidly growing field having potential applications in many areas. Nanoparticles (NPs) have been studied for cell toxicity, immunotoxicity, and genotoxicity. Tetrazolium-based assays such as MTT, MTS, and WST-1 are used to determine cell viability. Cell inflammatory response induced by NPs is checked by measuring inflammatory biomarkers, such as IL-8, IL-6, and tumor necrosis factor, using ELISA. Lactate dehydrogenase (LDH) assay is used for cell membrane integrity. Different types of cell cultures, including cancer cell lines have been employed as *in vitro* toxicity models. It has been generally agreed that NPs interfere with either assay materials or with detection systems. So far, toxicity data generated by employing such models are conflicting and inconsistent. Therefore, on the basis of available experimental models, it may be difficult to judge and list some of the more valuable NPs as more toxic to biological systems and vice versa. Considering the potential applications of NPs in many fields and the growing apprehensions of FDA about the toxic potential of nanoproducts, it is the need of the hour to look for new internationally agreed free of bias toxicological models by focusing more on *in vivo* studies.

Keywords: Cytotoxicity, *in vitro*, Metal nanoparticles, Toxicology, Review

Corresponding Author: Mohammad Abdollahi
Dept. of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, International Campus, Tehran University of Medical Sciences, Tehran, Iran; Tel/Fax: (+98-21) 66959104; E-mail: Mohammad.Abdollahi@UToronto.Ca, Mohammad@TUMS.ac.Ir

INTRODUCTION

Engineered nanoparticles (NPs) are commercially produced materials having at least one dimension less than 100 nm[1]. Nano-technology has brought a great revolution in the industrial sector. Due to their distinctive physicochemical and electrical properties, nano-sized materials have gained considerable attraction in the field of electronics, biotechnology, and aerospace engineering. In the field of medicine NPs are being employed as a novel delivery system for drugs, proteins, DNA, and monoclonal antibodies[2-4]. So far, NPs have been prepared from metal and non-metal, polymeric materials and bioceramics. The majority of NPs having medical applications are liposomes, polyethylene glycol, and dendrimers[5]. Humans are exposed to various nano-scale materials since childhood, and the new emerging field of nanotechnology has become another threat to human life[6]. Because of their small size, NPs find their way easily to enter the human body and cross the various biological barriers and may reach the most sensitive organs[7]. Scientists have proposed that NPs of size less than 10 nm act similar to a gas and can enter human tissues easily and may disrupt the cell normal biochemical environment[8]. Animals and human studies have shown that after inhalation and through oral exposure, NPs are distributed to the liver, heart, spleen, and brain in addition to lungs and gastrointestinal tract[9-11]. In order to clear these NPs from the body, the components of the immune system are activated. The estimated half life of NPs in human lungs is about 700 days posing a consistent threat to respiratory system. During metabolism, some of the NPs are congregated in the liver tissues[6-12]. NPs are more toxic to human health in comparison to large-

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The molecular mechanisms of liver and islets of Langerhans toxicity by benzene and its metabolite hydroquinone in vivo and in vitro

Haji Bahadar[a], Faheem Maqbool[a], Sara Mostafalou[b], Maryam Baeeri[a], Mahdi Gholami[a], Elmira Ghafour-Boroujerdi[a] & Mohammad Abdollahi[ac]

[a] Department of Toxicology and Pharmacology, Faculty of Pharmacy, Pharmaceutical Sciences Research Center, International Campus, Tehran University of Medical Sciences, Tehran, Iran,

[b] School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran, and

[c] Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

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Assessment of benzene induced oxidative impairment in rat isolated pancreatic islets and effect on insulin secretion

Haji Bahadar[a], Faheem Maqbool[a], Sara Mostafalou[b], Maryam Baeeri[a], Mahban Rahimifard[c], Mona Navaei-Nigjeh[c], Mohammad Abdollahi[a,c,*]

[a] Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, International Campus, Tehran, Iran

[b] School of Pharmacy, Ardebil University of Medical Sciences, Ardebil, Iran

[c] Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Benzene (C_6H_6) is an organic compound used in petrochemicals and numerous other industries. It is abundantly released to our environment as a chemical pollutant causing widespread human exposure. This study mainly focused on benzene induced toxicity on rat pancreatic islets with respect to oxidative damage, insulin secretion and glucokinase (GK) activity. Benzene was dissolved in corn oil and administered orally at doses 200, 400 and 800 mg/kg/day, for 4 weeks. In rats, benzene significantly raised the concentration of plasma insulin. Also the effect of benzene on the release of glucose-induced insulin was pronounced in isolated islets. Benzene caused oxidative DNA damage and lipid peroxidation, and also reduced the cell viability and total thiols groups, in the islets of exposed rats.

In conclusion, the current study revealed that pancreatic glucose metabolism is susceptible to benzene toxicity and the resultant oxidative stress could lead to functional abnormalities in the pancreas.

1. Introduction

Benzene (C_6H_6) is an organic compound, used as an industrial solvent and a component of petrochemicals. It is one of the environmental contaminants released from various sources affecting human life. Refined petroleum products generally contain benzene 2–3% by volume. But in certain regions of the world, the use of benzene in petrochemicals has reached to more than 5% by volume (Verma and Tombe, 2002; Karakitsios et al., 2007). Release of benzene in our environment takes place from industrial wastes, combustion of petrochemicals, and cigarette smoke. Its absorption takes place from all natural routes and rapidly metabolized in the liver and bone marrow. And the resultant toxic metabolites and free radicals cause various lethal effects on the body (Travis et al., 1990; Bahadar et al., 2014a).

Free radicals and reactive oxygen species (ROS) have been thought as important physiological mediators playing an

* *Corresponding author at:* Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran. Tel./fax: +98 21 66959104.
E-mail addresses: Mohammad.Abdollahi@UToronto.Ca, Mohammad@TUMS.Ac.Ir (M. Abdollahi).

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Molecular mechanisms involved in lead induced disruption of hepatic and pancreatic glucose metabolism

Sara Mostafalou[a,b], *Maryam Baeeri*[b], *Haji Bahadar*[b,c], *Mohammad Soltany-Rezaee-Rad*[b], *Mahdi Gholami*[b], *Mohammad Abdollahi*[b,*]

[a] *School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran*
[b] *Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran*
[c] *International Campus, Tehran University of Medical Sciences, Tehran, Iran*

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Liver

ABSTRACT

Lead (Pb) is a toxic heavy metal known to be associated with pathology of various human chronic diseases. This study has focused on the effect of lead on glucose homeostasis with regard to metabolic function of pancreas and liver. Islets of Langerhans were isolated from the pancreas of rats and exposed to lead for 24 h, then insulin release along with markers of ER stress and oxidative stress were evaluated. In another part, lead was administered to rats for 32 days and after evaluating criteria of diabetes, the activity of gluconeogenesis and glycogenolysis enzymes, and markers of oxidative stress and inflammation were measured in the liver. Lead disrupted insulin secretory function of islets through activating GSK-3β and ER stress, and increased activity of gluconeogenic enzymes in the liver featured by glucose intolerance. Chronic exposure to lead can disrupt glucose homeostasis by affecting pancreas and liver mainly through induction of insulin resistance.

1. Introduction

The heavy metal lead (Pb) is an abundant environmental toxicant with a wide range and long history of use dating back to Roman times. Despite wide toxicological studies, there is still debate on the hazards of lead for the general population through long time exposure to low levels of this toxicant in drinking water, food, and air (Karrari et al., 2012; Mehrpour et al., 2012). During the last decade, the exposure levels below

Abbreviations: 8OHG, 8-hydroxy-2-deoxy guanosine; AUC, area under curve; BLL, blood lead level; CHOP, CCAAT/enhancer-binding protein (C/EBP) homologous protein; eIF2B, initiation factor 2B; ER, endoplasmic reticulum; FBS, fasting blood sugar; G6P, glucose 6-phaophatase; GLUT2, glucose transporte 2; GP, glycogen phosphorylase; GRP78, glucose regulated protein 78; GSIS, glucose stimulated insulin secretion; GSK-3β, glycogen synthase kinase-3 beta; GTT, glucose tolerance test; HOMA-IR, homeostatic model assessment-insulin resistance; HOMA-β, homeostatic model assessment-beta cells function; IR, insulin receptor; IRS, insulin receptor substrate; MTT, thiazolyl blue tetrazolium bromide; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; PEPCK, phosphoenolpyruvate carboxykinase; PI-3K, phophatidil inositil-3 kinase; ROS, reactive oxygen species; TBARS, thiobarbituric acid reactive substances; TNF-α, tumor necrosis factor-alpha.

* Corresponding author. Tel.: +98 21 66959104; fax: +98 21 66959104.
E-mail addresses: Mohammad@TUMS.Ac.Ir, Mohammad.Abdollahi@UToronto.Ca (M. Abdollahi).

Journal of Diabetes & Metabolic Disorders

REVIEW ARTICLE Open Access

Growing burden of diabetes in Pakistan and the possible role of arsenic and pesticides

Haji Bahadar[1,2], Sara Mostafalou[2] and Mohammad Abdollahi[1*]

Abstract

This review is undertaken to address the possible role of arsenic and pesticides in the prevalence of diabetes in Pakistan and to highlight a resourceful targeted research in this area.

A bibliographic search of scientific databases was conducted with key words of "epidemics of diabetes in Pakistan", "diabetes in Asia", "diabetes mellitus and environmental pollutants", "diabetes mellitus and heavy metals", "diabetes mellitus and pesticides", "prevalence of pesticides in Pakistan", and "heavy metals contamination of drinking water, "vegetables and fruits in Pakistan". More than 200 articles were examined. Studies reporting the prevalence of diabetes mellitus (DM), pesticides and heavy metal contamination of drinking water, fruits and vegetables were included in the study. According to WHO 2011 report, about 12.9 million people are suffering from DM and the number is constantly increasing. Water pollution is a major public health threat in Pakistan. Most of the people in Pakistan are exposed to arsenic and pesticides either in drinking water or through vegetables, fruits, and other edible items with various concentrations above the WHO/FAO permissible limits. Being an agricultural country, a 1169% increase has been recorded with the use of different types of pesticides since last two decades, and almost similar rise in the burden of diabetes.

There is a growing global concern of arsenic and pesticides exposure with the incidence of DM. Besides other factors, the environmental attributors in the incidence of DM in Pakistan have not been conclusively elucidated yet which in turn deserve a resourceful targeted research.

Keywords: Arsenic, Diabetes mellitus, Environmental pollutants, Heavy metals, Pakistan, Pesticides, Review

Introduction

Pollution is the addition of substances or energy to the environment, likely to produce harmful effects on human health and ecosystem. Heavy industrialization and scientific developments have led to the addition of detrimental chemicals to the environment in the form of heavy metals, agrochemicals, pesticides and hydrocarbons [1]. Environmental pollution has been a major health concern throughout the world since very long, but the risks are higher in underdeveloped countries. In low developed countries, environmental pollution contributes about 8-9% of total disease burden [2].

Pakistan, a country with a population exceeding 180 million, having four provinces along with federally administered tribal areas, is the 6th populous country of the world with a very small economy [3].

Arsenic exposure in Pakistan

The presence of arsenic (As) in drinking water has become a major public health concern around the world. Arsenic has been recognized globally as the most toxic inorganic contaminant of drinking water [4]. Water sources of Asian countries, including Pakistan are among the most affected ones for As contamination [5,6].

Regional status of arsenic exposure in Pakistan

Sindh province

Approximately 36% people in Sindh province consume drinking water or vegetables containing As above the WHO limit [7]. The ground water sources in some rural areas in Sindh province contain As up to 1.1 mg/L [8]. A study published by Arain et al. reported the contamination of vegetables with As. The vegetables grown in the south

* Correspondence: Mohammad@TUMS.Ac.Ir
[1]Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, International Campus, Tehran University of Medical Sciences, Tehran, Iran
Full list of author information is available at the end of the article

4- Kamal Niaz

First Name	Last Name	Program	Level	School
Kamal	Niaz	Pharmacology and Toxicology	PhD	Pharmaceutical Sciences Research Center

Published Articles:

	Title of the Article
1	A review of environmental and occupational exposure to xylene and its health concerns
2	STAT3 targeting by polyphenols: Novel therapeutic strategy for melanoma
3	Can bacterium ud1023 lessen the uptake and Bioaccumulation of heavy metals in plants? An update
4	CYP2D: Brain Enzyme Involved in Induction of Analgesia and Codeine Dependency
5	Molecular evidence on the protective effect of ellagic acid on phosalone-induced senescence in rat embryonic fibroblast cells
6	Emerging Issue of Escherichia Coli Resistance: A Threat to Public Health
7	Effect of styrene exposure on plasma parameters, molecular mechanisms and gene expression in rat model islet cells
8	Endo-cannabinoids system and the toxicity of Cannabinoids with a biotechnological approach
9	Molecular mechanisms of action of styrene toxicity in blood plasma and liver
10	Smokeless tobacco (*paan* and *gutkha*) consumption, prevalence, and contribution to oral cancer

Editorial

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Emerging Issue of *Escherichia Coli* Resistance: A Threat to Public Health

Kamal Niaz, Faheem Maqbool, Mohammad Abdollahi*

Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran 1417614411, Iran

***Correspondence:** Mohammad Abdollahi, Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran, Tel: +98-21-66959104; E-mail: Mohammad.Abdollahi@utoronto.ca or Mohammad@tums.ac.ir

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Introduction

Over the past decade, extensive use of antibiotics in veterinary and humans contributed to bacterial resistance in the environment. The contribution of resistant bacterial strains in the environment occurred through feces, excreta of animals and humans. The enormous intake of antibiotics have resulted resistance in the normal microbiota of gastrointestinal tract (GIT) among healthy humans [1]. Furthermore, veterinarians used broad spectrum antibiotics for pets' safety [2]. In the present editorial, we tried to document the resistance of *E. coli* to various antibiotics with special reference to animals and humans.

Investigative exposure to drug-resistant extra-intestinal pathogenic *E. coli*

The massive practice of antibiotics in pets such as in dog lead to the existence of antibiotics resistant bacteria in feces, which have the possibility to infect public space, like parks and may contributed to public acquired infectious diseases [3]. Dogs and other domestic animals might be the important contributors in spreading of antibiotic resistance against *E. coli*. Furthermore, individuals returning from parks and other areas that contain canine feces unintentionally spread the resistant bacteria via shoe (Figure 1) [3]. For instance 9% of extra-intestinal pathogenic *E. coli* multiple drug-resistant was calculated from the total quantity of *E. coli* identified in the shoe samples. Therefore, in order to draw attention to these sites, as potential point of exposure is important; dissemination of antibiotic resistant *E. coli* bacteria can put large population in urinary tract infection [4]. Canines and humans isolation of multi-drug resistant *E. coli* clonal groups found to be closely related, suggesting possible cross-hosts species transfer infections [5,6]. Ultimately, extensive uses of antimicrobial agents lead to resistance in animals as well as in humans. Furthermore, in animals 50% of antimicrobial and chemotherapeutic agents are given each year to increase productivity [7].

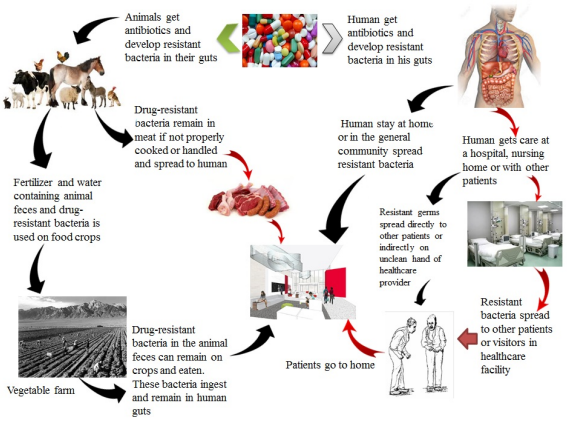

Figure 1: How antibiotics resistance spreads.

Incidence of extended-spectrum β-lactamase-producing *E. coli* (ESBL-EC)

The occurrence of ESBL-EC infection has improved in community hospital. Researchers and microbiologists should draw attention to the maternity centers, community hospitals and healthcare related ESBL-EC infection [8].

Approximately, 20 hospitals in the Southeast of United State patients' record were reviewed. By investigative analysis, it was found that admittance time, history, examinations and demographic evidence the scientists also pledge increased infections occurred due to antibiotics amongst public adherents who had inadequate contact to health maintenance facility. However, these infections developed due to other environmental risk factors such as unhygienic condition, genetics and malnutrition. In the study they have measured antibiotic-resistant pathogenesis a challenging situation in the large hospitals. This extended study confirmed that resistance to antibiotics of normal micro-flora happened in entirely health maintenance system. They also investigated that infection burden increasing in health facilities of the rural areas due to unavailability of health care units [8]. As aforementioned people living with domestic animals could possibly be at high risk to develop different species-cross infections.

Antibiotics are tremendously essential in health care settings. The statistical figures indicated that *E. coli* collapsed

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Review article:

A REVIEW OF ENVIRONMENTAL AND OCCUPATIONAL EXPOSURE TO XYLENE AND ITS HEALTH CONCERNS

Kamal Niaz[1], Haji Bahadar[1], Faheem Maqbool[1], Mohammad Abdollahi[1,2,*]

[1] Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, International Campus, Tehran, Iran
[2] Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran 1417614411, Iran

* Corresponding author: Mohammad Abdollahi**,** Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran. Tel/Fax: +98-21-66959104;
E-mail: Mohammad.Abdollahi@utoronto.ca; Mohammad@tums.ac.ir

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ABSTRACT

Xylene is a cyclic hydrocarbon, and an environmental pollutant. It is also used in dyes, paints, polishes, medical technology and different industries as a solvent. Xylene easily vaporizes and divides by sunlight into other harmless chemicals. The aim of the present review is to collect the evidence of the xylene toxicity, related to non-cancerous health hazards, as well as to provide possible effective measurement to minimize its risk ratio. For current study a bibliographic search of more than 250 peer-reviewed papers in scientific data including PubMed, and Google Scholar about xylene was done. But approximately 130 peer-reviewed papers relevant to xylene were included (Figure 1). All scientific data was reviewed with key words of "xylene toxicity", "xylene toxic health effects", "environmental volatile organic compounds", "human exposure to xylene", "xylene poisoning in laboratory workers", "effects of xylene along with other hydrocarbons", "neurotoxicity of selected hydrocarbons", and "toxic effects of particular xylene isomers in animals". According to these studies, xylene is released into the atmosphere as fugitive emissions from petrochemical industries, fire, cigarette, from different vehicles. Short term exposure to mixed xylene or their individual isomers result in irritation of the nose, eyes and throat subsequently leading toward neurological, gastrointestinal and reproductive harmful effects. In addition long term exposure to xylene may cause hazardous effects on respiratory system, central nervous system, cardiovascular system, and renal system. The health concerns of xylene are well documented in animals and human. It is important to improve health policies, launch xylene related health and toxicity awareness campaigns, to get rid of its dangerous outcomes. Chronic diseases have become a threat to human globally, with special prominence in regions, where xylene is used with other chemicals (benzene, toluene etc.) especially in petroleum and rubber industry. The mechanism of toxicity and interactions with endocrine system should be followed up which is the main threat to human health.

Keywords: xylene, health hazards of xylene, genotoxicity, hepatotoxicity, neurotoxicity, review

Abbreviations: TWA = time-weighted average; p = para; m = meta; o = ortho; Bd wt = body weight; d =day (s); DNA = deoxy ribonucleic acid; CYP = cytochrome P; GABA = gamma-aminobutyric acid; Gd = gestational day; SGPT = serum glutamic pyruvic transaminase; x = time (s); mo = month (s); yr = year (s); mg = milligram; kg = kilogram; CNS = central nervous system; GIT = gastrointestinal tract; RER; rough endoplasmic reticulum, RBC = red blood cells; WBC = white blood cells, ppbv = parts per billion volume, EPA = Environmental Protection Agency, NPL = National Priorities List, VOC = volatile organic compound, MDA = malondialdehyde, SOD = superoxide dismutase, GSH-Px = glutathione peroxidase, VOCs = volatile organic compounds

Review Article

STAT3 targeting by polyphenols: Novel therapeutic strategy for melanoma

Saeideh Momtaz[1,2]
Kamal Niaz[1,3]
Faheem Maqbool[1,3]
Mohammad Abdollahi[1,3]*
Luca Rastrelli[4]
Seyed Mohammad Nabavi[5]*

[1]Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran

[2]Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran

[3]International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran

[4]Dipartimento di Farmacia, University of Salerno, Fisciano, SA, Italy

[5]Applied Biotechnology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

Abstract

Melanoma or malignant melanocytes appear with the low incidence rate, but very high mortality rate worldwide. Epidemiological studies suggest that polyphenolic compounds contribute for prevention or treatment of several cancers particularly melanoma. Such findings motivate to dig out novel therapeutic strategies against melanoma, including research toward the development of new chemotherapeutic and biologic agents that can target the tumor cells by different mechanisms. Recently, it has been found that signal transducer and activator of transcription 3 (STAT3) is activated in many cancer cases surprisingly. Different evidences supply the aspect that STAT3 activation plays a vital role in the metastasis, including proliferation of cells, survival, invasion, migration, and angiogenesis. This significant feature plays a vital role in various cellular processes, such as cell proliferation and survival. Here, we reviewed the mechanisms of the STAT3 pathway regulation and their role in promoting melanoma. Also, we have evaluated the emerging data on polyphenols (PPs) specifically their contribution in melanoma therapies with an emphasis on their regulatory/inhibitory actions in relation to

Abbreviations: *AP-1, activator-1; ATP, adenosine triphosphate; Bax, Bcl-2-associated X protein; BCC, basal cell carcinoma; Bcl-x_L, B-cell lymphoma-extra large; bFGF, basic fibroblast growth factor; CDK-4, cyclin-dependent kinase 4; CIS, cytokines inducible SH2-containing protein; COX-2, cyclooxygenase; CSF-1, colony-stimulating factor-1; DCT, dopachrome tautomerase; DNA, deoxyribonucleic acid; ECM, extracellular matrix; EGCG, epigallocatechin gallate; EGF, epidermal growth factor; EGFR, epidermal growth factor receptor; ERK, extracellular signal–regulated kinases; ESCs, embryonic stem cells; Fas/CD95, first apoptosis signal/cluster of differentiation 95; FLIP, FLICE-like inhibitory protein; GM-CSF, granulocyte-macrophage colony-stimulating factor; HDACs, histone deacetylases; HGF, hepatocyte growth factor; HIES, hyper-immunoglobulin E syndrome; IL, interlukin; IFN-γ, interferon gamma; iNOS, inducible nitric oxide synthase; JAK/STATs, janus kinase-signal transducer and activator of transcription; JNK, c-Jun N-terminal kinase; LIF, leukemia inhibitory factor; MAPKs, mitogen-activated protein kinases; Mcl-1, myeloid cell leukemia 1; MM, multiple myeloma; MMPs, matrix metalloproteinases; MSH, melanocyte stimulating hormone; mTOR, the mechanistic target of rapamycin; NF-κB, nuclear factor-κB; NLK, nemo-like kinase; PDGF, platelet derived growth factor; PI3K, phosphatidylinositol 3-kinase; PIAS, protein inhibitors of activated STATs; PKC, protein kinase C; PP2A, protein phosphatase 2A; PPs, polyphenols; PTP1B, phospho-tyrosine phosphatase 1B; RTKs, receptor tyrosine kinases; SCC, squamous cell carcinoma; SOCS, suppressors of cytokines signaling; STAT3, signal transducer and activator of transcription 3; SURM, small ubiquitin related modifier; TC-PTP, T cell-protein tyrosine phosphatase; TGF-β, transforming growth factor-β; TRAIL, TNF-related apoptosis-inducing ligand; TYRP1, tyrosinase-related protein-1; UV, ultraviolet; VEGF, vascular endothelial growth factor; WHO, World Health Organization; Wnt, wingless signaling*

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Address for correspondence: Mohammad Abdollahi, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran. Tel/Fax: +98-21-66959104 E-mail: Mohammad.Abdollahi@UToronto.ca or Mohammad@TUMS.Ac.ir or Seyed Mohammad Nabavi Applied Biotechnology Research Center, Baqiyatallah University of Medical Sciences, Tehran, P.O. Box 19395-5487, Iran. Tel.: +98-21-88617712; Fax: +98-21-88617712; E-mail: Nabavi208@gmail.com.

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Guest editorial:

CAN BACTERIUM UD1023 LESSEN THE UPTAKE AND BIOACCUMULATION OF HEAVY METALS IN PLANTS? AN UPDATE

Kamal Niaz[1], Faheem Maqbool[1], Haji Bahadar[2], Mohammad Abdollahi[1] *

[1] Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, International Campus, Tehran, Iran
[2] Department of Pharmacy, Kohat University of Science and Technology Kohat, Pakistan

* Corresponding author: Mohammad Abdollahi, Dean, Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran. Tel/Fax: +98-21-66959104; E-mail: Mohammad.Abdollahi@uToronto.ca or Mohammad@tums.ac.ir

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Abbreviations: Ni – Nickel; Cd – Cadmium; TL – Thallium; As – Arsenic; DEHP - Di-(2-ethylhexyl) phthalates; DBP - Di-n-butyl phthalates; AMF - Arbuscular mycorrhizal fungi; MHB - Mycorrhizal helping bacteria; PGPR - Plant growth promoting rhizobacteria; ↑ - Increased; ↓ - Reduced

Pollution of water and soil with heavy metals highlights one of the most important public health threats. Soil and plants are polluted with heavy metals like nickel (Ni), cadmium (Cd), thallium (Tl) and arsenic (As) which mostly comes from the irrigation system, chemical industry, agrochemicals, and pesticides in the environment. The plant root signifies the first barrier to the selective accumulation of ions and heavy metals present in the soil. Kinetic data, uptake for nutrient ions and chemically related nonnutrient analogs suggest that metabolic processes associated with root absorption of nutrients regulate both rate of absorption and the affinity of specific nonnutrient ions. Differnet detailed kinetic studies of Ni, Cd, and Tl uptake by intact plants demonstrate multiphasic root absorption processes over a wide range of concentration (Cataldo and Wildung, 1978). For example, wheat and some vegetables have been reported to bio-accumulate heavy metals more than WHO/FAO permissible level. In addition, excessive application of pesticides and herbicides in the agriculture for the protection of plants from diseases and high production is also a threat to humans (Bahadar et al., 2014). Some of the trace elements (phosphorus, nitrogen, potassium) are necessary for the plant growth, but with that plants also take noxious metals and metalloids. The metals concentrations are different among various plants species and body parts. A study conducted in the Hamadan Province, Iran proves that metals (copper, zinc, iron and magnesium) accumulation depends on different factors like metals concentration, pH, electrical conductivity, nutrients in the subsoil (substrata). The results showed that zinc and copper concentration in aboveground and underground tissues plants were significantly positive related to their total subsoil amount and soil phosphorus had negative affectson copper, iron and zinc

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CYP2D: Brain Enzyme Involved in Induction of Analgesia and Codeine Dependency

Kamal Niaz[1,2], Faheem Maqbool[1,2], Maryam Baeeri[2], Mohammad Abdollahi[1,2,*]

1 International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran;

2 Department of Toxicology and Pharmacology, Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.

***Corresponding author.** Tel: +98-21-66959104; E-mail: Mohammad@tums.ac.ir

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Commentary

Abstract

Smoking is predisposed by social, environmental and genetic factors including variation in CYP2A6, CYP2D and CYP2B6, which encode nicotine and codeine metabolizing enzymes. In early adolescence, CYP2A6-induced slow nicotine metabolism was related with higher dependence and reduced cigarette consumption. Our commentary has fully extended prior work illustrating that slow nicotine metabolism mediated by CYP2A6, CYP2D and possibly CYP2B6, risk for tobacco addiction during adolescence. Inherited differences in the rate of nicotine and codeine elimination may induce neural responses. Thus smoking signals during early self-discipline can provide an understanding of possible mechanism involved for differences in smoking behaviors and response to cessation treatment. The levels and tissue distribution of codeine, codeine-6-glucuronide (C6G), norcodeine, morphine and the morphine metabolites like morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G) are present in blood, liver and brain. CYP2D6 and CYP2D genotypes in brain have not just laid a passive target role with receptor for drugs, pollutants, pesticides but also acted as active metabolizers.

Keywords: Nicotine; Codeine addiction; Metabolites; CYP2D.

1. Introduction

Tobacco leaf contains various alkaloids and the most abundant one is codeine. Other alkaloids present in tobacco are nicotine, anabaseine, myosmine, β-nicotyrine, cotinine, 2,3-bipyridyl, anatabine, anabasine, nor-nicotine, heavy metals, *N*-methylanabasine, and nicotine *N*-oxide. According to data of IARC [1] and Counts et al. [2] that the nicotine concentration in the commercial available tobacco products ranges from 6 to 18 mg/g. This is too high concentration of nicotine in tobacco. In the tobacco, nicotine is found in three forms; non-protonated (free base), mono-protonated and di-protonated form.

It has been reported previously that almost, 90% of the chain-smokers start smoking in the teenage [3]. A significant ratio of 40-75% of smoking activities is affected by genetic transfer and social interaction [4,5]. Genetic alteration alters the metabolism leading to a subsequent clearance of nicotine. In addition, individuals with less smoking routine have slower rate of metabolism of blood and tissues as compared to chronic smokers. The primary metabolism of nicotine occur in the liver by CYP2A6 and converted into cotinine and then to 3-hydroxycotinine (3-HC) by the same enzyme. The formation of 3-HC and cotinine ratio provides a reliable and constant quantity for nicotine metabolism. As the normal nicotine metabolite ratio is 7-10 [6,7].

Traditionally, tobacco has been consumed as part of culture in some countries of the world. Betel quid, areca nuts, and slaked lime used in smokeless products and electronic smoking cigarette are the prominent products of nicotine and codeine source. Approximately, 10% of the nicotine to cotinine conversion occurs via a cytochrome P450 (CYP) enzyme [8]. In the adolescent chain smokers, CYP2B6*6 allele form was linked to minor self-discipline rates in the placebo arm of a bupropion smoking termination clinical trial; 15% of persons with one or two copies CYP2B6*6 accomplished self-discipline [9]. In another study, the CYP2B6*6 allele was additional common in nicotine dependent individuals associated with those that are not dependent [10]. Furthermore, CYP2B6*6 also affect the risk of inquisitive nicotine in teenagers, which increase codeine analgesia. The main aim of the present commentary is to highlight that cigarette smoking may lead to codeine addiction in brain, which also centrally activates codeine to morphine.

The studies of near past identified that codeine is only metabolized in the liver by enzyme CYP2B, but

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Molecular evidence on the protective effect of ellagic acid on phosalone-induced senescence in rat embryonic fibroblast cells

Maryam Baeeri [a], Saeideh Momtaz [a, b], Mona Navaei-Nigjeh [a, c], Kamal Niaz [a, d], Mahban Rahimifard [a], Seyedeh Farnaz Ghasemi-Niri [a], Nima Sanadgol [a, e], Mahshid Hodjat [a], Mohammad Sharifzadeh [a, f], Mohammad Abdollahi [a, d, f, *]

[a] Toxicology and Diseases Group, Pharmaceutical Sciences Research Group, Tehran University of Medical Sciences, Tehran, Iran
[b] Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran
[c] Department of Tissue Engineering, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran
[d] International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran
[e] Department of Biology, Faculty of Sciences, University of Zabol, Zabol, Iran
[f] Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Science, Tehran, Iran

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ABSTRACT

Salient evidence testifies the link between organophosphorus (OPs) exposure and the formation of free radical oxidants; and it is well accepted that free radicals are one of the basic concerns of senescence. To show the oxidative features of phosalone (PLN) as a key member of OPs, to induce senescence in rat embryonic fibroblast (REF) cells and to demonstrate the beneficial effects of the known antioxidant ellagic acid (EA) in diminishing the PLN-induced toxic effects, the levels of cell viability, oxidative stress markers, inflammatory cytokines, telomerase activity, and the expression of the genes related to senescence were investigated. Our results lend support to the hypothesis that PLN enhances the entire premature senescence parameters of REF cells. This accounts for the mechanistic approval of the role of OPs in induction of senescence in rat fibroblasts. Moreover, incorporation of EA diminished PLN toxicity mainly through suppression of p38 and p53 at gene and protein levels, and tempered the inflammation factors (TNF-α, IL-1β, IL-6 and NF-κB), which further affected cell division. Analysis of cell cycle showed that the percentage of G0/G1 arrest, in REF cells treated by EA was elevated as compared to control and PLN treated cells.

Abbreviations: ABC, avidin-biotin-peroxidase complex; ATM, ataxia-telangiectasia mutated; ATP, adenosine triphosphate; ATR, ATM- and Rad3-Related; BCA, bicinchoninic acid; CDKN1A, cyclin-dependent kinase inhibitor p21; Ct, cycle number; DCFH-DA, 2′,7′-dichlorofluorescin diacetate; DMEM, dulbecco's modified eagle's medium; DMSO, dimethyl sulfoxide; DNA, deoxyribonucleic acid; DNA-PK, DNA-dependent protein kinase; DTT, DL-dithiothreitol; EA, ellagic acid; EDTA, ethylene diamine tetra acetic acid; US EPA, United States Environment Protection Agency; FBS, fetal bovine serum; FDA, food and drug administration; FRAP, ferric reducing antioxidant power; GAPDH, glyceraldehyde 3-phosphate dehydrogenase; HCl, hydrochloric acid; HRP, horseradish peroxidase; IC50, inhibitory concentration; IL-1β, interleukine-1β; IL-6, interleukine-6; LD50, lethal dose; LPO, lipid peroxidation; MDA, malondialdehyde; MTT, 3-4,5 dimethylthiazol-2-yl-2,5-diphenyltetrazolium bromide; NF-κB, nuclear factor-kappa-B; OPs, organophosphorus; OSRDs, oxidative stress related diseases; PBS, phosphate-buffered saline; PI, propidium iodide; PLN, phosalone; p38, p38 mitogen activated protein kinases; PRAK, p38-regulated/activated protein kinase; PS, phosphatidylserine; PVDF, polyvinylidene fluoride; RB, retinoblastoma; REF, rat embryonic fibroblast; ROS, reactive oxygen species; RT-PCR, real time-reverse transcription polymerase chain reaction; SASPP, senescence-associated-secretoryphenotype proteins; SA-β-GAL, senescence associated β-galactosidase; SDS-PAGE, sodium dodecyl sulfate polyacrylamide gel electrophoresis; TAP, total antioxidant power; TBA, thiobarbituric acid; TBARS, thiobarbituric acid reactive substances; TBS, tris-buffered saline; TGF-β, transforming growth factor-beta; TMB, 3,3′,5,5′-tetramethylbenzidine; TNF-α, tumor necrosis factor-alpha; TP53, Tumor protein; TPTZ, tri (2-pyridyl)-s-triazine; TTM, total thiol molecules; TUMS, Tehran University of Medical Sciences; X-gal, 5-bromo-4-chloro-3-indolyl-β-d-galactopyranoside; WHO, word health organization.

* Corresponding author. Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.
E-mail addresses: Mohammad@TUMS.Ac.Ir, Mohammad.Abdollahi@UToronto.Ca (M. Abdollahi).

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Research Paper

Effect of styrene exposure on plasma parameters, molecular mechanisms and gene expression in rat model islet cells

Kamal Niaz[a,b,d], Fatima Ismail Hassan[a,b], Faheem Mabqool[a,b], Fazlullah Khan[a,b,d], Saeideh Momtaz[c,b], Maryam Baeeri[b], Mona Navaei-Nigjeh[b], Mahban Rahimifard[b], Mohammad Abdollahi[a,b,d,*]

[a] International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran
[b] Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran
[c] Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran
[d] Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Styrene is an aromatic hydrocarbon compound present in the environment and have primary exposure through plastic industry. The current study was designed to evaluate styrene-induced toxicity parameters in rat plasma fasting blood glucose (FBG) level, oral glucose tolerance, insulin secretion, oxidative stress, and inflammatory cytokines in cellular and molecular levels. Styrene was dissolved in corn oil and administered at different doses (250, 500, 1000, 1500, 2000 mg/kg/day and control) to each rat, for 42 days. In treated groups, styrene significantly increased fasting blood glucose, plasma insulin ($p < 0.001$) and glucose tolerance. Glucose tolerance, insulin resistance and hyperglycemia were found to be the main consequences correlating gene expression of islet cells. Styrene caused a significant enhancement of oxidative stress markers ($p < 0.001$) and inflammatory cytokines in a dose and concentration-dependent manner in plasma ($p < 0.001$). Moreover, the activities of caspase-3 and −9 of the islet cells were significantly up-regulated by this compound at 1500 and 2000 mg/kg/day styrene administrated groups ($p < 0.001$). The relative fold change of GLUD1 was downregulated ($p < 0.05$) and upregulated at 1500 and 2000 mg/kg, respectively ($p < 0.01$). The relative fold changes of GLUT2 were down regulated at 250 and 1000 mg/kg and up regulated in 500, 1500 and 2000 mg/kg doses of styrene ($p < 0.01$). The expression level of GCK indicated a significant upregulation at 250 mg/kg and downregulation of relative fold changes in the remaining doses of styrene, except for no change at 2000 mg/kg of styrene for GCK. Targeting genes (GLUD1, GLUT2 and GCK) of the pancreatic islet cells in styrene exposed groups, disrupted gluconeogenesis, glycogenolysis pathways and insulin secretory functions. The present study illustrated that fasting blood glucose, insulin pathway, oxidative balance, inflammatory cytokines, cell viability and responsible genes of glucose metabolism are susceptible to styrene, which consequently lead to other abnormalities in various organs.

1. Introduction

Styrene is one of the volatile aromatic organic compounds (VAOC), used as a solvent in many industrial settings, which is derived from benzene. This compound is the precursor of polystyrene and other copolymers. Styrene is produced in large quantity in the United States, while a small amount is naturally produced by bacteria, fungi, and plants (Braun-Lüllemann et al., 1997; Burback and Perry, 1993;

Abbreviations: FBG, fasting blood glucose; VAOC, volatile aromatic organic compound; ROS, reactive oxygen species; MCP-1, monocyte chemoattractant protein-1; IL-8, interleukin-8; NF-κB, nuclear factor-kappa-B; SO, styrene oxide; h, hours; MAPK, mitogen-activated protein kinase; ERKs-1/2, extracellular signal-regulated kinases-1/2; GSK-3, glycogen synthase kinases-3; MeHg, methyl mercury; NaCl, Sodium chloride; TPTZ, 2,4,6-tripyridyl-S-triazine; TBA, thiobarbituric acid; EDTA, ethylene diamine tetra acetic acid; IL-1β, interleukine-1β; ELISA, enzyme-linked immunosorbent assay; BSA, Bovine serum albumin; DCFH-DA, 2′,7′-Dichlorofluorescin diacetate; HEPES, 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; TUMS, Tehran University of Medical Sciences; OGTT, Oral glucose tolerance test; HOMA-IR, homeostasis assessment of insulin resistance; TBARS, thiobarbituric acid reactive substances; DCF-DA, 2′, 7′-dichlorofluorescin diacetate; TAP, total Antioxidant Power; TTM, total thiol molecules; PI, propidium iodide; RT-PCR, real time-reverse transcription polymerase chain reaction; GDH, glutamate dehydrogenase; GLUT2, glucose transporter-2; GCK, glucokinase; GAPDH, glyeraldehyde-3-dehydrogenase; GIT, gastrointestinal tract; IRS-1, insulin receptor substrate-1; NAC, N-acetyl cysteine

* Corresponding author at: Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.
E-mail addresses: mohammad@tums.ac.ir, mohammad.abdollahi@utoronto.ca (M. Abdollahi).

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Review article:

ENDO-CANNABINOIDS SYSTEM AND THE TOXICITY OF CANNABINOIDS WITH A BIOTECHNOLOGICAL APPROACH

Kamal Niaz[1,2,3], Fazlullah Khan[1,2,3], Faheem Maqbool[1,2], Saeideh Momtaz[4,3,2], Fatima Ismail Hassan[1,2,3], Navid Nobakht-Haghighi[2,5], Mahban Rahimifard[2], Mohammad Abdollahi[1,2,3*]

[1] International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran
[2] Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran
[3] Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[4] Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran
[5] Faculty of Pharmacy, Eastern Mediterranean University, Famagusta, North Cyprus Mersin 10, Turkey

***** Corresponding author: Mohammad Abdollahi, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran. Tel/Fax: +98-21-66959104; E-mail: mohammad.abdollahi@utoronto.ca or mohammad@tums.ac.ir

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ABSTRACT

Cannabinoids have shown diverse and critical effects on the body systems, which alter the physiological functions. Synthetic cannabinoids are comparatively innovative misuse drugs with respect to their nature of synthesis. Synthetic cannabinoids therapy in healthy, chain smokers, and alcoholic individuals cause damage to the immune and nervous system, eventually leading to intoxication throughout the body. Relevant studies were retrieved using major electronic databases such as PubMed, EMBASE, Medline, Scopus, and Google Scholar. The extensive use of *Cannabis Sativa* L. (*C. Sativa*) and its derivatives/analogues such as the nonpsychoactive dimethyl heptyl homolog (CBG-DMH), and tetrahydrocannabivarin (THCV) amongst juveniles and adults have been enhanced in recent years. Cannabinoids play a crucial role in the induction of respiratory, reproductive, immune and carcinogenic effects; however, potential data about mutagenic and developmental effects are still insufficient. The possible toxicity associated with the prolong use of cannabinoids acts as a tumor promoter in animal models and humans. Particular synthetic cannabinoids and analogues have low affinity for CB1 or CB2 receptors, while some synthetic members like Δ9-THC have high affinity towards these receptors. Cannabinoids and their derivatives have a direct or indirect association with acute and long-term toxicity. To reduce/attenuate cannabinoids toxicity, pharmaceutical biotechnology and cloning methods have opened a new window to develop cannabinoids encoding the gene tetrahydrocannabinolic acid (THCA) synthase. Plant revolution and regeneration hindered genetic engineering in *C. Sativa.* The genetic culture suspension of *C. Sativa* can be transmuted by the use of *Agrobacterium tumefaciens* to overcome its toxicity. The main aim of the present review was to collect evidence of the endo-cannabinoid system (ECS), cannabinoids toxicity, and the potential biotechnological approach of cannabinoids synthesis.

Keywords: synthetic cannabinoids, acute, chronic, toxicity, biotechnology

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RESEARCH ARTICLE

WILEY ENVIRONMENTAL TOXICOLOGY

Molecular mechanisms of action of styrene toxicity in blood plasma and liver

Kamal Niaz[1,2,3] | Faheem Mabqool[1,2,3] | Fazlullah Khan[1,2,3] | Fatima Ismail Hassan[1,2] | Maryam Baeeri[3] | Mona Navaei-Nigjeh[3] | Shokoufeh Hassani[3] | Mahdi Gholami[3] | Mohammad Abdollahi[1,2,3]

[1]International Campus—Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran

[2]Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran

[3]Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Correspondence
Mohammad Abdollahi, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.
Email: mohammad@tums.ac.ir
or
mohammad.abdollahi@utoronto.ca

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Abstract

Styrene is an aromatic colorless hydrocarbon available in liquid form and highly volatile. In its pure form, it gives a sweet smell. The primary source of exposure in the environment is from plastic materials, rubber industries, packaging materials, insulations, and fiber glass and carpet industry. Natural sources of styrene include: few metabolites in plants which are transferred through food chain. The current study was designed to evaluate styrene toxicity, including: superoxide dismutase (SOD) and protein carbonyl, oxidative stress, glucose-6-phosphatase (G6Pase), glycogen phosphorylase (GP), and phosphoenolpyruvate carboxykinase (PEPCK) activities, adenosine triphosphate (ATP) to adenosine diphosphate (ADP) ratio, and changes in gene expressions such as glutamate dehydrogenase 1 (GLUD1), glucose transporter 2 (GLUT2), and glucokinase (GCK) in the rat liver tissue. For this purpose, styrene was dissolved in corn oil and was administered via gavage, at doses 250, 500, 1000, 1500, 2000, mg/kg/day per mL and control (corn oil) to each rat with one day off in a week, for 42 days. Plasma SOD and protein carbonyl of plasma were significantly up-regulated in 1000, 1500, and 2000 mg/kg/day styrene administrated groups ($P < .001$). In addition, styrene caused an increase in lipid peroxidation (LPO) and reactive oxygen species (ROS) in the dose-dependent manners in liver tissue ($P < .001$). Furthermore, the ferrous reducing antioxidant power (FRAP) and total thiol molecules (TTM) in styrene-treated groups were significantly decreased in liver tissue ($P < .001$) with increasing doses. In treated rats, styrene significantly increased G6Pase activity ($P < .001$) and down-regulated GP activity ($P < .001$) as compared to the control group. The PEPCK activity was significantly raised in a dose-dependent manner ($P < .001$). The ATP/ADP ratio of live cells was significantly raised by increasing the dose ($P < .001$). There was significantly an up-regulation of GLUD1 and GCK at 2000 mg/kg group ($P < .01$) and a down-regulation for GLUT2 at the same dose. While in the rest of group, GLUT2 showed up-regulation of relative fold change. By targeting genes such as GLUD1, GLUT2, and GCK, disruption of hepatic gluconeogenesis, glycogenolysis, and insulin secretory functions are obvious. The present study illustrates that induction of oxidative stress followed by changes in G6Pase, GP, and PEPCK activities and the genes responsible for glucose metabolism are the mechanisms of styrene's action in the liver.

KEYWORDS

gene expression, gluconeogenesis, glucose, insulin, oxidative stress, styrene

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REVIEW

epiH
Epidemiology and Health

Smokeless tobacco (*paan* and *gutkha*) consumption, prevalence, and contribution to oral cancer

Kamal Niaz[1,2,3], Faheem Maqbool[1,2,3], Fazlullah Khan[1,2,3], Haji Bahadar[4], Fatima Ismail Hassan[1,2,3], Mohammad Abdollahi[1,2,3]

[1]*International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran;* [2]*Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran;* [3]*Toxicology and Diseases Group, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran;* [4]*Institute of Paramedical Sciences, Khyber Medical University, Peshawar, Pakistan*

Smokeless tobacco consumption, which is widespread throughout the world, leads to oral submucous fibrosis (OSMF), which is a long-lasting and devastating condition of the oral cavity with the potential for malignancy. In this review, we mainly focus on the consumption of smokeless tobacco, such as *paan* and *gutkha*, and the role of these substances in the induction of OSMF and ultimately oral cancer. The list of articles to be examined was established using citation discovery tools provided by PubMed, Scopus, and Google Scholar. The continuous chewing of *paan* and swallowing of *gutkha* trigger progressive fibrosis in submucosal tissue. Generally, OSMF occurs due to multiple risk factors, especially smokeless tobacco and its components, such as betel quid, areca nuts, and slaked lime, which are used in *paan* and *gutkha*. The incidence of oral cancer is higher in women than in men in South Asian countries. Human oral epithelium cells experience carcinogenic and genotoxic effects from the slaked lime present in the betel quid, with or without areca nut. Products such as 3-(methylnitrosamino)-proprionitrile, nitrosamines, and nicotine initiate the production of reactive oxygen species in smokeless tobacco, eventually leading to fibroblast, DNA, and RNA damage with carcinogenic effects in the mouth of tobacco consumers. The metabolic activation of nitrosamine in tobacco by cytochrome P450 enzymes may lead to the formation of N-nitrosonornicotine, a major carcinogen, and micronuclei, which are an indicator of genotoxicity. These effects lead to further DNA damage and, eventually, oral cancer.

KEY WORDS: Fibrosis, Oral cancer, Areca, Smokeless tobacco, Prevalence

INTRODUCTION

The term "smokeless tobacco" refers to the consumption of unburned tobacco, in the form of chewing, spitting, dipping, and snuff. Consumers chew the tobacco in the mouth and spit out the juice that builds up. Nicotine and other constituents are absorbed in the lining of oral cavity. People of many regions, including India, Pakistan, other Asian countries, and North America, have a long history of smokeless tobacco use. Approximately 28 chemical constituents present in smokeless tobacco are carcinogenic in nature, among which nitrosamine is the most prominent [1].

People mostly use *paan* and *gutkha* due to a lack of awareness and education. They are not aware of the harmful effects associated with the use of these substances, and it has been reported that these products are consumed for perceived beneficial effects, such as mouth freshening, aid in digestion, germ-killing, astringency, mood enhancement, tension relief, and oral cleaning [1]. *Gutkha* is sweet in taste, and children consider it to be a form of candy. Many people believe that *gutkha* is a mouth freshener, but its pleasant taste and sweetness aggregate microbes, causing damage to teeth. The use of *paan* and *gutkha* is difficult to control in most countries where it is widespread, and their extensive use leads to oral cancer [2]. The consumption of smokeless tobacco and areca nut is high in South Asian countries in the form of *paan*. In various South Asian languages, *paan* simply means "leaf." Various in-

Correspondence: Mohammad Abdollahi
Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran
E-mail: mohammad@tums.ac.ir

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5- Fatima Ismail Hassan

First Name	Last Name	Program	Level	School
Fatima	Ismail Hassan	Pharmacology and Toxicology	PhD	Pharmaceutical Sciences Research Center

Published Articles:

	Title of the Article
1	Congenital Abnormalities: Consequence of Maternal Zika Virus Infection: A Narrative Review

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Infectious Disorders - Drug Targets, **2017,** *17,* **1-11**

REVIEW ARTICLE

Congenital Abnormalities: Consequence of Maternal Zika Virus Infection: A Narrative Review

Fatima Ismail Hassan[a,b], Kamal Niaz[a,b], Faheem Maqbool[a,b], Fazlullah Khan[a,b] and Mohammad Abdollahi[a,b,c,*]

[a]*Department of Toxicology and Pharmacology, Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran;* [b]*International Campus, Tehran University of Medical Sciences, Tehran, Iran;* [c]*Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran*

Mohammad Abdollahi

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Abstract: ***Background*:** Zika virus (ZIKV) is a deadly flavivirus that has spread from Africa to Asia and European countries. The virus is associated with other viruses in the same genus or family, transmitted by the same mosquito species with known history of fatality. A sudden increase in the rate of infection from ZIKV has made it a global health concern, which necessitates close symptom monitoring, enhancing treatment options, and vaccine production.

***Objectives*:** This paper reviewed current reports on birth defects associated with ZIKV, mode of transmission, body fluids containing the virus, diagnosis, possible preventive measures or treatments, and vaccine development.

***Methods*:** Google scholar was used as the major search engine for research and review articles, up to July, 2016. Search terms such as "ZIKV", "ZIKV infection", "ZIKV serotypes", "treatment of ZIKV infection", "co-infection with zika virus", "flavivirus", "microcephaly and zika", "birth defects and Zika", as well as "ZIKV vaccine" were used.

***Results*:** ZIKV has been detected in several body fluids such as saliva, semen, blood, and amniotic fluid. This reveals the possibility of sexual and mother to child transmission. The ability of the virus to cross the placental barrier and the blood brain barrier (BBB) has been associated with birth defects such as microcephaly, ocular defects, and Guillian Barre syndrome (GBS). Preventive measures can reduce the spread and risk of the infection. Available treatments only target symptoms while vaccines are still under development.

***Conclusion*:** Birth defects are associated with ZIKV infection in pregnant women; hence the need for development of standard treatments, employment of strict preventive measures and development of effective vaccines.

Keywords: Birth defects, infection, microcephaly, review, vaccine, ZIKV.

*Address correspondence to this author at the Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran;
Tel/Fax: +98-21-66959104; E-mails: Mohammad.Abdollahi@UToronto.Ca, and Mohammad@TUMS.Ac.Ir

6- Bilqees Sameem

First Name	Last Name	Program	Level	School
Bilqees	Sameem	Pharmacology	PhD	Pharmaceutical Sciences Research Center

Published Articles:

	Title of the Article
1	A review on tacrine-based scaffolds as multi-target drugs (MTDLs) for Alzheimer's disease

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Review article

A review on tacrine-based scaffolds as multi-target drugs (MTDLs) for Alzheimer's disease

Bilqees Sameem [a], Mina Saeedi [b, c, *], Mohammad Mahdavi [d], Abbas Shafiee [e]

[a] School of Pharmacy, International Campus (TUMS-IC), Tehran University of Medical Sciences, Tehran, Iran
[b] Medicinal Plants Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[c] Persian Medicine and Pharmacy Research Center, Tehran University of Medical Sciences, Tehran, Iran
[d] Drug Design and Development Research Center, Tehran University of Medical Sciences, Tehran, Iran
[e] Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Alzheimer's disease (AD) is a multifactorial neurological disorder among elderly people and combinatorial factors such as genetic, lifestyle, and environmental are involved in onset and disease progression. It has been demonstrated that loss of cholinergic transmission is one of the most significant causes of AD. One strategy currently being investigated for the development of new therapeutics relates to the enhancement of cholinergic system through several ways. At this juncture, anticholinesterase inhibitors have absorbed lots of attention and different marketed drugs such as donepezil, rivastigmine, tacrine, and galantamine have been developed. 9-Amino-1,2,3,4-tetrahydroacridine known as tacrine was introduced in 1945 as an efficient anticholinesterase agent. The mechanism of action of tacrine was proved to inhibit the metabolism of acetylcholine and therefore extending its activity and raising levels in the cerebral cortex. However, extensive use of tacrine was limited since it showed various side effects and toxicity. Thus, lots of efforts were carried out to prepare tacrine analogues to overcome the related adverse effects. This review describes differently synthesized tacrine-based scaffolds as cholinesterase inhibitors to manage Alzheimer's disease (AD).

Contents

* Corresponding author. Medicinal Plants Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
E-mail addresses: m-saeedi@sina.tums.ac.ir (M. Saeedi), shafieea@tums.ac.ir (A. Shafiee).

Chapter Four

School of Medicine

1- Hamid Reza Fami-Tafreshi

First Name	Last Name	Program	Level	School
Hamid Reza	Fami-Tafreshi	Physiology	PhD	Medicine

Published Articles:

	Title of the Article
1	Improve in Neurogenesis with Socialization can Reduce Behaviors that are Related to Poor Prognosis in Withdrawal Period in Male Rats
2	Social isolation is associated with reduced neurogenesis, impaired spatial working memory performance, and altered anxiety levels in male rats
3	Long-term morphine addiction reduces neurogenesis and memory performance and alters emotional reactivity and anxiety levels in male rats

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Research Article

Improve in Neurogenesis with Socialization can Reduce Behaviors that are Related to Poor Prognosis in Withdrawal Period in Male Rats

Famitafreshi H[1], Karimian M[2*], Hassanzadeh G[3] and Fatima S[1]

Abstract

Introduction: Morphine withdrawal period is associated with a wide variety of problems. Neurogenesis seems necessary for brain functions. Socialization is a lifelong process that helps getting behavioural norms from society. The aim of this study is to investigate if better neurogenesis in socialization can alleviate problems encountered during withdrawal period.

Method and material: Rats were randomly divided to: control rats, isolated rats, withdrawal isolated rats and withdrawal socialized rats. Animals received morphine 7 days and 14 days Brdu was injected. At the end of experiment, memory, neurogenesis, emotional reactivity and sucrose, NaCl consumption was assessed.

Results: Rats in withdrawal socialized group had better reference memory and working memory, and they decrease relapse. Furthermore, neurogenesis was higher in withdrawal socialized rats as compared to isolated rats. Enough neurogenesis is necessary for proper brain function. Sucrose preference test and force swim test were well performed in withdrawal socialized rats. These indicate lower incidence of co morbid psychiatric disorder in withdrawal period. Salt consumption as indicator of more relapse to drug abuse was seen to be higher in withdrawal isolated group of animals.

Conclusion: Socialization during withdrawal period can help to better tolerate withdrawal period and its adverse effects. So socialization reduces relapse and establishes behavioural norms for successful healthy life.

Keywords

Neurogenesis; Sucrose; Salt; Withdrawal; Isolation; Socialization; Emotional reactivity; Memory

Introduction

Substance abuse is a complex and devastating disorder accompanied by many adverse effects. Addiction cannot be always managed successfully which results in enormous financial and social burden. Relapse to substance abuse is often attributed to mesolimbic dopamine system whose efferent and afferent connections are the neural substrate for the rewarding effects of drugs of abuse [1]. Studies using brain imaging have shown that neuronal activity in the orbit frontal cortex, a brain area thought to promote the ability to control behavior, is disturbed in drug addicts [2].

Drug abuse adversely affects brain function and disturbed brain in return contributes to development of drug abuse sides-effects. These sides effect vary in degree of severity and personal traits [3]. After drug abuse there is a period of psychiatric co morbid. Theses co morbid can contribute to relapse to drug of abuse. Treatment of this co morbid can reduce relapse to drug abuse [4]. Of this co morbid conditions are depression and personality changes [4]. So by promoting these behavioral changes to proper traits we can reduce relapse to drug of abuse. Delineating brain mechanism for curing of this co morbid can help establishing good treatment. It should be noted that assessment of above signs is not issue of this study and in previous studies it has been studied by various dosages including our dosages [5].

Previous studies has shown that environmental enrichment (EE) can affect the process of brain diseases and processes such as depression, Alzheimer, drug addiction, learning neurogenesis and emotions. During EE, a large group of rats are put together in larger cage than the standard cage and are given toys and equipment, enabling more social contact, and providing a greater surface area per rat, and a more stimulating environment [6]. In other extreme is social isolation with many adverse effects on many brain and behavioral processes such as learning, memory and dopamine metabolism in nucleus accumbens [7]. Also in one study social isolation has increased vulnerability to addiction [8]. In the middle of this extreme is socialization that is describing in animal studies two rats putting together in one cage [9]. Socialization is a lifelong process that helps to be fit in society and adjust behavioral norms for living. Without socialization it seems co morbid pschychiatric symptoms develop. Managing people in withdrawal period is important because by timely intervention for co morbid conditions that increase risk of relapse, relapse to drugs decreases. These co morbid conditions are depression and emotional disturbances.

Neurogenesis in some regions of brain like dentate gyrus of hippocampus and sub ventricular zone [10] has been linked to learning and memory and preventing psychiatric disease [11]. Increase in neurogenesis can improve symptoms of brain diseases such as depression [12]. So because neurogenesis better in social state, withdrawal severity can be reduced in social state, because it improves brain functions such as memory [13]. Considering that neurogenesis can positively affect brain functions like cognition, successful withdrawal can be linked to improved rate of neurogenesis. In addition, subject's emotional state may also influence cognitive functions [14].

Some studies have proposed that disturbance in taste sensations can be associated with addiction and its relapse [15]. It has been recently documented that common genes mediate addiction and taste [16]. Thus, altered taste sensations may increase individual's susceptibility towards drug abuse and can predict likelihood of drug relapse.

***Corresponding author:** Morteza Karimian, Professor of Physiology, Tehran University of Medical Sciences, Tehran, Iran, Tel: +98 216405 3269; E-mail: karimian@tums.ac.ir

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Author Affiliations

Top

[1]*Department of Physiology, International campus, Tehran University of Medical Sciences, Tehran, Iran*
[2]*Professor of Physiology, Tehran University of Medical Sciences, Tehran, Iran*
[3]*Anatomy Department, Tehran University of Medical Sciences, Tehran, Iran*

Open Access Animal Physiology

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ORIGINAL RESEARCH

Social isolation is associated with reduced neurogenesis, impaired spatial working memory performance, and altered anxiety levels in male rats

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Hamidreza Famitafreshi[1]
Morteza Karimian[2]
Hamed Fanaei[3]
Fatemeh Attari[4]
Sulail Fatima[1]

[1]Department of Physiology, International Campus, [2]Department of Physiology, Tehran University of Medical Sciences, Tehran, [3]Department of Physiology, Zahedan University of Medical Sciences, Zahedan, [4]Department of Neuroscience, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

Correspondence: Morteza Karimian
Department of Physiology, Tehran University of Medical Sciences, Enghelab Street, Poorsina Avenue, Tehran 14399-55991, Iran
Tel +98 21 6641 9484
Fax +98 21 6641 9484
Email karimian@tums.ac.ir

Background: Social isolation has some adverse behavioral effects. It has been shown that neurogenesis is essential for improvement of behavioral function. The aim of this study was to examine the effects of social isolation on neurogenesis, brain-derived neutrotrophic factor levels, learning abilities, and anxiety levels in rats.

Methods: Twenty male Sprague-Dawley rats were randomly divided into two groups, ie, an isolated group and a socialized group. After a 7-day adaption period, the animals received intraperitoneal bromodeoxyuridine (BrdU) 50 mg/kg for 14 days. Two types of memories were examined: spatial working memory using the Morris water maze and short-term memory using the Y-maze. Anxiety levels were examined using the elevated plus maze. Neurogenesis was assessed by immunostaining brain sections with anti-BrdU antibody.

Results: Neurogenesis was significantly reduced in the isolated group (10 cells/400×) as compared with the socialized group (232 cells/400×). Memory performance was markedly reduced in isolated animals than in socialized animals (working memory 50.87 seconds vs 31.71 seconds; reference memory 55.44 seconds vs 39.73 seconds; and in probe trials 24.72 seconds vs 18.11 seconds). Y-maze performance remained unchanged between the two groups (71.41 seconds vs 64.97 seconds). Anxiety levels were reduced in isolated animals, as indicated by more time spent in the open arms (73 seconds vs 11 seconds) and a higher number of entries into the open arms (4.1 vs 1.4) of the elevated maze. BDNF levels decreased significantly more in the isolated group than in the socialized group (467±37.69 vs 370.7±12.19, P=0.0311).

Conclusion: These results show that social isolation has adverse effects on the hippocampus and learning abilities, and may make one more susceptible to brain diseases like depression and Alzheimer's disease.

Keywords: adaptation, learning, anxiety, susceptible, BDNF, memory, neurogenesis

Introduction

Social isolation refers to a complete absence of or insufficient contact with other members of society. It is not the same as loneliness, which is rooted in a temporary lack of contact with other humans. Social isolation has two components, ie, mental and physical.[1] Evidence that social isolation might be related to fundamental aspects of cognition comes from animal studies showing that isolation may impair learning and alter anxiety levels,[1] latent inhibition,[2] social behavior,[3] performance on the forced swim test,[4] and reversal learning.[5]

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ORIGINAL RESEARCH

Long-term morphine addiction reduces neurogenesis and memory performance and alters emotional reactivity and anxiety levels in male rats

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Hamidreza Famitafreshi
Morteza Karimian
Narges Marefati

Department of Physiology, Tehran University of Medical Sciences-International Campus, Tehran, Iran

Introduction: Substance abuse is a behavioral disorder associated with a wide variety of devastating effects. Neurogenesis in dentate gyrus of hippocampus is essential for brain functions like memory formation. Therefore, this may play an important role in achieving successful withdrawal.

Methods and materials: Twenty Sprague-Dawley rats were randomly divided into two experimental groups: control and addiction. To induce morphine dependence, animals received morphine (0.75 mg/rat) for 21 days. The performance of animals in Morris water maze and elevated plus maze tests was evaluated after day 20. At the end of the study, the rats were decapitated, and their brains were sectioned to study neurogenesis by counting BrdU-positive cells.

Results: Hippocampal neurogenesis was significantly reduced in rats in the addicted group. Also, reference and working memory performance were impaired in animals in the addicted group. A decrease in emotional reactivity and anxiety was observed in animals in the addicted group when compared with that in the control group.

Conclusion: Addiction adversely affects brain functions and neurogenesis; thus treatment to increase neurogenesis is the better option for the persons with substance abuse.

Keywords: hippocampal neurogenesis, morphine addiction, striatum, morphine-induced, hippocampus, substance abuse

Introduction

Neurogenesis is a process that occurs in some parts of brain like dentate gyrus of hippocampus and subventricular zone of lateral ventricles.[1] Adequate neurogenesis is essential for brain functions, but it may be influenced by many pathological conditions like Alzheimer, depression, and addiction.[2–4] Drug addiction, a compulsive urge to take drugs like cocaine, heroin, and alcohol, can adversely affect mesolimbic system.[5] Mesolimbic system is the most known region of brain that is responsible for side effects of drugs.[6] It is important to study adult hippocampal neurogenesis because cognitive functions are an important part of brain function and healthy life.[7–10] Also, hippocampus, as part of the limbic system, may be necessary for tolerance of drugs and reduction of relapse. However, mechanisms involving addiction-induced side effects are not elucidated to date. Previous studies have shown that cocaine has adverse effect on neurogenesis; however, the effect of long-term use of other substances such as morphine has not been studied. The aim of this research is to study the effect of long-term morphine addiction on neurogenesis and brain functions like memory, emotional reactivity, and anxiety levels to delineate the behaviors that help addiction

Correspondence: Morteza Karimian
Department of Physiology, Tehran University of Medical Sciences, Tehran, Amir Abad, Keshavarz Boulevard, Tehran 1417653761, Iran
Tel/Fax +98 21 6641 9484
Email karimian@tums.ac.ir

2- Imran Khan

First Name	Last Name	Program	Level	School
Imran	Khan	Pharmacology	PhD	School of Medicine

Published Articles:

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2	Anti-pruritic activity of pioglitazone on serotonin-induced scratching in mice: Possible involvement of PPAR-gamma receptor and nitric oxide
3	Proconvulsant effect of post-weaning social isolation stress may be associated with dysregulation of opioid system in the male mice
4	The involvement of NMDA receptor/NO/cGMP pathway in the antidepressant like effects of baclofen in mouse force swimming test
5	Involvement of Inflammatory Cytokines in Antiarrhythmic Effects of Clofibrate in Ouabain-Induced Arrhythmia in Isolated Rat Atria

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Involvement of the nitrergic system in the proconvulsant effect of social isolation stress in male mice

Shayan Amiri [a,b,1], Armin Shirzadian [a,b,1], Arya Haj-Mirzaian [a,b], Muhammad Imran-Khan [c], Maryam Rahimi Balaei [d], Nastaran Kordjazy [a,b], Ahmad Reza Dehpour [a,b], Shahram Ejtemaei Mehr [a,b,*]

[a] Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, P.O. Box 13145-784, Tehran, Iran
[c] International Campus, Tehran University of Medical Sciences, Tehran, Iran
[d] Department of Human Anatomy and Cell Science, College of Medicine, Faculty of Health Science, University of Manitoba, Winnipeg, MB, Canada

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ABSTRACT

Social isolation stress (SIS) in adolescence is accompanied by neurobehavioral disturbances and pathophysiological changes in certain regions of the CNS such as the hippocampus. In this study, we tested whether SIS impacts seizure susceptibility in postnatal male mice due to a role of hippocampal nitric oxide (NO). To do this, we used the pentylenetetrazole (PTZ) model of clonic seizures, open-field test, hole-board test, forced swimming test, and plasma corticosterone assay. We aimed to evaluate if 4 weeks of SIS is capable of decreasing seizure threshold along with altering affective and neuroendocrine responses in isolated conditioned (IC) animals in comparison with socially conditioned (SC) animals. In addition, we applied subeffective doses of NO precursor L-arginine (25, 50, and 100 mg/kg) and NOS inhibitors 7-NI (15 and 40 mg/kg), aminoguanidine (50 and 100 mg/kg), and L-NAME (10 and 15 mg/kg) to both IC and SC groups prior to the determination of seizure threshold. Injection of a single dose of all mentioned drugs did not induce changes in seizure threshold of SC mice. On the other hand, L-NAME and 7-NI, but not aminoguanidine, modulated the proconvulsant effect of SIS, while L-arginine augmented the latter effect. We also measured the hippocampal nitrite levels after the administration of the aforementioned drugs. Social isolation stress increased the nitrite levels in comparison with those in SC mice, whereas 7-NI and L-NAME, unlike aminoguanidine, mitigated the effect of SIS. Additionally, L-arginine boosted the effects of SIS on nitrite production. In summary, we showed that SIS enhanced seizure susceptibility in the PTZ model of clonic seizures through the activation of the nitrergic system in the hippocampus. Also, we proved that nNOS, but not iNOS, accounts for these changes following SIS.

1. Introduction

People with epilepsy (PWE) experience greater psychosocial challenges compared with the general population, thereby contributing to poor quality of life [1]. Among psychosocial problems, stress and social isolation have been reported as the most determinant factors which affect the severity of epilepsy and social functioning of PWE, respectively [2,3]. Previous studies have reported that social isolation stress (SIS) in the adolescent period induces considerable psychobiological abnormalities, neurobehavioral disturbances, and hypothalamic–pituitary–adrenocortical (HPA) axis malfunction [4,5]. In addition, the social isolation paradigm has been suggested as a reliable animal model for the investigation of neurobehavioral changes in psychiatric disorders similarly seen in humans [6]. Under chronic stress circumstances, the neurotoxic action of excitatory neurotransmitters such as glutamate causes an overproduction of nitric oxide (NO) via the excessive activity of nitric oxide synthase (NOS) [7,8].

Nitric oxide contributes to a variety of physiological and pathophysiological processes in the hippocampus (HIPP), such as learning, memory, depression, and seizure susceptibility [9–13]. Among NOS isoforms, both iNOS (inducible NOS) and nNOS (neuronal NOS) have been reported to increase the NO levels in the HIPP in response to stressful paradigms [14,15]. In addition, early stressful life events have negative enduring effects on the HIPP which are relevant to increased susceptibility to seizures in adulthood [16]. Recently, it has been demonstrated that endogenous NO is a key factor for initiation of seizure-like events [17]. In another study, Watanabe et al. showed that elevated NO levels in the murine brain are associated with increased seizure susceptibility in the pentylenetetrazole (PTZ) model of convulsive seizures. They also showed that PTZ-induced convulsive seizure is sensitive to small changes of NO levels in the brain; therefore, it is a valid animal model for the evaluation of epileptic activity [13,18]. Surprisingly, there are few studies about the effects of social isolation,

* Corresponding author at: Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, P.O. Box 13145-784, Tehran, Iran.
E-mail addresses: ejtemam@gmail.com, ejtemam@tums.ac.ir (S.E. Mehr).
[1] Please note that the first two authors are considered as the first author.

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Behavioural pharmacology

Anti-pruritic activity of pioglitazone on serotonin-induced scratching in mice: Possible involvement of PPAR-gamma receptor and nitric oxide

Milad shafizadeh [a,b], Armin Rajaba [a,b], Muhammad Imran khan [a,c], Sattar Ostadhadi [a,b], Hosein Rastegar [d], Ahmadreza Dehpour [a,b,*]

[a] Experimental Medicine Research Center, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Pharmacology, School of Medicine, International campus, Tehran University of Medical Sciences, Tehran, Iran
[d] Food and Drug Research Center, Ministry of Health and Medical Education,Tehran, Iran

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ABSTRACT

Pioglitazone is a member of peroxisome proliferator-activated receptor gamma (PPARγ) agonists, particularly used in management of type II diabetes. However it also has effects in some dermatological disorders. The current study was designed to investigate the effects of oral administration of pioglitazone and the association of nitric oxide, in serotonin-induced scratching in mice. In order to produce the scratching activity, serotonin (141 nm/site) was administered intradermally in the nape of the neck. Pioglitazone in concentrations of 10, 20, 40 and 80 mg/kg, was peroral administered (p.o) as a single dose, 4 h before the serotonin injection. PPAR-γ antagonist, GW9662 (2 mg/kg, i.p); a non-specific nitric oxide synthase (NOS) inhibitor, NG-nitro-L-arginine methyl ester (L-NAME; 1 mg/kg, i.p); or a nitric oxide precursor, L-arginine (100 mg/kg, i.p.); adminstrated 15 min before pioglitazone were analyzed for anti-scratching activity. Results obtained showed that pioglitazone (40 and 80 mg/kg, p.o) reduced the scratching in a dose-dependent manner. GW9662 inverted the anti-scratching effect of pioglitazone (80 mg/kg). Acute dose of L-NAME (1 mg/kg, i.p) also prevented the anti-scratching property of pioglitazone (80 mg/kg, p.o); although L-arginine was used in sub-effective dose (100 mg/kg, i.p), however it potentiated the anti-scratching behavior when co-injected with pioglitazone (20 mg/kg, p.o). The results indicate that acute pioglitazone has an anti-scratching effect on serotonin-induced scratching in mice. It is concluded that anti-scratching outcome of acute pioglitazone is initiated via activation of PPAR-γ receptor and to some extent by the NO pathway.

1. Introduction

Pruritus (itch) is an unpleasant cutaneous sensation usually coupled by instant craving to scratch. It may be either due to primary skin diseases, or a dermatological manifestation of some underlying systemic disease (Stander et al., 2007). Pruritus may also be observed during inflammatory process, metabolic diseases, malignancies, infectious process, psychiatric disorders, drug use and stress (Steinhoff et al., 2006).

Peroxisome proliferator activated receptors (PPARs) are the ligand-stimulated transcription factors which have been classified as α, δ/ β and γ (Berger and Moller, 2002; Chinetti et al., 2000). Following activation, PPARs regulate widespread biological processes, many of which are crucial for the skin e.g. lipid storage and lipocyte differentiation (Boyd, 2007; Friedmann et al., 2005).

However some prior studies have shown that Thiazolidinediones (TZDs) as a potent exogenous PPARγ agonists (Bell-Parikh et al., 2003; Berger et al., 2005) with these own constellation of pharmacological properties are effective in patients with dermatological disorders such as; lipodystrophy, melanoma, necrobiosis lipoidica, hirsutism, angiosarcoma and other soft-tissue sarcomas (Boyd, 2007). Various clinical studies reported the beneficial effects of PPAR-γ agonists on pruritus in a variety of dermatological disorders (Ellis et al., 2000; Pershadsingh et al., 1998; Sepmeyer et al., 2007). But due to lack of strong experimental evidence, further investigation is needed to elucidate the role of PPAR-γ agonists in pruritus.

* Correspondence to: Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, P.O. Box 13145-784, Tehran, Iran.
Tel.: +98 21 88973652; fax: +98 21 66402569.
E-mail address: dehpoura@sina.tums.ac.ir (A. Dehpour).

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Proconvulsant effect of post-weaning social isolation stress may be associated with dysregulation of opioid system in the male mice

Muhammad Imran Khan [a,b], Armin Shirzadian [a,b], Arya Haj-Mirzaian [a,b], Shahram Ejtemaei Mehr [a,b], Ahmad Reza Dehpour [a,b], Maryam Rahimi-Balaei [c,*], Shayan Amiri [a,b,*]

[a] Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Pharmacology, School of Medicine, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Human Anatomy and Cell Science, College of Medicine, Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada

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ABSTRACT

Opioid system has been reported to be involved in the consequences of post-weaning social isolation stress (SIS) such as hypoalgesia and social behaviors. Also, previous studies have shown that SIS increases mu opioid receptor expression in the regions of the brain associated with epileptogenesis such as basolateral amygdala and cortex. Interestingly, experiencing SIS increases seizure risk in the adulthood. Regarding the SIS-induced alterations in the opioid system, we hypothesize that increase in opioidergic system activity (mostly by mu receptor) may be associated with increase in vulnerability to seizures. In non-stressed mice, morphine at low doses (1 mg/kg) has an anticonvulsant effect on seizure threshold while higher doses (60 mg/kg) are proconvulsant. To support the hypothesis, we showed that administration of anticonvulsant dose of morphine (1 mg/kg) to socially isolated male mice not only was not able to reverse the negative effect of SIS on seizure susceptibility to pentylenetetrazole but also enhanced it. These results support our hypothesis that proconvulsant effect of post-weaning social isolation stress may be associated with dysregulation of opioid system in the adult male mice.

Introduction

Post-weaning social isolation stress and seizure risk

Loneliness or perceived social isolation (SI), a painful social condition, contributes to fatigue, depression and predisposes individuals to various diseases [1,2]. The adolescence period of life is most sensitive state to the adverse effects of loneliness [3]. Many animal studies have been focused in the adolescence stage to find out the underlying pathophysiological mechanisms of SI. In the animal studies, maladaptive neurobehavioral changes as well as development of psychopathological abnormalities has pervasive outcomes of experiencing the SI in the adolescence [4,5]. There are evidences reported that SI increases the seizure risk in both humans and rodents. Studies on people with epilepsy showed that SI not only decrease the quality of their lives but also exacerbates the seizures [6]. Moreover, Matsumoto et al. reported that applying 7 weeks of SI to adolescent mice alters GABAergic system which leads to a decrease in seizure threshold in adult subjects [7]. In this context, it is believed that SI is able to antagonize the effects of $GABA_A$ receptor agonist [8] and enhance the proconvulsant effect of picrotoxin [7].

Opioid system and seizure modulation

Opioid agonists and their receptors are diversely expressed with varying degree in different parts of central and peripheral nervous systems as well as in endocrine tissues and their target sites. In this regard, opioid system plays a role in modulation of a variety of functions like social behaviors, pain, addiction, neurotransmission, and seizure susceptibility [9,10]. It is well documented that opioids like morphine, have both anticonvulsant and proconvulsant effects in different experimental models of seizure [11,12]. The dual effect of morphine is linked to its dose. Various studies have reported that acute administration of morphine (0.5, 1, and 3 mg/kg) exert anticonvulsant effect in various paradigms of seizure models [11,13]. Also in our lab we showed that low dose of agmatine has synergistic anticonvulsant effect with morphine

* Corresponding authors at: Department of Human Anatomy and Cell Science, College of Medicine, Faculty of Health Sciences, University of Manitoba, Winnipeg, P.O. Box: R3E0J9, Manitoba, Canada. Tel./fax: +1 2048012181 (M. Rahimi-Balaei). Experimental Medicine Research Center, Tehran University of Medical Sciences, P.O. Box: 13145-784, Tehran, Iran. Tel.: +98 9196822007; fax: +98 2166402569 (S. Amiri).

E-mail addresses: rahimibm@myumanitoba.ca (M. Rahimi-Balaei), sh-amiri@farabi.tums.ac.ir (S. Amiri).

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Research paper

The involvement of NMDA receptor/NO/cGMP pathway in the antidepressant like effects of baclofen in mouse force swimming test

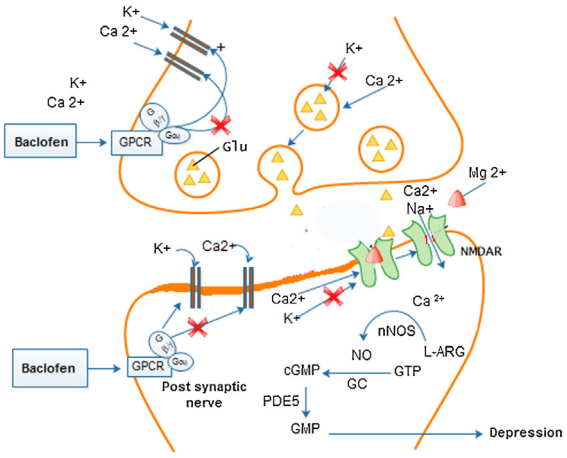
Muhammad Imran Khan[a,b,e,1], Sattar Ostadhadi[b,c,1], Samira Zolfaghari[d], Shahram Ejtemaei Mehr[a,b], Gholamreza Hassanzadeh[e], Ahmad-Reza Dehpour[a,b,c,*]

[a] Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Pharmacology, School of Medicine, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[c] Brain and Spinal Injury Repair Research Center, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran
[d] Department of Tissue Engineering and Applied Cell Sciences Iran University of Medical Sciences, Iran
[e] Department of Neuroscience, School of Advanced Technologies in Medicine, International Campus, Tehran University of Medical Science, Iran

HIGHLIGHTS

- Baclofen has an anti-depressant like effect in forced swimming test.
- This effect increased by inhibition of nitric oxide production.
- This effect increased by NMDA receptor antagonist.
- This effect decreased by PDE5 inhibition.
- The antidepressant-like action of baclofen mediated by NMDA receptors and NO-GMP pathway in forced swimming test

GRAPHICAL ABSTRACT



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ABSTRACT

In the current study, the involvement of *N*-methyl-D-aspartate receptor (NMDAR) and nitric oxide (NO)/cyclic guanosine monophosphate (cGMP) system in the antidepressant-like effects of baclofen was evaluated by using animal model in forced swimming test. Followed by an open field test for the evaluation of locomotor activity, the immobility time for mice in force swimming test was recorded. Only the last four min was analyzed. Administration of Baclofen (0.5 and 1 mg/kg, i.p.) reduced the immobility interval in the FST. Prior administration of L-arginine (750 mg/kg, i.p.,) a nitric oxide synthase substrate or sildenafil (5 mg/kg, i.p.) a phosphodiesterase 5 into mice suppressed the antidepressant-like activity of baclofen (1 mg/kg, i.p.).Co-treatment of 7-nitroindazole (50 mg/kg, i.p.,) an inhibitor of neuronal nitric oxide synthase, L-NAME (10 mg/kg, i.p.,) a non-specific inhibitor of nitric oxide synthase or MK-801 (0.05 mg/kg, i.p.) an NMDA receptor antagonist with subeffective dose of baclofen (0.1 mg/kg, i.p.), reduced the immobility time in the FST as compared to the drugs when used alone. Co-administrated of lower doses of MK-801 (0.01 mg/kg) or L-NAME (1 mg/kg) failed to effect immobility time however,

* Corresponding author at: Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, PO Box 13145-784, Tehran, Iran. Fax: +98 21 6640 2569.
E-mail address: Dehpour@sina.tums.ac.ir (A.-R. Dehpour).
[1] Please note that the first two authors are considered as the first author.

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Research Article

Involvement of Inflammatory Cytokines in Antiarrhythmic Effects of Clofibrate in Ouabain-Induced Arrhythmia in Isolated Rat Atria

Somayeh Moradi,[1] Vahid Nikoui,[2,3] Muhammad Imran Khan,[4] Shayan Amiri,[1,5] Farahnaz Jazaeri,[1] and Azam Bakhtiarian[1,5]

[1]*Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*
[2]*Razi Institute for Drug Research, Iran University of Medical Sciences, Tehran, Iran*
[3]*Department of Pharmacology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran*
[4]*Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, International Campus, Tehran, Iran*
[5]*Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran*

Correspondence should be addressed to Azam Bakhtiarian; bakhtiar@tums.ac.ir

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Considering the cardioprotective and anti-inflammatory properties of clofibrate, the aim of the present experiment was to investigate the involvement of local and systemic inflammatory cytokines in possible antiarrhythmic effects of clofibrate in ouabain-induced arrhythmia in rats. Rats were orally treated with clofibrate (300 mg/kg), and ouabain (0.56 mg/kg) was administered to animals intraperitoneally. After induction of anesthesia, the atria were isolated and the onset of arrhythmia and asystole was recorded. The levels of inflammatory cytokines in atria were also measured. Clofibrate significantly postponed the onset of arrhythmia and asystole when compared to control group ($P \leq 0.05$ and $P \leq 0.01$, resp.). While ouabain significantly increased the atrial beating rate in control group ($P \leq 0.05$), same treatment did not show similar effect in clofibrate-treated group ($P > 0.05$). Injection of ouabain significantly increased the atrial and systemic levels of all studied inflammatory cytokines ($P \leq 0.05$). Pretreatment with clofibrate could attenuate the ouabain-induced elevation of IL-6 and TNF-α in atria ($P \leq 0.01$ and $P \leq 0.05$, resp.), as well as ouabain-induced increase in IL-6 in plasma ($P \leq 0.05$). Based on our findings, clofibrate may possess antiarrhythmic properties through mitigating the local and systemic inflammatory factors including IL-6 and TNF-α.

1. Background

The fibrate class of hypolipidemic drugs is used extensively in treatment of metabolic syndrome in which hyperlipidemia and hypertension are most prominent manifestations of this disorder. Fibrates are ligands of the peroxisome proliferator-activated receptors (PPARs) [1, 2]. These receptors are ligand-dependent transcription factors and belong to the nuclear steroid/thyroid/retinoic acid receptor superfamily [3, 4]. PPARs consisted of three isotypes including α, β, and γ. PPAR-α possesses an important role in lipid metabolism [5]. PPAR-α is predominantly expressed in tissues with high fatty acid oxidation rate including heart, liver, and kidney [6]. It has been shown that fibrates protect heart against experimental ischemia/reperfusion injury in animals through PPARs [7, 8]. Interestingly, previous studies have shown that cardioprotective effects of fibrates are not observed in PPAR-α knockout mice, indicating that PPAR-α plays a critical role in cardioprotective effects of fibrates [7, 8]. Since majority of hyperlipidemic patients are suffering from comorbid cardiovascular diseases, it is clear that many of the cardiovascular patients use clofibrate. It has been demonstrated that PPAR-α agonists have anti-inflammatory properties [9–12], and inflammatory cytokines have been reported to be involved in atrial and ventricular arrhythmias [13–15]. Therefore, the aim of present study was to investigate

3- Leili Beytollahi

First Name	Last Name	Program	Level	School
Leili	Beytollahi	Bacteriology	PhD	School of Medicine

Published Articles:

	Title of the Article
1	Antimicrobial activity of photodynamic therapy in combination with colistin against a pan-drug resistant Acinetobacter baumannii isolated from burn patient
2	The efficacy of photodynamic and photothermal therapy on biofilm formation of Streptococcus mutans: An in vitro study

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Antimicrobial activity of photodynamic therapy in combination with colistin against a pan-drug resistant *Acinetobacter baumannii* isolated from burn patient

Ebrahim Boluki[a], Hossein Kazemian[b], Hadi Peeridogaheh[c], Mohammad Yousef Alikhani[d], Sima Shahabi[e], Leili Beytollahi[f], Roghayeh Ghorbanzadeh[g,*]

[a] Private practice, and Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Microbiology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
[d] Department of Microbiology, Medical School, Hamadan University of Medical Sciences, Hamadan, Iran
[e] Research Center for Science and Technology in Medicine, Tehran University of Medical Sciences, Tehran, Iran
[f] Department of Microbiology, school of Medicine, International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran
[g] Private practice, Tehran, Iran

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ABSTRACT

Nosocomially-acquired multi-, extensively-, and pandrug resistant (MDR, XDR, and PDR) strains of microorganisms such as *Acinetobacter baumannii* remain a serious cause of infection and septic mortality in burn patients. Treatment of patients with nosocomial burn wound infections is often complicated by drug-resistant strains of *A. baumannii*. Today, many researchers are focusing on the investigation of novel non-antibiotic strategies such as photodynamic therapy (PDT). We report a new PDT strategy that suppresses colistin resistance in PDR *A. baumannii* by interfering with the expression of a pmrA/pmrB two-component system. In the current study, *A. baumannii* with a PDR feature isolated from a burn patient was used as a test strain. PDT was carried out using toluidine blue O (TBO) and light-emitting diode (LED) as a photosensitizer and radiation source, respectively. The antimicrobial susceptibility profiles were assessed for cells surviving PDT. The effects of sub-lethal PDT (sPDT) on the expression of the pmrA/pmrB two-component signal transduction system were evaluated by real-time quantitative reverse transcription PCR. Results of drug susceptibly testing (DST) in LED and TBO groups separately showed that the bacteria were resistant to all tested antibiotics, while the DST result of the LED + TBO group showed highly declining bacterial growth when compared with the control group. Reduction in the expression of *pmrA* and *pmrB* was observed in the treated strains after sPDT. This represents the first conclusive example of a direct role for the PDT in breaking antibiotic resistance by directly modulating two-component system activity.

1. Introduction

Burn wounds are commonly infected with bacterial pathogens and have a high risk of infection by nosocomially-acquired multidrug-resistant (MDR) bacteria. These patients are also immunosuppressed, which makes them susceptible to many infection agents [1]. In deep partial-thickness and full-thickness burns, removing devitalized tissue, early excision, grafting, and topical antimicrobial therapy is the current standard of care and the primary method for reducing infection risk and length of hospital stay [2,3]. Insufficient initial antimicrobial therapy to treat burn wound infections results in higher mortality rates [2]. If a Gram-negative MDR pathogen is isolated from burn wound infections, colistin should be considered [2,3]. However, not only does colistin have a narrow therapeutic window, but worldwide reports indicate that the extensive use of colistin as a last resort to control gram-negative MDR pathogen infections has led to a worrying growing trend of colistin resistance among this bacteria [4]. This presents serious challenges to clinicians facing lack of affordable and effective treat-

* Corresponding author.
E-mail addresses: e.boluki@outlook.com (E. Boluki), Hosayn.kazemian@yahoo.com (H. Kazemian), h.piridogahe@gmail.com (H. Peeridogaheh), y.alikhani.phd@gmail.com (M.Y. Alikhani), s.shahabi.1973@gmail.com (S. Shahabi), shapee32@yahoo.com (L. Beytollahi), r.gdent81@gmail.com (R. Ghorbanzadeh).

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The efficacy of photodynamic and photothermal therapy on biofilm formation of *Streptococcus mutans*: An in vitro study

Leili Beytollahi[a,1], Maryam Pourhajibagher[b,1], Nasim Chiniforush[c], Roghayeh Ghorbanzadeh[d], Reza Raoofian[e,f], Babak Pourakbari[g], Abbas Bahador (Ph.D.)[a,b,c,h,*]

[a] Department of Microbiology, School of Medicine, International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran
[b] Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[c] Laser Research Center, Dentistry Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[d] Private Practice, Tehran, Iran
[e] Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran
[f] Innovative Research Center, Islamic Azad University, Mashhad Branch, Mashhad, Iran
[g] Pediatrics Infectious Disease Research Center, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[h] Dental Research Center, Dentistry Research Institute, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Background: The alternative antibacterial treatments of photodynamic therapy (PDT) and photothermal therapy (PTT) significantly affect microbiota inactivation. The aim of the present research was the assessment of the antimicrobial and anti-biofilm effects of PDT with toluidine blue O (TBO) and PTT with indocyanine green (ICG) on *Streptococcus mutans* as a cariogenic bacterium.
Materials and methods: The *S. mutans* ATCC 35668 strain was treated with final concentrations of 0.1 mg/mL TBO and 1 mg/mL ICG with energy densities of 17.18 and 15.62 J/cm^2, respectively. Cell viability was evaluated after culturing and anti-biofilm potential was analyzed using crystal violet assay and scanning electron microscopy.
Results: The number of *S. mutans* colony forming unit (CFU)/mL was significantly lower in the groups submitted to PDT (12.5–100 μg/mL TBO) and PTT (62.5–1000 μg/mL) compared to the control (untreated group). 0.1 mg/mL TBO-PDT and 1 mg/mL ICG-PTT showed stronger inhibitory effects on biofilm formation in *S. mutans* than other concentration levels, with a reduction of 63.87% and 67.3%, respectively.
Conclusion: Photo-elimination by high concentrations of TBO-PDT and ICG-PTT exhibited significantly stronger inhibitory effects on biofilm formation and cell viability in *S. mutans*.

1. Introduction

Dental caries occur as the result of a shift in a complex host-bacterial community interaction that leads to the formation of plaque biofilm on the human tooth surface [1]. Acidogenic communities and acid tolerant species are responsible for the development of caries [2].

Streptococcus mutans as a cariogenic bacterium was found to be the dominant species in many, but not in all, subjects with dental caries [3,4]. *S. mutans* can degrade the carbohydrates with the formation of abundant acid, and tolerate low pH environments [5].

Anti-caries procedures can be performed using antiseptic agents and mechanical and chemical disruption of oral microbial biofilm, such as by tooth brushing [6,7]. However, the use of these methods is limited by mechanical damage to the oral mucosa, the disruption of normal bacterial flora, the emergence of drug-resistant strains of microorganisms, and failure to maintain a certain concentration of antimicrobial compounds in the oral cavity [6–8].

Alternative techniques, such as photodynamic therapy (PDT) and photothermal therapy (PTT) can be used to remove biofilm from a tooth surface, considering the limitations of traditional treatments [9,10]. A combination of an appropriate photosensitizer (PS)

* Corresponding author at: Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Keshavarz Blvd, 100 Poursina Ave., Tehran, Iran.
E-mail addresses: abahador@sina.tums.ac.ir, ab.bahador@gmail.com (A. Bahador).
[1] [a]Equal contribution.

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4- Mohammed Elshiekh

First Name	Last Name	Program	Level	School
Mohammed	Elshiekh	Physiology	Ph.D	School of Medicine

Published Articles:

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1	Up-regulation of nitric oxide synthases by erythropoietin alone and in conjunction with ischemic preconditioning in ischemia reperfusion injury of rat kidneys
2	Ameliorative Effect of Recombinant Human Erythropoietin and Ischemic Preconditioning on Renal Ischemia Reperfusion Injury in Rats

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Up-regulation of nitric oxide synthases by erythropoietin alone and in conjunction with ischemic preconditioning in ischemia reperfusion injury of rat kidneys

Mohammed Elshiekh[1], Mehri Kadkhodaee[2], Behjat Seifi[2], Mina Ranjbaran[2] and Hassan Askari[2]

[1] *Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, International campus, Tehran, Iran*

[2] *Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

Abstract. The effects of erythropoietin (EPO) alone or in conjunction with ischemic preconditioning (IPC) on nitric oxide synthase as well as comparing their effects on oxidative stress and proinflammatory cytokines are studied. Rats underwent bilateral renal ischemia of 50 min followed by 24 h reperfusion. They were administered EPO (5000 iu/kg i.p.) and/or subjected to IPC and sacrificed after 24 h, then plasma and tissue samples were obtained. Treatment of either EPO or IPC and their combination attenuates oxidative stress, decreases histological damages, inhibits proinflammatory response, and up-regulates iNOS and eNOS gene expression compared to IR group. In addition, EPO+IPC and EPO treatment produced significant up-regulation in iNOS gene expression compared to IPC group. In IPC and EPO+IPC groups, more powerful effect on up-regulation of eNOS gene expression was shown compared to EPO group. Our findings suggest that treatment with EPO or IPC and their combination improve renal function and preserves tubular damage induced by IR injury. These advantageous effects were closely related to reducing oxidative stress, suppressing proinflammatory response and enhancing generation of NO. IPC was more powerful in enhancement of eNOS gene expression compared to EPO that was more effective in increasing of iNOS gene expression.

Key words: Ischemia reperfusion — Oxidative stress — Proinflammatory response — iNOS — eNOS

Introduction

Renal ischemia-reperfusion (IR) injury, an inflammatory pathophysiological process, leads to acute kidney failure, delayed graft function, and early mortality in patients subjected to kidney transplantation (Kosieradzki and Rowinski 2008). Several factors have crucial roles in the pathophysiology of IR injury, such as vascular endothelium, leukocytes, reactive oxygen species and adhesion molecules as well as inflammatory mediators (Elahi et al. 2009). Overproduction of ROS results in an increase in lipid peroxidation (MDA) by devastated unsaturated fatty acids in the cell membrane producing a decrease in endogenous antioxidants enzymes such as SOD (Wang et al. 2013).

Correspondence to: Mehri Kadkhodaee, Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran 1417613151, Iran
E-mail: kadkhodm@tums.ac.ir

Nitric oxide (NO) as a biological mediator plays an important role in a variety of biological processes and is a fundamental component in the fields of biochemistry, physiology, immunology and neuroscience (Omer et al. 2012). NO is known as an essential mediator of physiological and pathological processes of renal IR injury (Lopez-Marti et al. 2003). NO is produced from L-arginine by the enzyme nitric oxide synthase (NOS), which exists in three forms. Two are constitutive, neuronal nitric oxide synthase (nNOS, also known as NOS I) and endothelial nitric oxide synthase (eNOS, also known as NOS III) and one is inducible (iNOS, also known as NOS II, Ignarro 2000). Recent studies suggest the presence of a potentially new isoform of NOS in mitochondria (mtNOS) which was characterized as a constitutive NOS isoform (Giulivi et al. 1998; Ghafourifar et al. 1999). NO regulates neutrophil recruitment by suppressing the expression of adhesion molecules in the vascular endothelium producing increased blood flow to ischemic regions (Laroux et al. 2001).

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Ameliorative Effect of Recombinant Human Erythropoietin and Ischemic Preconditioning on Renal Ischemia Reperfusion Injury in Rats

Mohammed Elshiekh,[1] Mehri Kadkhodaee,[2,*] Behjat Seifi,[2] Mina Ranjbaran,[2] and Parisa Ahghari[3]

[1]Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, International campus, Tehran, IR Iran
[2]Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, IR Iran
[3]Department of Physiology, Faculty of Medicine, Hamedan University of Medical Sciences, Hamedan, IR Iran

*Corresponding author: Mehri Kadkhodaee, Department of Physiology, School of Medicine, Tehran University of Medical Sciences, P. O. Box: 1417613151, Tehran, IR Iran. Tel: +98-2188259862, Fax: +98-2166419484, E-mail: kadkhodm@tums.ac.ir

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Abstract

Background: Ischemia-reperfusion (IR) injury is one of the most common causes of renal dysfunction. There is increasing evidence about the role of the reactive oxygen species (ROS) in these injuries and endogenous antioxidants seem to have an important role in decreasing the renal tissue injury.

Objectives: The aim of this study was to compare the effect of recombinant human erythropoietin (EPO) and ischemic preconditioning (IPC) on renal IR injury.

Materials and Methods: Twenty four male Wistar rats were allocated into four experimental groups: sham-operated, IR, EPO + IR, and IPC + IR. Rats were underwent 50 minutes bilateral ischemia followed by 24 hours reperfusion. Erythropoietin (5000 IU/kg, i.p) was administered 30 minutes before onset of ischemia. Ischemic preconditioning was performed by three cycles of 3 minutes ischemia followed by 3 minutes reperfusion. Plasma concentrations of urea and creatinine were measured. Kidney samples were taken for reactive oxidative species (ROS) measurement including superoxide dismutase (SOD) activity, glutathione (GSH) contents, and malondialdehyde (MDA) levels.

Results: Compared to the sham group, IR led to renal dysfunction as evidenced by significantly higher plasma urea and creatinine. Treatment with EPO or IPC decreased urea, creatinine, and renal MDA levels and increased SOD activity and GSH contents in the kidney.

Conclusions: Pretreatment with EPO and application of IPC significantly ameliorated the renal injury induced by bilateral renal IR. However, both treatments attenuated renal dysfunction and oxidative stress in kidney tissues. There were no significant differences between pretreatment with EPO or application of IPC.

Keywords: Erythropoietin, Ischemia-Reperfusion Injury, Ischemic Preconditioning, Oxidative Stress, Renal Ischemia Reperfusion Injury

1. Background

Renal ischemia-reperfusion (IR) injury is major cause of acute kidney injury, a common clinical problem associated with an increasing prevalence and high mortality rate (1). The severity of the injury depends on the duration of ischemia and subsequent reperfusion phase. Reperfusion causes damage through generation of reactive oxygen species and inflammation rather than restoration of normal function (2). Therefore, the need for additional therapeutic modalities to prevent renal IR injury is quite urgent.

Erythropoietin is a glycoprotein hormone that was originally identified as the humoral factor, which control production of erythroid precursor cells. However, many evidence suggests that EPO has several functions independent of its effects on red blood cells production. Recently, studies in vitro and vivo have shown that EPO attenuates cell damage (3). The proper effects of the EPO-related changes are not fully clearly, even though it has anti-apoptotic, antioxidative and anti-inflammatory properties. Its pro-angiogenic potential seems to be related to EPO-mediated protective effect.

Ischemic preconditioning (IPC), defined as brief sublethal periods of ischemia followed by reperfusion before master ischemia, is a way to minimize subsequent events of IR injury (4, 5). Researches show that IPC regimen can protect the target organs or distant parts of organs and tissues (6, 7). This phenomenon has been demonstrated firstly in myocardium (8). Protective effects of IPC on IR injury have been frequently demonstrated in other organs such as skeletal muscle (9).

Antioxidants have been presented to be protective against IR interposed oxidative damage in different ani-

5- Seifu Feyisa

First Name	Last Name	Program	Level	School
Seifu	Feyisa	Bacteriology	PhD	School of Medicine

Published Articles:

	Title of the Article
1	Evaluation of efflux pump gene expression among drug susceptible and drug resistant strains of Mycobacterium tuberculosis from Iran
2	Molecular characterization of Mycobacterium tuberculosis isolates from Tehran, Iran by restriction fragment length polymorphism analysis and spoligotyping

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Short communication

Evaluation of efflux pump gene expression among drug susceptible and drug resistant strains of *Mycobacterium tuberculosis* from Iran

Jalil Kardan Yamchi [a], Mehri Haeili [b], Seifu Gizaw Feyisa [c], Hossein Kazemian [a], Abdolrazagh Hashemi Shahraki [d], Fatemeh Zahednamazi [a], Abbas Ali Imani Fooladi [e], Mohammad Mehdi Feizabadi [a,*]

[a] Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran
[c] Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran
[d] Department of Epidemiology, Pasteur Institute of Iran, Tehran, Iran
[e] Applied Microbiology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

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ABSTRACT

Absence of mutations within the genes encoding drug targets in some phenotypically drug resistant strains of *Mycobacterium tuberculosis* suggests possible involvement of alternative mechanisms such as over-expression of efflux pumps. We investigated the expression level of *Rv1410c*, *Rv2459*, *Rv1218c* and *Rv1273c* efflux pumps gene by real-time quantitative reverse transcription PCR (qRT-PCR) in 31 clinical isolates of *M. tuberculosis*. Susceptibility to first-line drugs was performed using the proportion method. Twenty one isolates were characterized with drug resistance (DR), and among them 12 showed a significantly elevated level of expression (>4 fold) for at least one of the studied genes encoding for efflux pumps. Point mutations in the *katG* (codons 315 or 335) and *rpoB* (codons 456 and 441) genes were found in 42.85% and 66.6% of drug resistant isolates, respectively. Only one isolate showed mutation at position −15 of the *inhA* promoter region. Among the 7 isolates (33.33%) which had no mutation in the studied regions of drug target genes, 5 isolates showed over-expression for efflux pumps. Our results demonstrated that over-expression of efflux pumps can contribute to drug resistance in *M. tuberculosis*.

Emergence and distribution of drug resistant strains of *Mycobacterium tuberculosis* (MTB) pose a major threat for tuberculosis (TB) control programs. Occurrence of mutations in some drug target genes is considered as the main cause of multi-drug resistant tuberculosis (MDR-TB) development (Rodrigues et al., 2012). The lack of mutations in resistance conferring genes in some clinical isolates of MTB, raises the hypothesis of other drug resistance mechanisms such as efflux pumps (Nikaido, 2001). In this study, we aimed to investigate the expression of four putative efflux pump genes among drug susceptible (DS), MDR and extensively drug resistant (XDR) *M. tuberculosis* clinical isolates from Iran, the setting where the first totally drug resistant (TDR) strains of *M. tuberculosis* were identified for the first time (Velayati et al., 2009). It is important to note that, TDR-TB is not recognized by WHO and these cases are defined as strains which are resistant to a wider range of drugs compared to XDR isolates. The selected genes coding for putative efflux pumps were *Rv1218c* (tetronasin-transport ATP-binding protein ABC transporter), *Rv1273c* (drugs-transport transmembrane ATP-binding protein), *Rv1410c* (aminoglycosides/tetracycline transport integral membrane protein) and *Rv2459* (conserved integral membrane transport protein) (Lew et al., 2011). Proteins encoded by *Rv1218c* and *Rv1273c* were classified as belonging to the ATP-binding transport protein family (ABC transporters) and the two other efflux pumps are classified as belonging to the major facilitator super family (MFS). These efflux pumps were selected according to previous studies (Calgin et al., 2013; Gupta et al., 2010; Wang et al., 2013) and http://tuberculist.epfl.ch/.

A total of 31 *M. tuberculosis* clinical isolates obtained from TB patients in different provinces of Iran in 2013 were included in this study. Drug susceptibility testing against first-line drugs (rifampicin: 40 μg/mL, isoniazid: 0.2 μg/mL, streptomycin: 4.0 μg/mL and ethambutol: 2.0 μg/mL) was performed by the proportion method according to the WHO guidelines (WHO, 2008; WHO and IUATLD, 1998).

For each strain, total RNA extraction was carried out from a loopful of mycobacterial colonies developed on antibiotic free Lowenstein–Jensen (LJ) medium incubated at 37 °C for 3–4 weeks. Total RNA extraction was performed using GeneJET RNA Purification kit (Thermo, Dreieich, Germany) according to manufacturer instructions. After treatment of total RNA with DNAse I enzyme (Thermo), cDNA was synthesized by RevertAid First Strand cDNA Synthesis kit (Thermo) according to the manufacturer's protocol. Real time qRT-PCR was performed using SYBR Green Low ROX Master Mix (Amplicon, Brighton, UK) in a BIOER

* Corresponding author
E-mail address: mfeizabadi@tums.ac.ir (M.M. Feizabadi).

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Major Article

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Molecular characterization of *Mycobacterium tuberculosis* isolates from Tehran, Iran by restriction fragment length polymorphism analysis and spoligotyping

***Seifu Gizaw Feyisa*[1], *Mehri Haeili*[2], *Fatemeh Zahednamazi*[3], *Nader Mosavari*[4], *Mohammad Mohammad Taheri*[4], *Gholamreza Hamzehloo*[5], *Samin Zamani*[3] and *Mohammad Mehdi Feizabadi*[3]**

[1]. Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran. [2]. Department of Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran. [3]. Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. [4]. Department of Tuberculosis, Razi Vaccine & Serum Research Institute, Hessarak, Karaj, Iran. [5]. Regional TB reference laboratory, Tehran, Iran.

ABSTRACT

Introduction: Characterization of *Mycobacterium tuberculosis* (MTB) isolates by DNA fingerprinting has contributed to tuberculosis (TB) control. The aim of this study was to determine the genetic diversity of MTB isolates from Tehran province in Iran. **Methods**: MTB isolates from 60 Iranian and 10 Afghan TB patients were fingerprinted by standard IS*6110*-restriction fragment length polymorphism (RFLP) analysis and spoligotyping. **Results**: The copy number of IS*6110* ranged from 10-24 per isolate. The isolates were classified into 22 clusters showing ≥ 80% similarity by RFLP analysis. Fourteen multidrug-resistant (MDR) isolates were grouped into 4 IS*6110*-RFLP clusters, with 10 isolates [71% (95% CI: 45-89%)] in 1 cluster, suggesting a possible epidemiological linkage. Eighteen Iranian isolates showed ≥ 80% similarity with Afghan isolates. There were no strains with identical fingerprints Spoligotyping of 70 isolates produced 23 distinct patterns. Sixty (85.7%) isolates were grouped into 13 clusters, while the remaining 10 isolates (14.2%) were not clustered. Ural (formerly Haarlem4) (n = 22, 31.4%) was the most common family followed by Central Asian strain (CAS) (n = 18, 25.7%) and T (n = 9, 12.8%) families. Only 1strain was characterized as having the Beijing genotype. Among 60 Iranian and 10 Afghan MTB isolates, 25% (95% CI: 16–37) and 70% (95% CI: 39-89) were categorized as Ural lineage, respectively. **Conclusions**: A higher prevalence of Ural family MTB isolates among Afghan patients than among Iranian patients suggests the possible transmission of this lineage following the immigration of Afghans to Iran.

Keywords: *Mycobacterium tuberculosis*. IS*6110*-RFLP. Spoligotyping.

INTRODUCTION

Tuberculosis (TB) is a global health problem that infects millions of people worldwide each year. According to the 2014 World Health Organization (WHO) global TB report, in 2013 there were 9.0 million new TB cases, which resulted in 1.5 million deaths[1]. Despite a promising decline in the incidence rate of TB in Iran from 36 cases per 100,000 people in 1990 to 17 cases per 100,000 people in 2010[2], TB continues to be a major public health concern in Iran. Risk factors such as drug addiction, human immunodeficiency virus (HIV) infection, drug-resistant *Mycobacterium tuberculosis* (MTB) strains, population ageing[3], and sharing borders with 4 countries that have high rates of TB incidence, namely Afghanistan, Pakistan, Turkmenistan, and Iraq[4] [5],have contributed to a persistent problem of TB in Iran. According to a recent report, approximately 21 per 100,000 Iranians suffered from TB in 2013[6].

Tehran, the capital of Iran, is the 5th biggest city in the world. It has a population of more than 12 million people and an annual population growth rate of 1.44[7]. The population density (persons per km^2) and average number of people per household in Tehran are 890 and 3.3, respectively[7]. Over the years, Tehran has experienced inward migration of people from elsewhere in Iran and from neighboring countries. More than 450,000 Afghans currently live in Tehran[7]. Significant developments in deoxyribonucleic acid (DNA) technology and molecular biology methods in the 21st century have greatly assisted the rapid diagnosis, immediate initiation of therapy, and identificati n of the source of infection of TB, which are crucial for stopping its further transmission. DNA fingerprintin based on IS*6110* is an internationally standardized genotyping technique. IS*6110* restriction fragment length polymorphism (RFLP) analysis relies on the analysis of IS*6110* copy numbers and their locations within the genome of MTB. It is considered to be the most effective method for discriminating between MTB isolates among the molecular techniques that have been

***Corresponding author*:** Dr. Mohammad Mehdi Feizabadi.
e-mail: mfeizabadi@tums.ac.ir
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6- Sikiru Afolabi Adebileje

First Name	Last Name	Program	Level	School
Sikiru Afolabi	Adebileje	Medical Physics	Ph.D	School of Medicine

Published Articles:

	Title of the Article
1	Accurate classification of brain gliomas by discriminate dictionary learning based on projective dictionary pair learning of proton magnetic resonance spectra

Research article

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Accurate classification of brain gliomas by discriminate dictionary learning based on projective dictionary pair learning of proton magnetic resonance spectra

Sikiru Afolabi Adebileje,[a,b] Keyvan Ghasemi,[b,c] Hammed Tanimowo Aiyelabegan[d] and Hamidreza Saligheh Rad[a,b]*

ABSTRACT **Proton magnetic resonance spectroscopy is a powerful noninvasive technique that complements the structural images of cMRI, which aids biomedical and clinical researches, by identifying and visualizing the compositions of various metabolites within the tissues of interest. However, accurate classification of proton magnetic resonance spectroscopy is still a challenging issue in clinics due to low signal-to-noise ratio, overlapping peaks of metabolites, and the presence of background macromolecules. This paper evaluates the performance of a discriminate dictionary learning classifiers based on projective dictionary pair learning method for brain gliomas proton magnetic resonance spectroscopy spectra classification task, and the result were compared with the sub-dictionary learning methods. The proton magnetic resonance spectroscopy data contain a total of 150 spectra (74 healthy, 23 grade II, 23 grade III, and 30 grade IV) from two databases. The datasets from both databases were first coupled together, followed by column normalization. The Kennard–Stone algorithm was used to split the datasets into its training and test sets. Performance comparison based on the overall accuracy, sensitivity, specificity, and precision was conducted. Based on the overall accuracy of our classification scheme, the dictionary pair learning method was found to outperform the sub-dictionary learning methods 97.78% compared with 68.89%, respectively. Copyright © 2016 John Wiley & Sons, Ltd.**

Keywords: proton magnetic resonance spectroscopy; brain gliomas; dictionary pair learning; sub-dictionary learning

Introduction

Proton magnetic resonance spectroscopy (^{1}H-MRS) is a powerful noninvasive technique that complements the structural images of conventional magnetic resonance imaging (cMRI), which aids biomedical and clinical applications by identifying and visualizing the compositions of various metabolites within the tissues of interest (brain, heart, etc.).[1,2] An observed ^{1}H-MRS spectra of the brain are made up of complicated signals corresponding to several overlapping peaks of different metabolites, as well as baseline coming from various macromolecules and lipids coupled with noise and distortions;[1,3] an accurate classification of ^{1}H-MRS brain spectra signals is needed for efficient and effective diagnosis of diseases.

With a decision support system for classification,[4,5] the ^{1}H-MRS spectra , which are multivariate data, can achieve a higher reliability by developing a good statistical model to classify various tumorous ^{1}H-MRS data.[6,7] Several classification methods for ^{1}H-MRS data have been proposed,[8–11] but the sparse representation (SR) technique is a recent method for classification.[12–14]

Sparse representation is a parsimonious principle that shows the representation of a signal as a linear combination of basis vectors, which are chosen from a dictionary.[15,16] The SR method has been found to be robust to noise, while its basis vectors are non-orthogonal, which are sometimes found to be interpretable because of its sparseness property. The SR has achieved a remarkable success in various signal processing, image processing, and computer vision applications.[17–19]

Dictionary learning (DL), which is a subclass of SR, is obtained by finding a desired dictionary that can effectively represent the signal of interest.[20,21] Analysis and synthesis types of dictionaries have been widely studied in literatures and are found to play active roles in signal representation.[22] Synthesis-based SR method has been found to allow easy learning of a desired dictionary from a training set and can model complexity better of the local signal structures. However, the synthesis representation coefficient of signals is usually obtained via an lp-norm ($p < 1$) sparse coding process,

* *Correspondence to: Hamidreza Saligheh Rad, Department of Medical Physics and Biomedical Engineering, Faculty of Medicine, Sina Campus, PO Box 1417613151, Tehran University of Medical Sciences, Tehran, Iran. E-mail: h-salighehrad@tums.ac.ir*

a *Department of Medical Physics and Biomedical Engineering, Tehran University of Medical Sciences – International Campus (TUMS-IC), Tehran, Iran*

b *Quantitative MR Imaging and Spectroscopy Group (QMISG), Tehran, Iran*

c *Department of Chemistry, Imam Khomeini International University, Tehran, Iran*

d *Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences – International Campus, Tehran, Iran*

7- Amin Hasanvand

First Name	Last Name	Program	Level	School
Amin	Hasanvand	Pharmacology	PhD	Medicine

Published Articles:

	Title of the Article
1	Anti-inflammatory effect of AMPK signaling pathway in rat model of diabetic neuropathy

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Inflammopharmacology

ORIGINAL ARTICLE

Anti-inflammatory effect of AMPK signaling pathway in rat model of diabetic neuropathy

Amin Hasanvand[1,2] · Hossein Amini-khoei[3,4] · Mohammad-Reza Hadian[5] · Alireza Abdollahi[6] · Seyed Mohammad Tavangar[7] · Ahmad Reza Dehpour[2,4] · Elika Semiei[2] · Shahram Ejtemaei Mehr[1,2]

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Abstract Diabetic neuropathy (DN) is characterized as Hyperglycemia activates thdisturbed nerve conduction and progressive chronic pain. Inflammatory mediators, particularly cytokines, have a determinant role in the pathogenesis of neuropathic pain. The activity of adenosine monophosphate protein kinase (AMPK), an energy charge sensor with neuroprotective properties, is decreased in diabetes. It has been reported that activation of AMPK reduces the systemic inflammation through inhibition of cytokines. In this study, we aimed to investigate the probable protective effects of AMPK on DN in a rat of diabetes. DN was induced by injection of streptozotocin (65 mg/kg, i.p.). Motor nerve conduction velocities (MNCV) of the sciatic nerve, as an electrophysiological marker for peripheral nerve damage, were measured. Plasma levels of IL-6, TNF-α, CRP were assessed as relevant markers for inflammatory response. Also, the expression of phosphorylated AMPK (p-AMPK) and non-phosphorylated (non-p-AMPK) was evaluated by western blotting in the dorsal root ganglia. Histopathological assessment was performed to determine the extent of nerve damage in sciatic nerve. Our findings showed that activation of AMPK by metformin (300 mg/kg) significantly increased the MNCV and reduced the levels of inflammatory cytokines. In addition, we showed that administration of metformin increased the expression of p-AMPK as well as decline in the level of non p-AMPK. Our results demonstrated that co-administration of dorsomorphin with metformin reversed the beneficial effects of metformin. In conclusion, the results of this study demonstrated that the activation of AMPK signaling pathway in diabetic neuropathy might be associated with the anti-inflammatory response.

✉ Shahram Ejtemaei Mehr
ejtemam@gmail.com

1 Department of Pharmacology, School of Medicine, International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran

2 Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

3 Department of Pharmacology, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran

4 Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran

5 Department of Physical Therapy, Rehabilitation Faculty, Tehran University of Medical Sciences, Tehran, Iran

6 Department of Pathology, Imam Khomini Complex Hospital, Tehran University of Medical Sciences, Tehran, Iran

7 Department of Pathology, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

8- Amir Hossein Abdolghaffari

First Name	Last Name	Program	Level	School
Amir Hossein	Abdolghaffari	Pharmacology	PhD	Medicine

Published Articles:

	Title of the Article
1	Antioxidant therapy in acute, chronic and post-endoscopic retrograde cholangiopancreatography pancreatitis: An updated systematic review and meta-analysis
2	Molecular and biochemical evidences on the protective effects of triiodothyronine against phosphine-induced cardiac and mitochondrial toxicity

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Molecular and biochemical evidences on the protective effects of triiodothyronine against phosphine-induced cardiac and mitochondrial toxicity

Amir Hossein Abdolghaffari [a,b,c,d], Amir Baghaei [d], Reza Solgi [d], Maziar Gooshe [e,f], Maryam Baeeri [d], Mona Navaei-Nigjeh [d], Shokoufeh Hassani [d], Abbas Jafari [d], Seyed Mehdi Rezayat [c,g], Ahmad Reza Dehpour [c,e], Shahram Ejtemaei Mehr [c], Mohammad Abdollahi [d,h,i,*]

[a] Department of Pharmacology, School of Medicine, International Campus, Tehran University of Medical Sciences (TUMS-IC), 1417653861 Tehran, Iran
[b] Pharmacology and Applied Medicine, Department of Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, 141554364 Karaj, Iran
[c] Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, 1417614411 Tehran, Iran
[d] Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran
[e] Experimental Medicine Research Center, Tehran University of Medical Sciences, 1417614411 Tehran, Iran
[f] Students' Scientific Research Center (SSRC), Tehran University of Medical Sciences, 1417614411 Tehran, Iran
[g] Department of Pharmacology and Toxicology, Pharmaceutical Sciences Branch & Pharmaceutical Sciences Research Center, Islamic Azad University (IAUPS), 194193311 Tehran, Iran
[h] International Campus, Tehran University of Medical Sciences, Tehran 1417614411, Iran
[i] Endocrinology & Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Aim: Aluminum phosphide (AlP) is a widely used fumigant and rodenticide. While AlP ingestion leads to high mortality, its exact mechanism of action is unclear. There are ample evidences suggesting cardioprotective effects of triiodothyronine (T3). In this study, we aimed to examine the potential of T3 in the protection of a rat model of AlP induced cardiotoxicity.

Main methods: In order to induce AlP intoxication animals were intoxicated with AlP (12 mg/kg; LD50) by gavage. In treatment groups, T3 (1, 2 and 3 μg/kg) was administered intra-peritoneally 30 min after AlP administration. Animals were connected to the electronic cardiovascular monitoring device simultaneously after T3 administration. Then, electrocardiogram (ECG), blood pressure (BP), and heart rate (HR) were monitored for 180 min. Additionally, 24 h after AlP intoxication, rats were deceased and the hearts were dissected out for evaluation of oxidative stress, cardiac mitochondrial function (complexes I, II and IV), ATP/ADP ratio, caspases 3 & 9, and apoptosis by flow cytometry.

Key findings: The results demonstrated that AlP intoxication causes cardiac toxicity presenting with changes in ECG patterns such as decrement of HR, BP and abnormal QRS complexes, QTc and ST height. T3 at a dose of 3 μg/kg significantly improved ECG and also oxidative stress parameters. Furthermore, T3 administration could increase mitochondrial function and ATP levels within the cardiac cells. In addition, administration of T3 showed a reduction in apoptosis through diminishing the caspase activities and improving cell viability.

Significance: Overall, the present data demonstrate the beneficial effects of T3 in cardiotoxicity of AlP.

1. Introduction

Aluminum phosphide (AlP) is a commonly used insecticide, rodenticide and fumigant. Poisoning by deliberate self-ingestion of AlP is a common cause of death and socioeconomic loss worldwide, especially in developing countries [2,13,26]. AlP is sold as pallet, tablet, porous blister pack, sachets, and as dusts [43].

While the exact mechanism of AlP toxicity is still unclear, several studies suggest that phosphine gas (PH_3) is a key player in AlP toxicity. PH_3 is a highly reactive radical, which can freely diffuse into intracellular compartments. PH_3 is released from AlP upon contact with water, moisture or hydrochloric acid of the stomach [43]. There are ample evidences suggesting that PH_3 can initiate a nucleophilic attack and reduce vital enzymes [3].

AlP intoxication is mostly fatal by causing multiorgan damage through denaturation of cell membranes [53,56,57]. While AlP can cause a wide range of clinical manifestations, circulatory failure is the most common cause of mortality and morbidity in AlP ingested patients [5,60]. Ventricular arrhythmias or dysfunction is a primary outcome of

* Corresponding author at: Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran.
E-mail addresses: Mohammad@TUMS.Ac.Ir, Mohammad.Abdollahi@UToronto.Ca (M. Abdollahi).

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META-ANALYSIS

Antioxidant therapy in acute, chronic and post-endoscopic retrograde cholangiopancreatography pancreatitis: An updated systematic review and meta-analysis

Maziar Gooshe, Amir Hossein Abdolghaffari, Shekoufeh Nikfar, Parvin Mahdaviani, Mohammad Abdollahi

Maziar Gooshe, Amir Hossein Abdolghaffari, Mohammad Abdollahi, Department of Toxicology and Pharmacology, Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, and Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran 1417614411, Iran

Amir Hossein Abdolghaffari, Pharmacology and Applied Medicine, Department of Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj 31375369, Iran

Amir Hossein Abdolghaffari, International Campus, ICTUMS, Tehran University of Medical Sciences, Tehran 1417614411, Iran

Shekoufeh Nikfar, Department of Pharmacoeconomics and Pharmaceutical Administration, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran 1417614411, Iran

Parvin Mahdaviani, Department of Pharmaceutics, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran 1417614411, Iran

Author contributions: Gooshe M and Abdolghaffari AH contributed equally to this paper; Gooshe M reviewed data and drafted the manuscript; Abdolghaffari AH prepared the bibliography, collected data and edited the manuscript; Nikfar S conducted the meta-analysis, reviewed the data and the manuscript; Mahdaviani P prepared the bibliography, collected data and prepared the tables; and Abdollahi M conceived the study and edited the manuscript.

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Correspondence to: Mohammad Abdollahi, PhD, Professor, Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, and Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran 1417614411, Iran. mohammad@tums.ac.ir
Telephone: +98-21-64122319
Fax: +98-21-66959104

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Abstract

AIM: To investigate the efficacy and adverse effects of antioxidant therapy in acute pancreatitis (AP), chronic pancreatitis (CP) and post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP).

METHODS: PubMed, Scopus, Google Scholar, Cochrane library database, and Evidence-based medicine/clinical trials published before August 2014 were searched. Clinical and laboratory outcomes of randomized trials of antioxidant therapy in patients with AP, CP and PEP were included. The methodological quality of the trials was assessed by the Jadad score based on the description of randomization, blinding, and dropouts (withdrawals). The results of the studies were pooled and meta-analyzed to provide estimates of the efficacy of antioxidant therapy.

RESULTS: Thirty four trials out of 1069 potentially relevant studies with data for 4898 patients were

9- Samaneh Sadat Seyyedi

First Name	Last Name	Program	Level	School
Samaneh sadat	Seyyedi	Medical Genetics	PhD	Medicine

Published Articles:

	Title of the Article
1	Protein-Protein Interaction Network could reveal the relationship between the breast and colon cancer
2	Deregulation of miR-1, miR486, and let-7a in cytogenetically normal acute myeloid leukemia: association with NPM1 and FLT3 mutation and clinical characteristics

Gastroenterology and Hepatology From Bed to Bench.

ORIGINAL ARTICLE

Protein-Protein Interaction Network could reveal the relationship between the breast and colon cancer

Mona Zamanian-Azodi[1], Mostafa Rezaei-Tavirani[1], Sara Rahmati-Rad[2], Hadi Hasanzadeh[3], Majid Rezaei Tavirani[4], Samaneh Sadat Seyyedi[5]

[1]*Proteomics Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[2]*Department of Cell and Molecular Biology, Faculty of Science, University of Tehran, Tehran, Iran.*

[3]*Cancer Research Center, Department of Medical Physics, Semnan University of Medical Science, Semnan, Iran*

[4]*Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran*

[5]*Department of Medical Genetics, Tehran University of Medical Sciences, International Campus (TUMS- IC), Tehran, Iran*

ABSTRACT

Aim: This study is aimed to elicit the possible correlation between breast and colon cancer from molecular prospective by analyzing and comparing pathway-based biomarkers.

Background: Breast and colon cancer are known to be frequent causes of morbidity and mortality in men and women around the world. There is some evidence that while the incident of breast cancer in young women is high, it is reported lower in the aged women. In fact, aged women are more prone to colorectal cancer than older men. . In addition, many studies showed that several biomarkers are common among these malignancies.

Patients and methods: The genes were retrieved and compared from KEGG database and WikiPathway, and subsequently, protein-protein interaction (PPI) network was constructed and analyzed using Cytoscape v:3.2.1 software and related algorithms.

Results: More than forty common genes were identified among these malignancies; however, by pathways comparison, twenty genes are related to both breast and colon cancer. Centrality and cluster screening identified hub genes, including SMAD2, SMAD3, (SMAD4, MYC), JUN, BAD, TP53. These seven genes are enriched in regulation of transforming growth factor beta receptor signaling pathway, positive regulation of Rac protein signal transduction, positive regulation of mitochondrial outer membrane permeabilization involved in apoptotic signaling pathway, and positive regulation of mitotic metaphase/anaphase transition respectively.

Conclusion: As there are numerous genes frequent between colorectal cancer and breast cancer, there may be a common molecular origin for these malignancies occurrences. It seems that breast cancer in females interferes with the rate of colorectal cancer incidence.

Keywords: Colon cancer, Breast cancer, Protein-Protein Interaction Network, Gene ontology.

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Introduction

Colon cancer accounts for the second most widespread fatal malignancy and with 30% inheritance bases in the world (1, 2). It manifests in the lower section of digestive system known as large intestine (colon) (3). Regular treatment for colon cancer comprise of surgery, chemotherapy and radiotherapy (1). An accumulation of mutations in tumor suppressor genes and oncogenes is the cause of cancer progression, which is a multistep process. This development requires many genetic alterations. The inactivation

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Reprint or Correspondence: **Mostafa Rezaei–Tavirani,** Ph.D. Proteomics Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
E-mail: Tavirany@yahoo.com

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ORIGINAL ARTICLE

Deregulation of miR-1, miR486, and let-7a in cytogenetically normal acute myeloid leukemia: association with NPM1 and FLT3 mutation and clinical characteristics

Samaneh Sadat Seyyedi[1] · Masoud Soleimani[2] · Marjan Yaghmaie[3] · Monireh Ajami[2] · Mansoureh Ajami[2] · Shahram Pourbeyranvand[4] · Kamran Alimoghaddam[3] · Seyed Mohammad Akrami[5]

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Abstract Cytogenetically normal acute myeloid leukemia (CN-AML) constitutes the largest subgroup of AML patients that is associated with molecular alteration. MiRNAs have been shown to be aberrantly expressed in CN-AML. In addition, specific miRNA (miR) expression patterns were found to be associated with certain genetic alterations in these patients. This study investigated the expression level of miR-1, miR-486, and let-7a in 45 CN-AML patients well characterized for FLT3 and/or NPM1 mutations using real-time quantitative RT-PCR and evaluated the association between candidate miRs expression and clinical features. Our data revealed that miR-1 was significantly overexpressed in CN-AML patients, and increasing expression of miR-1 correlated with NPM1 mutation ($P<0.05$) and lower hemoglobin level was also observed in patients with miR-1 overexpression ($P<0.05$). The expression of miR-1 was much higher in AML-M2 compared with other subtypes. Further, we found significantly increasing miR-486 expression in 40 of 45 (89 %) CN-AML patients. There was no significant association of upregulation of miR-486 with clinical parameters. The expression level of miR-486 was increased in AML-M2 subtype. The levels of let-7a were significantly increased in CN-AML patients compared to the healthy control and significantly higher in the NPM1±CN-AML patients. There was no correlation detected between the level of let-7a and FLT3+. An increasing expression level of let-7a was demonstrated in M2 subtype. In addition, our data showed no significant association between increasing let-7a and clinical characteristic. Comparison of peripheral blood and bone marrow results in 30 CN-AML patients showed that there is a considerable concordance between PB and BM in the results of candidate miR levels ($P<0.001$). In conclusion, further studies should also be performed to detect functional mechanism of these miRs.

Keywords Cytogenetically normal AML · miR-1 · miR-486 · let-7a

✉ Seyed Mohammad Akrami
akramism@tums.ac.ir

[1] Department of Medical Genetics, Tehran University of Medical Sciences, International Campus (TUMS—IC), Tehran, Iran

[2] Department of Hematology, School of Medical Sciences, Tarbiat Modares University, Tehran, Iran

[3] Hematology-Oncology and Stem Cell Transplantation Research Center, Tehran University of Medical Sciences, Tehran, Iran

[4] Department of Anatomy, School of Medical Sciences, Tarbiat Modares University, Tehran, Iran

[5] Department of Medical Genetics, Tehran University of Medical Sciences, Tehran, Iran

Introduction

Acute myeloid leukemia (AML) is a group of hematopoietic stem cell disorders that are characterized by the autonomous proliferation of myeloid progenitors and is also associated with genetic instability and molecular changes. Cytogenetic aberrations have classified AML patients into favorable, intermediate, and adverse prognostic groups [1, 2]. AML patients with cytogenetic normal (CN) who comprise the largest cytogenetic group of AML (approximately 45 %) fall into the intermediate category [3, 4]. This heterogeneous AML subgroup shows molecular alterations and gene mutation. Among these genetic abnormalities, Fms-like tyrosine kinase 3 (FLT3) lesions have been reported in about 25 % of AML cases, and patients with this abnormality are associated with a poor prognosis [5–7]. Nucleophosmin (NPM1) abnormalities were

10- Demeke Geremew Debebe

First Name	Last Name	Program	Level	School
Demeke	Geremew Debebe	Immunology	M.Sc.	Medicine

Published Articles:

	Title of the Article
1	Microbiological and Immunological Aspects of Narcolepsy
2	Th17 Cell Related Cytokine Profiles in Narcolepsy and Other Types of Excessive Daytime Sleepiness

Microbiological and Immunological Aspects of Narcolepsy

Demeke Geremew[1,2], **Meseret Workineh**[1], **Maryam Izad**[2,*]

[1]Department of Immunology and Molecular Biology, School of Biomedical and Laboratory Sciences, University of Gondar (UoG), Ethiopia
[2]Department of Immunology, School of Medicine, Tehran University of Medical Sciences International Campus (TUMS-IC), Iran

Abstract Narcolepsy is a chronic neurological disorder characterized by excessive day time sleepiness, cataplexy and hypnagogic and hypnopompic hallucination. Narcolepsy is caused by loss of hypocretine neuron. Hypocretine is an excitatory neuropeptide projecting in the central nervous system and maintains wakefulness. The mechanism of hypocretin loss in narcolepsy is elusive. However, an autoimmune mediated destruction of hypocretin neuron is suspected because of its firm association with HLA-DQB1*0602 genotype and polymorphism in the TCR-α chain. Furthermore, infection with streptococcus pyogenes, influenza A H1N1 strain and the Pandemrix vaccine itself has strong association with narcolepsy. We searched PubMed (1984 – 2015), Google Scholar (1984 – 2015), MEDLINE (1984 – 2015), and EMBASE (1984 – 2015). In the interim, bibliographies of identified articles were reviewed to find additional references. The purpose of this mini review is to summarize recent findings involving microbiological and immunological factors for narcolepsy development.

Keywords Narcolepsy, Cataplexy, Hypocretin, HLA-DQB1*0602, Pandemrix Vaccine

1. Introduction

Narcolepsy is a chronic neurological disorder caused by loss of hypocretine (Hcrt) neurons, wakefulness associated neurotransmitter in the lateral hypothalamus [1, 2]. The clinical features of narcolepsy includes: excessive daytime sleepiness, cataplexy, hypnagogic hallucinations, sleep paralysis, and disturbed nocturnal sleep patterns [1]. The International Classification of Sleep Disorders (ICSD-3) classified narcolepsy in to two main forms: type 1 & type 2 narcolepsy [3]. A typical feature of type 1 narcolepsy is sudden loss of muscle tone triggered by positive emotions [4, 5] such as laughter and surprise [5-9]. The usual onset of the disease is in childhood ,with highest incidence between 10–19 age groups [3], and once established the disease is life-long [10, 11]. Narcolepsy affects 0.03–0.16% of the general population in various ethnic groups [12], and the highest prevalence (0.16%) was reported from Japan [13]. In Europe, the average direct and indirect costs of narcolepsy were estimated to be €3200-18000 and €1000-11000 per case per year respectively [3].

Genetic and environmental factors play key roles for the development of narcolepsy [12, 14]. Among the different genetic predisposing factors, a specific human leukocyte antigen (HLA) subtype is the major trigger [15]. Furthermore, environmental association with upper airway infections; streptococcus pyogenes, and influenza A virus H1N1 vaccination and infection itself was reported to have an important effect on narcolepsy susceptibility [16-19]. Recent pathophysiological studies have shown that type 1 narcolepsy is caused by the early loss of Hcrt, but type 2 narcolepsy is rarely caused by Hcrt deficiency [20] indicating a more heterogeneous origin in its etiology [21]. In this review, we will discuss the main genetic and environmental triggers associated with microbiology and immunology, which leading to an autoimmune mediated destruction of Hcrt neurons in narcolepsy.

2. Causes of Narcolepsy

2.1. Genetic Triggers to Narcolepsy

In 1984, Juji and colleagues discovered a strong association of narcolepsy with HLA class II region [22]. Subsequently, Mignot et al. uncovered that HLA-DQ0602, a heterodimer protein encoded by HLA-DQA1*01:02 & DQB1*06:02 as the main predisposing genes [23, 24]. Moreover, other HLA alleles such as DQB1*03:01 also contribute to narcolepsy susceptibility, but the effect is weaker [3]. Nevertheless, HLA-DQB1*06:01, DQB1*05:01, DQA1*01(non- DQA1*01:02) and DQB1*06:03 are protective alleles to narcolepsy [3, 25].

Type 1 narcolepsy is strongly associated with HLA-DQ0602, especially with DQB1*06:02 (90-100%), the overwhelming effect of this allele on the risk suggests that

Original Research

Th17 Cell Related Cytokine Profiles in Narcolepsy and Other Types of Excessive Daytime Sleepiness

Demeke G. Debebe[1], Khosro Sadeghniat-Haghighi[2], Yadollah Shakiba[3], Ania Rahimi-Golkhandan[2], Maryam Izad[1]*

[1.] *Department of Immunology, School of Medicine, International Campus, Tehran University of Medical Sciences, Tehran, Iran*
[2.] *Occupational Sleep Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran*
[3.] *Department of Immunology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran*

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Abstract

Background and Objective: Narcolepsy is a chronic neurological disorder caused by loss of hypocretin (Hcrt) neurons. Both genetic and environmental factors play an important role for the development of narcolepsy. The mechanism of Hcrt loss in narcolepsy is elusive; however, an autoimmune mediated destruction of Hcrt neurons is suspected. The purpose of this study was to assess Th17 related cytokines: interleukin-6 (IL-6), IL-17, IL-23, and transforming growth factor beta (TGF-β) in the pathophysiology of narcolepsy and other types of excessive daytime sleepiness (EDS).

Materials and Methods: A total of 15 narcoleptic patients, 35 other patients with EDS and 48 age and sex matched healthy subjects were enrolled in this case-control study. Serum IL-6, IL-17, IL-23, and TGF-β levels were measured using sandwich enzyme-linked immunosorbent assay.

Results: There was no significant difference in IL-6 (P = 0.0618) and IL-23 (P = 0.7717) level among participants with narcolepsy, other patients with EDS and controls, whereas TGF-β was significantly decreased in the ones with narcolepsy and other EDS compared to healthy controls (P = 0.0039).

Conclusion: Decreased level of TGF-β in narcolepsy and other patients with EDS indicates a clue for the presence of dysregulation of inflammatory cascades in these patients. This study sheds a new insight on the pathophysiology of narcolepsy.

Keywords: Narcolepsy; Cataplexy; Hypocretin; Interleukin-6; Transforming growth factor beta; Interleukin-17; Interleukin-23

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Introduction

Narcolepsy is a chronic neurological disorder caused by the loss of hypocretin (Hcrt) [orexin (OX)]; a neuropeptide that projects all over the central nervous system (CNS) (1, 2). The clinical features of narcolepsy include excessive daytime sleepiness (EDS), cataplexy, hallucinations at sleep onset and awakening, sleep paralysis, and fragmented nocturnal sleep patterns (1). There are two types of narcolepsy: Type 1 narcolepsy [narcolepsy with cataplexy (NC)] and Type 2 narcolepsy [narcolepsy without cataplexy (NwC)] (2, 3). The distinctive attribute of Type 1 narcolepsy is a sudden loss of muscle tone elicited by positive emotions (3) such as laughter and surprise (4). The

***Corresponding author**: M. Izad, Department of Immunology, School of Medicine, International Campus, Tehran University of Medical Sciences, International Campus, Tehran, Iran.*
Tel: +989127197297, Fax: +982166419536
Email: izadm@sina.tums.ac.ir

Chapter Five

School of Rehabilitation

1- Mohammad Reza Hadian

First Name	Last Name	Program	Level	School
Mohammad Reza	Hadian	Physiotherapy	Professor/PhD	Rehabilitation

Published Articles:

	Title of the Article
1	Changes in Back Compressive Force When Measuring Maxi-mum Acceptable Weight of Lift in Iranian Male Students.
2	Is Cock-up Splint the Right Choice for All of the Carpal Tunnel Syndrome Patients? A Case Report.
3	Reliability of digital photography for assessing lower extremity alignment in individuals with flatfeet and normal feet types

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Original Article

Changes in Back Compressive Force When Measuring Maximum Acceptable Weight of Lift in Iranian Male Students

Ali SALEHI SAHL ABADI [1], ****Gebraeil NASL SARAJI*** [1], ***Adel MAZLOUMI*** [1], ***Hojjat ZERAATI*** [2], ***Mohammad Reza HADIAN*** [3], ***Amir Homayoun JAFARI*** [4]

1. *Dept. of Occupational Health, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*
2. *Dept. of Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*
3. *Dept. of Postgraduate Studies, Faculty of Rehabilitation, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran*
4. *Medical Physics and Biomedical Engineering Department, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

***Corresponding Author:** Email: jnsaraji@tums.ac.ir

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Abstract

Background: Low back pain caused by work, ranked the second after cardiovascular diseases, are among the most common reasons of patients' referral to the physicians in Iran. This study aimed to determine the changes in back compressive force when measuring maximum acceptable weight of lift in Iranian male students.

Methods: This experimental study was conducted in 2015 on 15 young male students were recruited from Tehran University of Medical Science. Each participant performed 18 different lifting tasks involving three lifting frequencies, with three lifting heights, and two box sizes. Each set of experiments was conducted during the 20 min work period using free-style lifting technique. The back compressive force evaluated with hand-calculation back compressive force method. Finally, Pearson correlation test, analysis of variance (ANOVA) and t-test were used for data analysis.

Results: The mean of back compressive force (BCF) for the small and large boxes at a frequency of 1lift/min at heights of F - K height, were 1001.02 (±86.74), 1210.57 (±93.77) Ib, respectively. There was a significant difference between mean BCF in terms of frequencies of lifts (P=0.02). The result revealed significant difference between frequencies of 1 lift/min and 6.67 lift/min (P=0.01). There was a significant difference between mean BCF in terms of the sizes of the two boxes (P=0.001). There was a significant relationship between the BCF and maximum acceptable weight of lift in all test conditions (P=0.001).

Conclusion: BCF is affected by box size, lifting frequency and weight of load.

Keywords: Back compressive force, Maximum acceptable weight of lift, Psychophysical methodology

Introduction

There are several harmful factors at work environment that causes fatigue, burnout, and early exhaustion of individuals, and lead to the waste of time and money. Some of the occupational factors are responsible for the incidence of musculoskeletal problems. Manual Material Handling (MMH) tasks are one of the common occupational factors (1). In most industries, and even in non-occupational settings, manual handling and lifting of weights happens very frequently; each of these tasks have their own specific requirements, and such tasks are one of the important reasons for the incidence of low back pain (2). Low back pain and other musculoskeletal disorders caused by work, ranked the second after cardiovascular diseases, are among the most important and common diseases and cause of patients' referral to the physicians in Iran (3). Moreover,

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Clinical Medical Reviews and Case Reports

Case Report: Open Access

Is Cock-up Splint the Right Choice for All of the Carpal Tunnel Syndrome Patients? A Case Report

Mahdi Hadidi[1], Mohammad-Reza Hadian[2,3]*, Ali Arab Kheradmand[4], Mahmood Farzan[5], Hamidreza Monsef[6], Maryam-Raheleh Dadras[7], Saeed Talebian[2] and Gholam Reza Olyaei[2]

[1]School of Rehabilitation, Tehran University of Medical Sciences (TUMS), Iran

[2]Professor, Faculty of Rehabilitation, Tehran University of Medical Sciences (TUMS), Iran

[3]Professor, Brain and Spinal Research center (BASIR, Imam Hospital), Tehran University of Medical Sciences (TUMS, TUMS-IC), Iran

[4]Associate Professor, surgeon, Imam Hospital, Tehran University of Medical Sciences (TUMS), Iran

[5]Professor, orthopedic surgeon, Imam Hospital, Tehran University of Medical Sciences (TUMS), Iran

[6]Associate Professor, Faculty of Pharmacy, Tehran University of Medical Sciences (TUMS), Iran

[7]Medical Physics, International Affairs, Iran University of Medical Sciences (IUMS), Iran

***Corresponding author:** *Dr. Mohammad-Reza Hadian, Professor, Faculty of Rehabilitation, Brain and Spinal Injury Research center (BASIR, Imam Hospital), Tehran University of Medical Sciences (TUMS, TUMS-IC), Tehran, Iran, Tel: +9821-77536134, Fax: +9821-77534133, E-mail: hadianrs@sina.tums.ac.ir, hadian_ras@yahoo.com*

Abstract

Introduction: Splinting the hand is a common treatment strategy for the patients with carpal tunnel syndrome.

Case presentation: A fifty-year-old woman was the exceptional one who her clinical signs and symptoms was deteriorated after the administration of splinting. She showed deterioration of clinical and electrophysiological parameters after two weeks of using splint combined with steroid [1]. After removing the splint, the patient showed relief of subsequent signs and symptoms.

Conclusion: It seems that some cautions should be considered in prescribing splints for CTS patients. We have discussed the clinical presentation, possible causes, and management of the patient and a brief review of literature were also presented.

Keywords

Splinting, Carpal Tunnel Syndrome (CTS), Iontophoresis

Introduction

Carpal Tunnel Syndrome (CTS) is the most common entrapment neuropathy of the upper limb [2]. It is more common in women than men and is seen in patients between 40-60 years old [3]. Entrapment of the median nerve within the carpal tunnel is secondary to the compression of the nerve between the transverse carpal ligament (flexor retinaculum) superiorly and the flexor tendons and carpal bones inferiorly [4].

Several treatment options either surgical and or non-surgical have been suggested for relieving the pressure on the nerve. The non-surgical methods have frequently recommended for patients with mild to moderate symptoms and include splinting the wrist in neutral position, physical therapy and medication [2,5]. However, in severe condition of CTS, conservative treatments seem to be less beneficial. Splinting, iontophoresis and phonophoresis are among the non-surgical treatments that have been recommended separately or in combination for CTS patients. Very few researches have focused on the efficacy of combined treatments for CTS patients [1,6-8].

Some previous researches have shown clinical improvements following splinting in spite of non-significant changes in electrophysiological parameters [7,8]. In this report, evidences from one woman who her clinical and electrophysiological signs and symptoms was deteriorated after the application of the splint and iontophoresis will be discussed.

Case Description

A fifty-year-old woman was referred to the Rehabilitation clinic of Tehran University of Medical Science for treatment of idiopathic bilateral CTS. She was out of fourteen women who were referred for CTS treatments in a clinical trial. Diagnosis of CTS was determined based on the clinical signs and symptoms and also electrophysiological findings by surgeons (hand specialist). Exclusion and inclusion Criteria such as Rheumatoid arthritis, previous fracture and dislocation of wrist, diabetes, Hyperthyroidism, myxedema, any

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DIAGNOSTIC METHODS: RELIABILITY STUDY

Reliability of digital photography for assessing lower extremity alignment in individuals with flatfeet and normal feet types

Zinat Ashnagar [a], Mohammad Reza Hadian [b, *], Gholamreza Olyaei [a], Saeed Talebian Moghadam [a], Asghar Rezasoltani [c], Hassan Saeedi [d], Mir Saeed Yekaninejad [e], Rahimeh Mahmoodi [a]

[a] Physical Therapy Department, School of Rehabilitation, Tehran University of Medical Sciences, Tehran, Iran
[b] School of Rehabilitation, Brain and Spinal Injury Research Center (BASIR), Tehran University of Medical Sciences, International Campus (TUMS, TUMS-IC), Tehran, Iran
[c] Faculty of Rehabilitation, Physiotherapy Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[d] Department of Orthotics and Prosthetics, Faculty of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran
[e] Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Aim: The aim of this study was to investigate the intratester reliability of digital photographic method for quantifying static lower extremity alignment in individuals with flatfeet and normal feet types.
Methods: Thirteen females with flexible flatfeet and nine females with normal feet types were recruited from university communities. Reflective markers were attached over the participant's body landmarks. Frontal and sagittal plane photographs were taken while the participants were in a standardized standing position. The markers were removed and after 30 min the same procedure was repeated. Pelvic angle, quadriceps angle, tibiofemoral angle, genu recurvatum, femur length and tibia length were measured from photographs using the Image j software.
Results: All measured variables demonstrated good to excellent intratester reliability using digital photography in both flatfeet (ICC: 0.79–0.93) and normal feet type (ICC: 0.84–0.97) groups.
Conclusion: The findings of the current study indicate that digital photography is a highly reliable method of measurement for assessing lower extremity alignment in both flatfeet and normal feet type groups.

1. Introduction

Flatfeet or pes planus is characterized by a chronically dropped or abnormally low medial longitudinal arch (MLA) often in association with calcaneal eversion and excessive pronation of the subtalar joint (Angin et al., 2014; Banwell et al., 2014; Neumann, 2010).

The Foot Posture Index (FPI) is a clinical tool of foot posture assessment that has been proposed to evaluate multiple segments and planes of the foot in a variety of clinical settings (Redmond et al., 2008). The six-item criterion FPI is a simple, quick and observational method which allows the clinician to assess static standing foot posture and classify it as neutral, pronated, or supinated (Redmond et al., 2006). The FPI has shown moderate intertester and high intratester reliability and good construct validity (Cornwall et al., 2008; Keenan et al., 2007). During the assessment of the relationship between static foot posture and foot mobility, it has been demonstrated that individuals with higher FPI scores had greater foot mobility and those with lower FPI had less foot mobility (Cornwall and McPoil, 2011).

The relationship between the FPI and rearfoot plane motion during walking has been investigated (Buldt et al., 2013; Chuter, 2010). The results demonstrated a strong, positive correlation between increasing FPI score (more pronated posture) and maximum rearfoot eversion (Chuter, 2010).

Flatfeet rarely exist without some degree of hyperpronation

* Corresponding author.
E-mail addresses: z-ashnagar@razi.tums.ac.ir (Z. Ashnagar), hadianrs@sina.tums.ac.ir (M.R. Hadian), olyaeigh@sina.tums.ac.ir (G. Olyaei), talebian@sina.tums.ac.ir (S. Talebian Moghadam), a_rezasoltani@sbmu.ac.ir (A. Rezasoltani), hassan_saeedi2@yahoo.co.uk (H. Saeedi), yekaninejad@yahoo.com (M.S. Yekaninejad), rahimeh.mahmoodi@gmail.com (R. Mahmoodi).

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2- Syed Asadullah Arslan

First Name	Last Name	Program	Level	School
Syed Asadullah	Arslan	Physiotherapy	PhD	Rehabilitation

Published Articles:

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1	Prevalence and Risk Factors of Low Back Pain Among the Office Workers of King Edward Medical University Lahore, Pakistan
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3	Investigating the anticipatory postural adjustment phase of gait initiation in different directions in chronic ankle instability patients
4	Reliability of Magnetic Resonance Imaging Findings Interpretation in Patients with Lumbar Disk Herniation

Research Paper: Prevalence and Risk Factors of Low Back Pain Among the Office Workers of King Edward Medical University Lahore, Pakistan

Syed Asadullah Arslan[1], Mohammad Reza Hadian[1,2*], Gholamreza Olyaei[1], Hussein Bagheri[1], Mir Saeed Yekaninejad[2], Sahar Ijaz[3], Ali Arab Kheradmand[4]

1. Department of Physiotherapy, School of Rehabilitation, International Campus, Tehran University of Medical Sciences, Tehran, Iran.
2. Brain and Spinal Injury Repair Research Center (BASIR), Tehran University of Medical Sciences, Tehran, Iran.
3. Department of Anatomy, School of Medicine, International Campus, Tehran University of Medical Sciences, Tehran, Iran.
4. Institute of Cancer, Imam Khomeini Hospital, Tehran, Iran.

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ABSTRACT

Purpose: In the present era, Low Back Pain (LBP) is a destructive health problem. It affects many people and accounts for huge economic loss. Office workers have a unique lifestyle while working in sedentary position with poor body posture for long periods of time. The musculoskeletal problems can result in inconvenience or pain with bad impact on the quality of life.

Methods: This cross-sectional study was done to find the prevalence and risk factors of LBP among the office workers of King Edward Medical University (KEMU), Lahore, Pakistan. After taking the ethical approval from Institutional Review Board (IRB), KEMU, Lahore, a sample size of 300 office workers was calculated by using proportion formula of sample size estimation with 5% margin of error from KEMU with effect from Jan 2015 to Sep 2015. Participants aged between 18 and 60 years with at least 1 year work experience completed the validated questionnaires.

Results: Results showed that point and lifetime prevalence of LBP among office workers of KEMU, Lahore, Pakistan was 29.20% and 69.20%, respectively. LBP prevalence rose with the increase in age, work experience, low education, low physical activity, sleep disturbance, smoking habit, more sitting and standing time, computer use, and low job satisfaction.

Conclusion: We concluded that different individual, ergonomic, and psychosocial factors were associated with LBP. Because of high prevalence of LBP among office workers of this university, better ergonomic facilities and awareness about sitting posture, regular exercise, good sleep, and psychological support to the workers were recommended to decrease the effects of predisposing risk factors of LBP.

*** Corresponding Author:**
Mohammad Reza Hadian, PhD
Address: *Brain and Spinal Injury Repair Research Center (BASIR), Tehran University of Medical Sciences, Tehran, Iran.*
Phone: *+98 (21) 77533939*
E-mail: *hadianrs@sina.tums.ac.ir*

The Test-Retest Reliability and Minimal Detectable Change of the Fugl-Meyer Assessment of the Upper Extremity and 9-Hole Pegboard Test in Individuals With Subacute Stroke

Sahar Toluee Achacheluee[1], Leila Rahnama[1*], Nouredin Karimi[1], Iraj Abdollahi[1], Shapour Jaberzadeh[2], Syed Asadullah Arslan[3]

1. Department of Physical Therapy, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.
2. Department of Physical Therapy, Faculty of Medicine, Monash University, Melbourne, Australia.
3. Department of Physiotherapy, School of Rehabilitation, International Campus, Tehran University of Medical Sciences, Tehran, Iran.

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ABSTRACT

Purpose: The first step to manage motor impairment of upper limb in patients with subacute stroke is having an accurate assessment tool. The Fugl-Meyer assessment of upper extremity and 9-hole pegboard test are used to evaluate motor function and hand dexterity in stroke survivals. The present study aimed to investigate the test-retest reliability and minimal detectable change (MDC) in these two tests.

Methods: A total of 15 patients with subacute stroke (54-76 years old) participated in this study. They were selected non-randomly from rehabilitation clinics and hospitals of Tehran, Iran, based on inclusive and exclusive criteria. Intraclass correlation coefficient (ICC), standard error measurement (SEM), and MDC were used for investigating intraday and interday reliability for 1 hour and 3 days.

Results: Intraday reliabilities of Fugl-Meyer and 9-hole pegboard were excellent with ICC of 0.98 and 0.98, also MDC of 1.96 and 8.59, respectively. The interday reliabilities of these tests were also excellent with ICC of 0.99 and 0.96, as well as MDC of 1.52 and 12.69, respectively. The absolute reliability (SEM) was less than 10% of maximum acquired scores indicating acceptable errors of measurement.

Conclusion: Results show that the Fugl-Meyer assessment and 9-hole pegboard test have excellent test-retest reliability. Therefore these tests can be used for appropriate treatment planning and clinical decision making in patients with subacute stroke.

1. Introduction

Stroke is a major cause of disability among elders in the world and affects mostly the upper extremity [1]. Upper limb disability does not recover in 50% of cases after stroke [2]. Almost 20% to 30% patients with stroke remain dependent even after recent progress in the treatment of patients with acute

*** Corresponding Author:**
Leila Rahnama, PhD
Address: *Department of Physiotherapy, University of Social Welfare and Rehabilitation Sciences, Kodakyar Ave., Daneshjo Blvd., Evin, Tehran, Iran.*
Phone: *+98 (21) 22180039*
E-mail: *lrahnama@gmail.com*

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Original research study

Investigating the anticipatory postural adjustment phase of gait initiation in different directions in chronic ankle instability patients

Zahra Ebrahimabadi[a], Sedigheh Sadat Naimi[b, *], Abbas Rahimi[b], Heydar Sadeghi[c], Seyed Majid Hosseini[b], Alireza Akbarzadeh Baghban[d], Syed Asadullah Arslan[e]

[a] Department of Physiotherapy, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[b] Physiotherapy Research Centre, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[c] Department of Kinesiology, School of Physical Education, Kharazmi University, Tehran, Iran
[d] Physiotherapy Research Centre, Department of Basic Sciences, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[e] Department of Physiotherapy, School of Rehabilitation, TUMS, Tehran, Iran

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ABSTRACT

Objective
The main objective of the present study was to analyze how supra spinal motor control mechanisms are altered in different directions during anticipatory postural phase of gait initiation in chronic ankle instability patients. It seems that supra spinal pathways modulate anticipatory postural adjustment phase of gait initiation. Yet, there is a dearth of research on the effect of chronic ankle instability on the anticipatory postural adjustment phase of gait initiation in different directions.

Method
A total of 20 chronic ankle instability participants and 20 healthy individuals initiated gait on a force plate in forward, 30° lateral, and 30° medial directions.

Results
According to the results of the present study, the peak lateral center of pressure shift decreased in forward direction compared to that in other directions in both groups. Also, it was found that the peak lateral center of pressure shift and the vertical center of mass velocity decreased significantly in chronic ankle instability patients, as compared with those of the healthy individuals.

Conclusion
According to the results of the present study, it seems that chronic ankle instability patients modulate the anticipatory postural adjustment phase of gait initiation, compared with healthy control group, in order to maintain postural stability. These changes were observed in different directions, too.

1. Introduction

Lateral ankle sprain is the most common injury among athletes (Hopkins et al., 2012; Steib et al., 2013) and 30%–75% of patients report repeated injury (Hopkins et al., 2012; Wikstrom et al., 2010; Munn et al., 2010) and experience symptoms including pain, weakness, and giving way after the initial injury (Konradsen et al., 2002; Brown et al., 2008; Pope et al., 2011). Chronic Ankle Instability (CAI) can cause osteoarthritis (Valderrabano et al., 2006); it can also affect athletes' life style in drastic ways. Similar to other chronic injuries, CAI is a complex injury which causes considerable decrease in the quality of life (Kim et al., 2012). Two main types of factors, including mechanical (such as joint laxity) and functional (such as sensorimotor deficit) factors, explain residual symptoms (Hopkins et al., 2012) in CAI patients (Hopkins et al., 2012; Hass et al., 2010; Gutierrez et al., 2009). However, few studies have primarily focused on investigating the issue of alternation in supra spinal motor control.

Anticipatory Postural Adjustment (APA) is a part of gait initiation, which plays a crucial role in facilitating forward body movement (Hiraoka et al., 2014). The APA, or preparatory phase of gait initiation, is constrained by the secondary motor area. During the preparatory phase, the APA is expressed as a backward and lateral shift of the Center of Pressure (COP) moves toward, first, the swing leg side, promoting the Center of Mass (COM) acceleration forward and, then, toward the stance leg side (Hass et al., 2010). Also, the COM falls and, finally, the swing limb unloads during the swing phase of gait initiation (Chastan et al., 2010). According to the previous studies, the APA phase of gait initiation is seriously impaired in older adults and patients with Parkinson's disease (Halliday et al., 1998; Uemura et al., 2012); the main reason for this is claimed to be alteration of the supra

* Corresponding author.
Email addresses: z.ebrahima@gmail.com (Z. Ebrahimabadi); naimi.se@gmail.com (S.S. Naimi); arahimiuk@yahoo.com (A. Rahimi); sadeghih@yahoo.com (H. Sadeghi); majid_hoseini@sbmu.ac.ir (S.M. Hosseini); akbarzad@gmail.com (A.A. Baghban); asadshahgilani@gmail.com (S.A. Arslan)

Reliability of Magnetic Resonance Imaging Findings Interpretation in Patients with Lumbar Disk Herniation

Sayed Mehdi Hussaini[1*], Noureddin Karimi[1], Kamran Ezzati[2], Samane Hossein Zadeh[3], Leyla Rahnama[1], Syed Asadullah Arslan[4]

1. Department of Physiotherapy, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.
2. Department of Physiotherapy, School of Medicine, Guilan University of Medical Sciences, Guilan, Iran.
3. Department of Statistics, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.
4. Department of Physiotherapy, School of Rehabilitation, Tehran University of Medical Sciences, International Campus, Tehran, Iran.

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Intervertebral disc, MRI, Reliability of results, Low back pain

ABSTRACT

Purpose: The present study aimed to find reliability of magnetic resonance imaging (MRI) in patients with lumbar disk herniation.

Methods: In this cross-sectional study, 110 individuals aged 20-50 years with chronic low back pain (LBP) of more than 3 months were enrolled by nonprobability convenient sampling method. Only disk herniated patients of L4-L5 and L5-S1, diagnosed by physicians on the basis of MRI, were included in the study. Sagittal and axial MRI scans were taken and examined to rule out acute pathology. Two examiners interpreted the MRI results without knowing the results of clinical tests and questionnaires. Reliability at intra- and inter-level was done twice with the interval of 5 days. Reliabilities of findings such as affected disk level, extent of disk herniation, nerve root involvement, dehydration, and ligamentum flavum involvement were also assessed.

Results: Intra- and inter-test values for disk level were 0.87 and 0.80, for disk grade were 0.81 and 0.76, for lateral canal stenosis were 0.81 and 0.75, for dehydration were 0.81 and 0.72, for spondylolisthesis were 0.88 and 0.81, and for ligamentum flavum involvement were 0.79 and 0.75.

Conclusion: Repeatability of MRI results in patients with lumbar disk herniation at intra- and inter-level was good to excellent.

1. Introduction

Low back pain (LBP) is one of the most common problems referred to medical professionals and 70%-80% of adults experience it at some point in their lives [1]. In the industrialized countries, LBP is very common and lumbar disk degenerative disease is one of the main causes of LBP all over the world [2]. LBP may occur due to degenerative changes, Stenosis of spinal cord, neoplasm, injury, infection, and arthritic effects [3]. Lumbar disk herniation (LDH) is the main spinal degenerative dis-

*** Corresponding Author:**
Sayed Mehdi Hussaini, MSc.
Address: *Department of Physiotherapy, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.*
Phone: *+98 (912) 7919716*
E-mail: *sayedmehdi.pt@gmail.com*

3- Hadi Sarafraz

First Name	Last Name	Program	Level	School
Hadi	Sarafraz	Physiotherapy	PhD	Rehabilitation

Published Articles:

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1	Reliability, agreement, and diagnostic accuracy of the Modified Lateral Scapular Slide test

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Original article

Reliability, agreement, and diagnostic accuracy of the Modified Lateral Scapular Slide test

A. Shadmehr [a], H. Sarafraz [b, *], M. Heidari Blooki [c], S.H. Jalaie [d], N. Morais [e]

[a] Department of Physiotherapy, School of Rehabilitation Tehran University of Medical Sciences, (TUMS), Tehran, Iran
[b] Department of Physiotherapy, School of Rehabilitation, International Campus, Tehran University of Medical Sciences (IC-TUMS), Tehran, Iran
[c] Iranian Red Crescent Society (IRCS), Rehabilitation Center, Bandarabbas, Iran
[d] Biostatistics, Department of Physiotherapy, School of Rehabilitation, Tehran University of Medical Sciences, (TUMS), Tehran, Iran
[e] Polytechnic Institute of Leiria, School of Health Sciences (ESSLei), Campus 2 – Morro Do Lena – Alto Do Vieiro, 2411-901 Leiria, Portugal

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ABSTRACT

Background: The Lateral Scapular Slide Test is a static test used in clinical settings to assess medio-lateral inferior angle displacement and scapular asymmetry at three different degrees of shoulder abduction. However, there is no evidence in the literature about the reliability and diagnostic accuracy of a modified LSST (arm elevation in the scapular plane with loading) in a symptomatic population.
Objective: To assess the intra- and inter-rater reliability, agreement, and diagnostic accuracy of the MLSST (Modified Lateral Scapular Slide Test) in subjects with and without shoulder symptoms. A new test position is examined, in which the arm is held in 90° of elevation in the scapular plane with 1 kg load.
Design: Within day intra- and inter-rater reliability, agreement, and diagnostic accuracy study.
Method: Participants included 25 (42 ± 2.7 years) subjects with shoulder symptoms and 25 (40 ± 2.1 years) asymptomatic control subjects. Two raters, blinded to each other's outcomes, measured the distance between the inferior scapular angle and T7 at arms by the side, hands on hips and 90° of arm elevation in the scapular plane with 1 kg load. Measurements were performed twice, bilaterally. Intra-class correlation coefficient (ICC), minimal detectable change ($MDC_{95\%}$) and diagnostic accuracy were calculated.
Results: The ICCs for intra- and inter-rater reliability were good to high in both shoulders of symptomatic and asymptomatic groups. The $MDC_{95\%}$ in the symptomatic group ranged between 0.67 and 1.40 cm in the symptomatic shoulder and 0.72–1.16 cm in the asymptomatic shoulder. The asymptomatic group presented a $MDC_{95\%}$ ranging between 0.63 and 1.52 cm in the dominant and 0.60–1.41 cm in the non dominant shoulder. Positive and negative likelihood ratios ranged between 0.67–5.50 and 0.81–1.11, respectively.
Conclusion: The MLSST had good reliability and agreement properties to assess scapular position in both groups. However, no test position had clinical utility as a diagnostic criterion for shoulder pathology.

1. Introduction

Shoulder joint function may be affected by changes in scapular position and motion. Several studies have shown that altered scapular position and motion, commonly termed scapular dyskinesis, can significantly impact on shoulder joint stability (Mueller et al., 2013), muscles' force generation (Kebaetse et al., 1999; Kibler and McMullen, 2003; Kibler et al., 2006) and length tension capacities (Borstad, 2006), range of motion (Kebaetse et al., 1999), and quality of movement (Ludewig and Reynolds, 2009). Any muscle imbalance affecting the shoulder complex may change scapular kinematics and the symmetry of shoulder motions. Thus, scapular asymmetry is often considered as a related factor to the development or perpetuation of shoulder pain and disability and used as a diagnostic criterion to identify patients at risk of developing shoulder symptoms (Lukasiewicz et al., 1999; Hebert et al.,

* Corresponding author. Department of Physiotherapy, School of Rehabilitation, International Campus, Tehran University of Medical Sciences, (IC-TUMS), Enghelab Ave, Pitch-e-shemiran, Zip: 11489, Tehran, Iran. Tel.: +98 2177533939; fax:+98 2177534133.
E-mail addresses: hsarafraz@razi.tums.ac.ir, sarafraz1361@yahoo.com (H. Sarafraz).

4- Muhammad Salman Bashir

First Name	Last Name	Program	Level	School
Muhammad	Salman Bashir	Physiotherapy	PhD	Rehabilitation

Published Articles:

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1	Evaluating the target, effect, action interaction (tea model) of spinal manipulation therapy on sacroiliac joint dysfunction

ORIGINAL ARTICLE

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EVALUATING THE TARGET, EFFECT, ACTION INTERACTION (TEA MODEL) OF SPINAL MANIPULATION THERAPY ON SACROILIAC JOINT DYSFUNCTION

[1]Muhammad Salman Bashir
[*2]Mohammad Reza Hadian
[3]Gholamreza Olyaei
[4]Saeed Talebian
[5]Rabiya Noor
[6]Syed Asadullah Arslan

ABSTRACT

Background: In physical therapy, usually the effects of treatment on any condition will be evaluated based on the mode of action on the target tissue. Some treatments will have direct and indirect effects. Due to indirect effects, there may be changes in other tissues or systems in and around the target tissue. The interaction between target, effect, and action was studied under TEA model. In sacroiliac joint dysfunction, Muscle Energy Technique (MET) and Spinal Manipulation Therapy (SMT) were proved as useful treatment approaches but one is targeted on muscles (MET) the other targets on joint (SMT). The indirect effects of both the approaches can't be neglected. This study focused on evaluating indirect effects of SMT.

Methods: A pilot study was conducted to see the effect of Spinal Manipulation Therapy on muscles (Transverse Abdominus, Internal Oblique) when applied in patients with sacroiliac joint dysfunction. 44 subjects diagnosed with sacroiliac joint dysfunction were recruited in the study. Resting thickness was measured by ultrasound before and after Spinal Manipulation Therapy. SPSS version 17 was used for statistical analysis. Paired t-test compared pre and post test results.

Results: After conducting Pilot study revealed that Pre resting thickness of Transverse Abdominus and Internal Oblique is (3.5±0.10) and (5.47± 0.15) Post resting Thickness of TrA (Transverse Abdominus) and Internal Oblique (IO) is (3.90±0.12) and (7.63±0.80) Results are significant as P-Value 0.000 that is <0.05.

Conclusion: Here is concluded that SMT is a useful method to treat muscles through its direct action is on the Sacroiliac joint in Sacroiliac joint dysfunction. So we can use it for treating muscles by applying on joints (Indirect method).

Keywords: Spinal Manipulation, Sacroiliac Joint, Muscle, Pain, Low backache, Ultrasonography.

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[1]Ph.D. Physiotherapy Student, School of Rehabilitation Tehran University of Medical Sciences - International Campus (IC-TUMS)
[3]Professor, School of Rehabilitation, Tehran University of Medical Sciences - International Campus (IC-TUMS)
[4]Professor, School of Rehabilitation, Tehran University of Medical Sciences - International Campus (IC-TUMS)
[5]Ph.D. Physiotherapy Student, School of Rehabilitation Tehran University of Medical Sciences - International Campus (IC-TUMS)
[6]Ph.D. Physiotherapy Student, School of Rehabilitation Tehran University of Medical Sciences - International Campus (IC-TUMS)

CORRESPONDING AUTHOR

[*2]Mohammad Reza Hadian

Professor, School of Rehabilitation, Brain & Spinal Injury Research Center, Vice Dean for Research Affairs Tehran University of Medical Sciences - International Campus (IC-TUMS)
Email: hadianrasan@gmail.com; hadian_ras@yahoo.com; hadianrs@sina.tums.ac.ir

Chapter Six

School of Nursing and Midwifery

1- Muaf Abdulla Karim

First Name	Last Name	Program	Level	School
Muaf Abdulla	Karim	Nursing	PhD	Nursing

Published Articles:

	Title of the Article
1	End-of-life care provision: experiences of intensive care nurses in Iraq
2	Old age satisfaction regarding geriatric home services in Erbil city
3	Assessment of Health Related to Quality of Life in Hypertensive and Diabetic Mellitus patients in Kurdistan/Iraq
4	Assessment of Nurses' Knowledge Regarding Needle Prick Injury in Erbil Hospitals
5	Assessing Level of Satisfaction of Breast Cancer Patients about Nursing Care in Rizgari Teaching Hospital in Erbil City

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End-of-life care provision: experiences of intensive care nurses in Iraq

Forough Rafii, Alireza Nikbakht Nasrabadi and Muaf Abdulla Karim

ABSTRACT

Background: Nurses play a key role in providing care for the critically ill in the intensive care unit (ICU). The physical, psychological, emotional and spiritual intimate care given by Kurdish nurses allows them to develop a therapeutic relationship with terminally ill patients in the ICU.

Aims: This study sought to explore the meaning of caring for terminally ill patients from the perspective of Kurdish ICU nurses.

Design: Van Manen's (1990) hermeneutic phenomenological design was adopted.

Method: The data were collected through in-depth semi-structured interviews with a purposive sample of 10 nurses working in ICUs. Interviews were transcribed and finally analysed according to Van Manen's method.

Results: Four major themes including emotional labour, death as a positive dimension, optimistic rather than futile care and working within constraints emerged.

Conclusions: Kurdish nurses in their caring encounters with terminally ill patients experienced a range of feelings from emotional strain to being optimistic while working within limited resources in the ICU. Further research is needed to explore the experiences of nurses with other cultures of caring for terminally ill patients in ICUs.

Relevance to practice: End-of-life care in ICU is emotionally challenging, therefore, nurses in this setting require psychological and spiritual support to ensure optimal care provision.

Key words: Critical care nursing • ICU follow-up • Intensive care • Phenomenological research • Qualitative research

INTRODUCTION

Death is an inevitable event (Haisfield-Wolfe, 1996); recent technological advances and the consequent extension of life expectancy have increased the complexity for end-of-life care (Beckstrand and Kirchhoff, 2005). Caring for critically ill patients happens in intensive care units (ICUs) where about 20% of patients have been known to die (Angus *et al.*, 2004). The mortality rate in ICUs of USA, Canada and Sweden has been reported to range between 10% and 20% (Cook *et al.*, 2004; Beckstrand *et al.*, 2006). Because of the complex nature of patients admitted to the ICU, death, end-of-life care and challenging decision-making is common place at the ICU (Shorter and Stayt, 2010). Hansen *et al.* (2009), however, report that many ICU nurses may lack essential knowledge and skills required to provide effective care for terminally ill patients and to offer support for their families and carers. Although, there are no firm statistical data about the mortality rate in private and general hospitals of Kurdistan region/Iraq or mortality rate in the ICUs of this region specifically, the death rate appears to be significant; therefore, the critical care nurses require developing essential skills in order to provide better care for these patients.

Authors: F Rafii, Professor, RN, MScN, PhD. Department of Medical Surgical Nursing, School of Nursing and Midwifery, Iran University of Medical Sciences, International Campus (IUMS-IC), Tehran, Iran; A Nikbakht Nasrabadi, Professor, RN, MScN, PhD. Department of Medical Surgical Nursing, School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran; M Abdulla Karim, RN, BSc N, MSc N, PhD. N. candidate in Nursing, Department of Medical Surgical Nursing, School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran

Address for correspondence: M Abdulla Karim, BSc N, MSc N, PhD. N. candidate, Department of Medical Surgical Nursing, School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran
E-mail: muafabdulla82@yahoo.com or abdullahkarim@razi.tums.ac.ir

BACKGROUND

Patients suffering from life-threatening diseases such as cancer, heart disease, stroke and chronic respiratory diseases are admitted to the ICU of hospitals (Payne

Old age satisfaction regarding geriatric home services in Erbil city

Sangar MA*, Karem FA*, Alireza NN**, Muaf AK**
*Hawler Medical University, Nursing College, Erbil, Kurdistan Region/ Iraq,
**Department of Medical Surgical Nursing, School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran

Correspondence to: Muaf Abdulla Karim, BScN, MScN, PhD candidate in Nursing, Department of Medical Surgical Nursing, School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran, Ministry of Health, Kurdistan Region, Erbil/ Iraq,
Phone: +9647504497296, +989145214619, E-mail: muafabdulla82@yahoo.com, abdullahkarim@razi.tums.ac.ir

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Abstract

Background and objectives: Life satisfaction is a vital imaginary situation in the psychosocial study of aging. Life satisfaction is a multi-dimensional issue that depends on many objective and subjective characteristics. In this study, the achievements are based on socio-demographic characteristics and old age satisfaction toward services in Geriatric home.

Methods: It is a cross sectional study which had been conducted in Geriatric home service in Erbil city during the period from 27/6/2014 to 4/2/2015. A questionnaire was made including sections for demographic characteristics, satisfaction with living conditions utilizing a face-to-face interview format. 25 males and females of old ages were interviewed. Each interview was used as method of data collection.

Results: Twenty-five old aged persons participated in this study in the geriatric home center in Erbil governorate. The majority of them were males; age group was 52-70 years and single. The average duration of staying was of 1-6 years (68%). Most of them did not have friends outside the geriatric home and could not get in contact with their family.

Conclusion: Interventions need to be planned to improve life satisfaction among old people. Appropriate old age policies containing important solutions to the problems of the old people are important to make them feel the element of culture.

Keywords: old age, life satisfaction, geriatric home services, Erbil

Introduction

Life satisfaction continues to be an important construct in the psychosocial study of aging. It is one of the subjective conditions of quality of life, which is the most commonly approved and seems to become one of the facets of victorious aging, both of them being key concepts in aging.

The economic structure, the erosion of societal values, weakening of social values, and social institutions such as the joint family were changed according to the urbanization, modernization, and globalization. Research reports were about life satisfaction, which is strongly related to socio-demographic and psychosocial variables [2].

Changes in the human body might cause difficulty in life. Often, that is why people enter long-term care communities. For some residents, aging was very dangerous or depressing. Others adapted well. The way you work with residents can make them feel better about themselves—and can make your work more pleasant [5].

The ageing process is of course a biological situation, which has its own dynamic; largely, it is not under the human's control. However, it is also subject to the constructions by which each society makes sense of old age. In the developed world, the chronological duration plays a paramount role. The age of 60 or 65, is roughly equivalent to retirement ages in most developed countries where it is said to be the beginning of old age [3].

Most of the developed countries have accepted the chronological age of 65 years as a definition of "elderly" or older person, but like many westernized concepts, this does not adapt well to the situation in Africa. While this definition is somewhat arbitrary, it is many times associated with the age at which one can begin to receive pension benefits. At the moment, there is no United Nations standard numerical criterion, but the UN agreed cutoff is 60+ years to refer to the older population [4,6].

Older people who are not able to manage the daily life by themselves may have a different view of life satisfaction than those with preserved self-care capacity. It may well be that the transition from being healthy and independent of help self-care capacity alters the view of aspects contributing to the activities of daily living to having to live with a reduced life satisfaction [1].

The modern socio economic system makes old age a serious social problem. Planned and purposeful activities, which will constructively engage older persons according to their capacity, must be organized. Those aged who are suffering from illness need special services in their old age homes [7,8].

There is no huge geriatric home service in each city in Kurdistan. There is only one public Geriatric home in Erbil. The aim of the study was to identify the socio-

Assessment of Health Related to Quality of Life in Hypertensive and Diabetic Mellitus patients in Kurdistan/Iraq

تقييم نوعية الحياه للمرضى المصابين بارتفاع ضغط الدم والداء السكري في كوردستان/العراق

Jamal Kareem Shakor, Department of Nursing- Darbandikhan Technical Institute/Slemani Polytechnic University/ Slemani, Iraq.
Saleem Saaed Qader, Medical Research Centre, Hawler Medical University, Erbil, Iraq.
Bootan Hasan Ahmed, Department of Medical Surgical Nursing, school of Nursing And Midwifery, Hawler University of medical science, Erbil/Iraq.
Muaf Abdulla Karim, Department of Medical Surgical Nursing/School of Nursing and Midwifery, Tehran University of Medical Science, International Campus (TUMS-IC), Tehran, Iran.
E-mail: muafabdulla82@yahoo.com

لخلاصة
خلفية البحث: ارتفاع ضغط الدم وداء السكري هما من الامراض المزمنة لذلك فان لديهما التاثير السلبي على نوعية الحياه للمرضى المصابين به.
الهدف: الهدف من هذه الدراسة هو تقييم نوعية الحياة للمرضى المصابين بارتفاع ضغط الدم وداء السكري من خلال قياس حالتهم الاقتصادية والاجتماعية، وحالتهم الطبية والمتعلقات المرضية الاخرى.
المنهجية:أجريت دراسة مقطعية في كوردستان العراق لاستبيان نوعية الحياة الصحية للمرضى المصابين بارتفاع ضغط الدم وداء السكري للفترة من ١٥ اب ٢٠١٣ ولغاية ١ كانون الثاني ٢٠١٤.واستخدم مقياس الصحة المتعلقة بنوعية الحياة. والمسمى **SF -12** (الاستمارة المختصرة) وتم اختيار العينة المناسبة والمتوفرة لجمع البيانات.
النتائج: كان متوسط المسح الصحي للاستبيان SF-١٢ هو ٣٩.٠ ± ١.٦٤ درجه ومتوسط مكونات الحالة الجسمية هو ٣٦.٦ ± ١.٩ ومتوسط االحالة النفسية هو ٤١.٥ ± ١.٦.وكانت نوعية الحياة الصحية للمرضى المصابين بارتفاع ضغط الدم ومرض السكري ضعيفة في كردستان العراق ومن ناحية أخرى كانت نوعية لحياه الصحية للمرضى الذين يعانون من ارتفاع ضغط الدم اقل وكان المتوسط ٣٩.٧ ± ١.٧ مقارنة مع مرضى السكري ٤١.٩ ± ١.٦ وان المشاركون من الإناث وكبار السن وغير المتزوجات والتي ليس لديها وظيفة أو تقاعد كانت نوعية حياتهم اسوأ. تم استخدام الاختبار التائي لتحليل البيانات.
الاستنتاج: إن نوعية الحياة الصحية لمرضى ارتفاع ضغط الدم ومرض السكري كانت سيئة في كردستان بالمقارنة مع بلدان أخرى وخصوصا للمشاركات بالبحث من العنصر النسوي وغير المتزوجات وليس لديهن وظيفة أو تقاعد
التوصيات : توصي الدراسة باجراء دراسات اخرى على مدى اطول لتقييم نوعية الحياة لكلا المرضين (ارتفاع ضغط الدم والداء السكري) وبشكل منفصل .
الكلمات المفتاحية :الامراض المزمنة،الصحة،نوعية الحياة،كردستان/عراق

Abstract
Background: Hypertension and diabetes mellitus are chronic diseases, therefore; they had negative effect on quality of life of affected patients.
Aim: The aim of this study was to assess health related to quality of life of hypertensive and diabetes mellitus patients through measuring their socioeconomic status, medical conditioning and co-morbidity.
Methodology: This is cross sectional study that has been carried out in Kurdistan- Iraq. Health Survey Questionnaire, Short form-12 was used for measuring health related quality of life. Conventional sampling method was carried out for collecting of data. T- Test was used to analyze the data
Result: Mean Health Survey Questionnaire, Short Form-12 score was 39.0±1.64, mean of physical component summary was 36.6±1.9 and mean of mental component summary of was 41.5±1.6. Health related quality of life among hypertensive and diabetes mellitus patients were poor in Kurdistan. On the other hand, poor health related quality of life was less observed in hypertension patients 39.7±1.7 as compared with diabetic patients 41.9±1.6.

Assessment of Nurses' Knowledge Regarding Needle Prick Injury in Erbil Hospitals

تقييم معرفة الممرضات عن الإصابة بوخز الإبرة في مستشفيات اربيل

Muaf Abdulla Karim, Department of Medical Surgical Nursing, School of Nursing and Midwifery, **Tehran University of Medical Science, International Campus (TUMS-IC), Tehran, Iran.**
Sangar Muhammad Ahmed, BSc N, MPH, Assistant lecture/Hawler Medical University, College of Nursing.
Kaify Jamil Qadir, BSc N, MSc N, assistant lecture /Hawler Medical University, College of Nursing.
Alireza Nikbakht Nasrabadi, BSc N, MSc N, PhD N, Professor, Department of Medical Surgical Nursing, School of Nursing and Midwifery, **Tehran University of Medical Science, International Campus (TUMS-IC), Tehran, Iran**
muafabdulla٨٢@yahoo.com

الخلاصة:
الخلفية : في كل يوم يتعرض العاملين في المجال الصحى إلى المخاطر الوخز بالإبر الملوثة أو الأدوات الجارحة. الممرضات هم اكثر العاملين الذين يتعرضون الوخز الإبر فى المستشفى والتي قد تنتج عنها مخاطر الالتهابات نتيجة الممارسات غير الأمينة فى التعامل مع الوخز بالابر والادوات الحادة.
الهدف : تهدف الدراسة الى تقييم معلومات الممرضات والمخاطر الناتجة عن الاستخدام غير الجيد للوخز بالإبر والأدوات الحادة .
المنهجية : أجريت الدراسة الوصفية فى بعض المستشفيات مدينة اربيل وقد شملت العينة (٦٠) ممرض وممرضة وتم اختياره بطريقة غرضية و قد تم تصميم الاسئلة لتحقيق اهداف البحث.تم استخدام الوسائل الاحصائية الوصفية والتحليلية في تحليل النتائج بالاستخدام SPSS Version ١٩ لتحليل المعلومات
النتائج: أظهرت نتائج الدراسة بين اغلب الممرضات ان معلوماتهم جيدة حول المخاطر الناتجة عن الوخز بالإبر والأدوات الحادة . ولا توجد أي علاقة مؤثرة بين معرفة المرضين تجاه إصابات وخز الإبر والبيانات الديموغرافية.
الاستنتاج : استنتج الباحثون أن المعرفة الممرضون بشأن إصابات وخز الإبر بشكل عام كانت جيدة.
التوصيات: إجراء برنامج التعليم التربوي للممرضين بشأن إصابة وخز الإبرة لتحسين معرفتهم حول هذا الموضوع لحماية أنفسهم من مخاطرها.
مفاتيح الكلمات :معرفة ،ممرض ، ممرضة ، الوخز بالابر

Abstract:
Background Every day, health care worker are exposed to dangerous and deadly blood borne pathogens through contaminated needle sticks, sharps, or splash exposures. In hospitals, nurses are the first level of the staff whom contact with risk of infection from unsafe practices related to needles and sharps.
Objective: Assess of nurse knowledge regarding needle prick injuries and its risks in Erbil hospitals.
Methodology: A descriptive study was conducted in some hospitals of Erbil City. The Sample size for the study was ٦٠ nurses. Purposive sample was selected and Data was analyzed by using descriptive and inferential statistic by SPSS version (١٩).
Results: It showed that the most of nurses had good knowledge regarding the needle prick injuries and its risks. Also there are no significance relationship between nurse's knowledge and their demographic data.
Conclusion: The researchers concluded that the nurse's knowledge regarding needle prick injuries generally were good
Recommendation: conducting educational teaching programme for nurses regarding needle prick injury to improve their knowledge about it to protect themselves from its risks
Key words: Needle prick injury, Knowledge, Nurses.

INTRODUCTION:

In hospitals, nurses are the first level of the staff whom contact with risk of infection from unsafe practices related to needles and sharps. They are expected to undertake activities related to patient care with the beginning of their clinical years.

Assessing Level of Satisfaction of Breast Cancer Patients about Nursing Care in Rizgari Teaching Hospital in Erbil City

تقييم مستوى الرضى عند المرضى المصابون بسرطان الثدي حول الرعاية التمريضية في مستشفى رزكاري مدينه اربيل

Muaf Abdulla Karim, Department of Medical Surgical Nursing, School of Nursing and Midwifery, Tehran University of Medical Science, International Campus (TUMS-IC), Tehran/Iran.
Bootan Hassan Ahmed, B.Sc. in Nursing, M.Sc. in Advanced Nursing, Assistant Lecturer, College of Nursing / Hawler Medical University.
Dr. Mahvash Sals ali, Professor, School of Nursing and Midwifery, Tehran University of Medical Science /International Campus (TUMS-IC), Tehran, Iran.
E-mail: muafabdulla82@yahoo.com

الخلاصة:
خلفية البحث: قناعة المريض اصبحت من المؤشرات المهمة لنوعية وكفاءة الخدمات قبل الرعاية الصحية.
الهدف:الهدف من الدراسة هو تقييم مستوى قناعة المصابات بسرطان الثدي بالخدمات التمريضية في مستشفى رزكاري في اربيل كردستان العراق.
المنهجية: أجريت دراسة مقطعية في ردهة الاورام السرطانية في مستشفى رزكارى التعليمي ، عينة الدراسة تكونت من 60 مريض استغرقت الدراسة 6 اشهر ، من الاول من حزيران الى 20 ايلول 2014 . وقد استخدم اسلوب المقابلة الشخصية لجمع المعلومات وكانت المعلومات الديموغرافية تتعلق بالجنس، المستوى التعليمي والتاريخ المرضي للعائلة ومدته والدخل الاقتصادي ومدة البقاء في المستشفى ونوعية العلاج واستخدم مقياس لتقيم قناعات المريض واستخدام مربع كاي.
النتائج:اشترك (60) من المرضى في الدراسة واستخدم مقياس لتقيم قناعات المريض واستخدم مربع كاي لإيجاد العلاقة بين مستوى قناعة المصابات والصفات الديموغرافية والعوامل الديمغرافية. واظهرت النتائج بان(30) من المصابات كانت قناعاتهم مابين (60-80) وكانت لديهم قناعة جيدة حول الرعاية التمريضية و (30) منهم كانت درجاتهم مابين (38-59) حول نسبة قناعتهم.
الاستنتاج:اظهرت الدراسة بان المرضى كانت لديهم اتجاها ايجابيا حول الخدمات التمريضية .
التوصيات : اجراء دراسات اوسع وشمول مستشفيات اخرى.
مفاتيح الكلمات:التقييم، مستوى القناعة، مرضى السرطان، الرعاية التمريضية.

Abstract:
Background: Patients' satisfaction has become an established outcome indicator of the quality and efficiency of the health care system.
Objective The aim of this study was to assess the level of Breast cancer patients' satisfaction toward nursing care in selected hospital of Erbil city in Iraqi Kurdistan Region.
Materials and Methods: A descriptive study was designed at oncology ward of Rizgari Teaching Hospital. Participants were interviewed and questions were asked. It started from 1st June to 20th September 2014.The questionnaire included demographical data: gender, educational qualification, history of cancer in the family, family income, type of hospital room and duration of stay in hospital, and type of treatment and frequency of hospitalization were analyzed by using Rating Scale.
Results: 60 patients participated in this study. Likert scale was used to assess the levels of satisfaction. Chi-square analysis was computed to find the associations between the levels of satisfaction and demographic variables. 30 patients had a scored between 60-80 and considered to have a good level of satisfaction toward nursing care. However, 30 participants had scoring between 38-59 and are considered to have average level of satisfaction.
Conclusion: The study concluded breast cancer patients had positive attitude toward nursing care. be conducted to assess the level of breast cancer patients' satisfaction toward nursing care
Recommendations: Further research including further oncology hospitals.

Keywords: Assess, Level of satisfaction, Cancer patients, Nursing care.

INTRODUCTION:

Cancer has become a major health problem in world. Recently, nearly 14.1 million cancer cases have been diagnosed breast cancer both in developed and less developed countries [(1)]. The incidence rate is almost 25% higher in men than in women [(2)]. However, among women the most

2- Vian Haji Rasul

First Name	Last Name	Program	Level	School
Vian Haji	Rasul	Nursing	PhD	Nursing

Published Articles:

	Title of the Article
1	Influencing factors on cervical cancer screening from the Kurdish women's perspective: A qualitative study

Influencing factors on cervical cancer screening from the Kurdish women's perspective: A qualitative study

Rasul VH*, Cheraghi MA**, Behboodi Moqadam Z***
*Faculty of Nursing and Midwifery, International Campus, Tehran University of Medical Sciences, Tehran, Iran; Shaqlawa Techniqueal Institute, Erbil Polytechnique University, Kurdistan Region, Iraq,
**Faculty of Nursing and Midwifery, International Campus, Tehran University of Medical Sciences, Tehran, Iran,
***Reproductive Health Faculty of Nursing and Midwifery, International Campus, Tehran University of Medical Sciences, Tehran, Iran

Correspondence to: Mohammad Ali Cheraghi, PhD, Associate professor in Nursing,
Faculty of Nursing and Midwifery, International Campus, Tehran University of Medical Sciences, Tehran, Iran,
Phone: (+98) 2166933600, Fax: (+98) 2166941668, E-mail: mcheraghi@tums.ac.ir

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Abstract

Aim: This study was aimed to explore and describe the Kurdish women's perception of cervical cancer screening.

Methods: A qualitative design based on a conventional content analysis approach. Purposive sampling was applied to 19 women chosen, who had a Pap smear or refused to have one. The study was performed in the Kurdistan Region, Iraq. Semi-structured in-depth individual interviews were carried out to collect data.

Results: Four main themes including conflict, belief, and awareness about cervical cancer screening and socio-cultural factors emerged during data analysis.

Conclusion: Cervical cancer has a high mortality rate in the developing countries. However, only a few Kurdish women participated in the cervical cancer screening in the Kurdistan Region, Iraq. Understanding the factors associated with the women's perception of cervical cancer could guide future educational planning and clinical interventions improve the cervical cancer screening.

Keywords: cervical cancer screening, Kurdish women, content analysis, qualitative research

Introduction

Cervical cancer is a major health problem and the second leading cause of cancer deaths among women worldwide. While about 500,000 women develop cervical cancer per annum, the survival rate is as low as 50% [1,2]. In addition, a great majority (over 86%) of the new cases of cervical cancer are reported from developing countries [3,4]. The primary aim of cervical cancer screening is to decrease the incidence of invasive cervical cancer by the early detection and treatment of the precursors of the cancer. The secondary aim is to reduce the mortality by the timely detection of the invasive cancers [5].

According to the World Health Organization (WHO), the crude incidence rate of cervical cancer in Iraq is 2.1 per 100,000 women of all ages. Moreover, 10.21 million Iraqi women aged 15 years and older are at risk of developing the disease [6].

The Kurdistan Region is an autonomous region in Northern Iraq. It covers an area of about 40,000 square kilometers and holds 8.35 million people (from 36 million people living in Iraq) [7].

Although some independent reports from different cities of Iraq have shown an increased incidence of different types of cancer, limited research has evaluated the cancer incidence in the country, especially in the Kurdistan Region. In the first study on cancer incidence in the Kurdistan Region, Ramadhan et al. (2011) reported evidence of an increased risk of all cancers, including cervical cancer, in recent years [8]. Exposure to numerous environmental and epidemiological changes in the Kurdistan Region of Iraq has elevated the risk of cancer in this region. For instance, due to the persistent effects of the chemical bombardment of Halabja City, Kurdistan, in 1988, the incidence of cancer in this city is 10 times higher than the normal rate [9].

According to the WHO scanning, even at every 10 years, can decrease the incidence of cervical cancer by 64% [10]. The idea behind the PAP-test is that cellular changes that may develop into cancer are detected at such an early stage that they can be removed through a simple operation, thus preventing the cancer [11]. The natural history of an invasive CC, a disease with long preneoplastic changes, more than 10 years in the majority of the cases, generally allows its early detection [12]. The survival rate of cervical cancer is directly related to the stage of diagnosis, i.e. patients with an early diagnosis have a significantly higher survival rate than those suffering from metastatic disease (91% vs. 14%]) [13,14].

3- Tiran Jamil Piro

First Name	Last Name	Program	Level	School
Tiran Jamil	Piro	Nursing	PhD	Nursing

Published Articles:

	Title of the Article
1	Iraqi Nurses' Perspectives on Safety Issues in Maternity Services

Nurs Midwifery Stud. 2015 September; 4(3): e29529. DOI: 10.17795/nmsjournal29529

Published online 2015 September 23. **Research Article**

Iraqi Nurses' Perspectives on Safety Issues in Maternity Services

Tiran Jamil Piro,[1] Shahrzad Ghiyasvandian,[2,*] and Mahvash Salsali[2]

[1]Medical-Surgical Nursing Department, School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, IR Iran
[2]School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Shahrzad Ghiyasvandian, School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, IR Iran. Tel: +98-2166937120, E-mail: shghiyas@tums.ac.ir

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Background: Studies introduce maternal and neonatal safety phenomena as important challenges to the public health, particularly in low-income countries. However, few researches are conducted on the identification of safety issues in maternity hospitals in Iraq. It was the first study on nurses' perspectives on safety issues in Kurdistan, Iraq.
Objectives: The current study aimed to describe nurses' perspectives on what constitutes a safe maternity service in Kurdistan, Iraq.
Patients and Methods: A qualitative design, based on a content analysis approach, was used. Ten Kurdish nurses who worked in the delivery room of Kurdistan, Iraq maternity hospital were recruited through purposive sampling. Semi-structured interviews were performed to collect data. All interviews were audiotaped and transcribed verbatim. Sampling continued to the level of data saturation. Data analysis was performed based on the steps suggested by Graneheim and Lundman.
Results: Thematic analysis led to the identification of six main categories including stressful job, lack of schedule and job description, providing care with limited resources, professional unaccountability, regional sociopolitical factors, and inadequate training.
Conclusions: Iraqi nurses identified factors such as limited health resources, lack of job description, and professional unaccountability as major safety issues in maternity services. These findings alarm the need to ensure the provision of females and neonates with appropriate care. This, however, would require coordination between Iraqi Kurdistan health authorities to provide midwifery care facilities, high-quality and relevant staff training, and an effective healthcare system in the maternity units.

Keywords: Qualitative Research; Nurses; Safety; Maternal-Child Nursing

1. Background

Every day, four million infants (younger than one month old) and half a million mothers die due to pregnancy-related causes. Since 99% of these deaths occur in low- and middle-income countries, research is warranted to identify the root causes of maternal and infant safety issues and propose solutions to such issues in lower income countries (1, 2). Pregnancy-related mortality is a serious health and social problem affecting many women and their families each year (3-6). Nurses working in maternity services believe that numerous problems can result in safety issues both for mothers and their babies in delivery rooms (7-10). In Middle East countries, access to a health professional for childbirth care is no longer a key constraint; the majority of women now deliver with doctors or midwives in maternal units (11). Maternal and neonatal care is identified as a patient safety problem in middle-income countries such as Iraq (11, 12). The Iraqi health care system is seriously impacted by different external and internal fights, international sanctions, and sociopolitical instability in recent years (13). Prenatal health services in Kurdistan, Iraq are similarly affected by problems common to maternity care services such as poor qualification of health care providers including nurses and midwives (13).

In the maternity hospital of Kurdistan, Iraq, a group of nurses are responsible for maternity care and they provide services during and after birth. In the absence of educated midwives, few nurses with university education work in departments such as maternity wards and delivery rooms. Previous studies highlighted the increasing challenge that nurses face to prepare themselves for the real clinical world of nursing. These nurses are not willing to work in the mentioned departments and also did not receive relevant trainings (14). Since they play the main role in midwifery and nursing care provisions, especially during labor, several patient safety and care issues have emerged in this department. However, the actual quality of maternity care and safety for mothers and their neonates, i.e. a great number of mothers especially in middle-income countries, through perspectives and statements of health care provider teams, receive relatively less research attention (2). There is also little information regarding the effectiveness of midwifery and nursing care on maternal safety, particularly among females in labor, according to statements and experiences of midwifes and maternity nurses (2). Hence, the current study was conducted on this problem based on nurses' statements. As the authors were not able to find any

4- Morteza Malekian

First Name	Last Name	Program	Level	School
Morteza	Malekian	Nursing	PhD	Nursing

Published Articles:

	Title of the Article
1	Iranian Clinical Nurses' Activities for Self-Directed Learning: A Qualitative Study

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Published by Canadian Center of Science and Education

Iranian Clinical Nurses' Activities for Self-Directed Learning: A Qualitative Study

Shahrzad Ghiyasvandian[1], Morteza Malekian[2] & Mohammad Ali Cheraghi[1]

[1] School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran

[2] School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran

Correspondence: Morteza Malekian, School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran. Tel(Fax): 98-313-265-7954. E-mail: mortezamalekian@ymail.com

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Abstract

Background: Clinical nurses need lifelong learning skills for responding to the rapid changes of clinical settings. One of the best strategies for lifelong learning is self-directed learning. The aim of this study was to explore Iranian clinical nurses' activities for self-directed learning.

Methods: In this qualitative study, 23 semi-structured personal interviews were conducted with nineteen clinical nurses working in all four hospitals affiliated to Isfahan Social Security Organization, Isfahan, Iran. Study data were analyzed by using the content analysis approach. The study was conducted from June 2013 to October 2014.

Findings: Study participants' activities for self-directed learning fell into two main categories of striving for knowledge acquisition and striving for skill development. The main theme of the study was 'Revising personal performance based on intellectual-experiential activities'.

Conclusions: Study findings suggest that Iranian clinical nurses continually revise their personal performance by performing self-directed intellectual and experiential activities to acquire expertise. The process of acquiring expertise is a linear process which includes two key steps of knowledge acquisition and knowledge development. In order to acquire and advance their knowledge, nurses perform mental learning activities such as sensory perception, self-evaluation, and suspended judgment step-by-step. Moreover, they develop their skills through doing activities like apprenticeship, masterly performance, and self-regulation. The absolute prerequisite to expertise acquisition is that a nurse needs to follow these two steps in a sequential manner.

Keywords: clinical nurses, self-directed learning, lifelong learning, qualitative study, Iran

1. Introduction

Rapid scientific advances have significantly decreased the half life of medical sciences (Gyawali, Jauhari, Shankar, Saha, & Ahmad, 2011) and posed big challenges to healthcare systems and fields, including nursing (Yang & Jiang, 2014). Accordingly, nurses are expected to have certain kinds of learning skills for managing rapid changes in healthcare settings. Moreover, as nursing is an applied science, nurses need to learn how to transfer their knowledge to practice. Papathanasiou, Tsaras and Sarafis (2014) also noted that nurses' active involvement in their own learning is an absolute prerequisite to lifelong learning.

One of the good strategies for lifelong learning is self-directed learning (Fisher & King, 2010). The concept of self-directed learning (SDL) originates from the Adult Learning Theory. This theory suggests that adults are pragmatic and problem-focused individuals whose learning is mainly affected by experiential rather than passive approaches (Roberson, 2011). SDL is a process in which learners actively participate in identifying their own learning needs, setting learning goals, allocating resources, developing and implementing appropriate strategies and plans, and evaluating learning outcomes either independently or with others' help (Knowles, Holton, & Swanson, 2008). It could help nurses identify their learning needs, plan for fulfilling the identified needs, and turn into independent experts (Montin & Koivisto, 2014). The positive outcomes of SDL include, but not limited to, greater self-control, self-confidence, autonomy, and lifelong learning skills (O'Shea, 2003).

5- Alireza Nikbakht Nasrabadi

First Name	Last Name	Program	Level	School
Alireza	Nikbakht Nasrabadi	Nursing	PhD	Nursing &Midwifery

Published Articles:

	Title of the Article
1	The Prevalence of Violence Against Iranian Women and Its Related Factors

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The Prevalence of Violence Against Iranian Women and Its Related Factors

Alireza Nikbakht Nasrabadi[1], Nahid Hossein Abbasi[1,2] & Neda Mehrdad[3]

[1] School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran

[2] Islamic Azad University of Ahvaz, Ahvaz, Iran

[3] Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Correspondence: Nahid Hossein Abbasi, School of Nursing and Midwifery, Tehran University of Medical Sciences, International Campus(TUMS-IC)Tehran, Iran; Islamic Azad University of Ahvaz, Nosrat st, Tohid sq. Ahvaz 1419733171, Iran. Tel: 98-21-66-921-144.. E-mail: nahid.habbasi @gmail.com

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doi:10.5539/gjhs.v7n3p37 URL: http://dx.doi.org/10.5539/gjhs.v7n3p37

Abstract

Background: Domestic violence against women is a public health problem with negative consequences, and it is an intractable and widespread problem. This type of violence affects the stability of the family.

Aim: The aim of this study was to estimate the prevalence of any violence against women referring to health centers and explore the associated risk factors with violence in Ahvaz, Iran.

Methods: A cross-sectional study was conducted on randomly chosen samples of 368 married women aged between 15-55 years in 2013. The samples were divided to two groups, with abused experience and without abused experience. The data were amassed by questionnaire form.

Results: The prevalence of violence against women was found to be around 63.8%, among them 58.8% were emotional abuse. The majority of women (84%) had never gone to a counseling center. Findings show 47% of women were silent, 27% got in a fight, 7% screamed, 6% abused their children, and 5% threw things when occurred violence against them. Experience of violence in women correlated with the marriage age of woman, numbers of children, and difference of marriage age between couple, marriage age of men, employed women, uneducated women and the rate of drugs use in their husbands.

Conclusions: Nurses and other health care providers can and should play a major role in empowering women living with violence and promote education, social policies and attitudes that proactively prevent violence.

Keywords: Iran, prevalence, violence, women

1. Background

Violence against women is a universal reality and is common in all countries, cultures and societies. It is at not rate acceptable or justifiable and is to be considered as one of the major women health problems. It is not only a women's dominant problem but also a major issue in women's human rights (WHO, 2013). The term violence against women includes forms of violence such as sexual partner violence and non-sexual partner violence. Evidence shows both a form of violence is widespread throughout the world, and it affects women's physical, sexual and mental health. These findings send the world a very vigorous message that violence against women is not a trivial subject related to some societies; rather it is a universal problem and challenge whose prevention seems to be vital (WHO, 2011; WHO, 2013). Women are significantly more likely than men to be perpetrators of dating violence during young adulthood (38% vs. 19%) (Jain et al., 2010). Based on the World Health Organization's report, the rate of violence against women is as following: Eastern Mediterranean countries (37%), African countries (36.3%) American countries (29.8%), European countries (25.4%), Western Pacific (24.6%) and other countries with high salaries (23.2%) (WHO, 2013).

Violence against women is a multi-dimensional phenomenon which is defined based on ethical, cultural and legal attractions and is an activity or attitude which hurts women. In fact, it is a real physical, sexual, emotional,

Chapter Seven

School of Nutritional Sciences

1- Abdel Hamid el Bilbeisi

First Name	Last Name	Program	Level	School
Abdel	Hamid el Bilbeisi	Nutritional Sciences	PhD by Research.	Nutrition

Published Articles:

	Title of the Article
1	Dietary Patterns and Metabolic Syndrome among Type 2 Diabetes Patients in Gaza Strip, Palestine
2	The Association between Physical Activity and the Metabolic Syndrome among Type 2 Diabetes Patients in Gaza Strip, Palestine
3	The Prevalence of Metabolic Syndrome and Its Related Factors among Adults in Palestine: A Meta-Analysis

ORIGINAL ARTICLE

Dietary Patterns and Metabolic Syndrome among Type 2 Diabetes Patients in Gaza Strip, Palestine

Abdel Hamid el Bilbeisi[1], Saeed Hosseini[1], Kurosh Djafarian[1]*

OPEN ACCESS

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Affiliation and Correspondence:
[1]Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, International Campus (TUMS- IC), Tehran, Iran
*Email: kdjafarian@tums.ac.ir

ABSTRACT

BACKGROUND: ***The prevalence of metabolic syndrome is raising worldwide; however, the role of diet in the origin of metabolic syndrome is not understood well. This study identifies major dietary patterns among type 2 diabetes mellitus patients with and without metabolic syndrome; and its association with metabolic syndrome components in Gaza Strip, Palestine.***
METHODS: ***This cross sectional study was conducted among 1200 previously diagnosed type 2 diabetes mellitus (both genders, aged 20 - 64 years) patients receiving care in primary healthcare centers in Gaza Strip, Palestine. Metabolic syndrome was defined based on the International Diabetes Federation criteria; dietary patterns were evaluated using a validated semi-quantitative food frequency questionnaire. Statistical analysis was performed using SPSS version 20.***
RESULTS: ***Two major dietary patterns were identified by factor analysis: Asian-like pattern and sweet-soft drinks-snacks pattern. After adjustment for confounding variables, patients in the highest tertile of the Asian-like pattern characterized by a high intake of whole grains, potatoes, beans, legumes, vegetables, tomatoes and fruithad a lower odds for (Metabolic syndrome, central obesity, high triglycerides, low HDL cholesterol and high blood pressure), (OR 0.766 CI 95% (.642-.914)), (OR 0.797 CI 95% (.652-.974)), (OR 0.791 CI 95% (.687-.911)), (OR 0.853 CI 95% (.743-.978)) and (OR 0.815 CI 95% (.682-.973)) respectively, (P value < 0.05 for all). No significant association was found between the sweet-soft drinks-snacks pattern with metabolic syndrome and its components.***
CONCLUSION: ***The Asian-like pattern may be associated with a lower prevalence of metabolic syndrome and its components among type 2 diabetes patients.***
KEYWORDS: ***Dietary patterns, Factor analysis, Metabolic syndrome, Type 2 diabetes mellitus, Palestine***

INTRODUCTION

Metabolic syndrome (MetS) is a constellation of abnormal cardio metabolic factors that increase risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM)(1). MetS is a major health problem worldwide; based on the International Diabetes Federation (IDF) appreciation about one quarter of the world's adult population

DOI: http://dx.doi.org/10.4314/ejhs.v27i3.4

ORIGINAL ARTICLE

The Association between Physical Activity and the Metabolic Syndrome among Type 2 Diabetes Patients in Gaza Strip, Palestine

Abdel Hamid el Bilbeisi[1], Saeed Hosseini[1], Kurosh Djafarian[1]*

OPEN ACCESS

Citation: Abdel H., Saeed H., Kurosh D. The association between physical activity and the metabolic syndrome among type 2 diabetes patients in Gaza Strip, Palestine. J Health Sci 2017;27(3):273. doi: http://dx.doi.org/10.4314/ejhs.v27i3.9
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Competing Interests: The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.
Affiliation and Correspondence:
[1]Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, International Campus (TUMS- IC), Tehran, Iran
*Email: kdjafarian@tums.ac.ir

ABSTRACT

BACKGROUND: Metabolic syndrome is a major health problem worldwide. Globally, the World Health Organization identified physical inactivity as the fourth leading risk factor for mortality. This study was conducted to evaluate the association between physical activities and metabolic syndrome and diabetes complications among type 2 diabetes patients in Gaza Strip, Palestine.
METEHODS: This cross-sectional study was conducted among 1200 previously diagnosed type 2 diabetes mellitus patients (from both genders, aged 20 to 64 years) receiving care in the primary health care centers. Metabolic syndrome was defined based on the International Diabetes Federation criteria. The International Physical Activity Questionnaire was used to measure physical activity. Statistical analysis was performed using SPSS version 20.
RESULTS: A significant inverse association was found between inactive patients and metabolic syndrome. In our study, 93.7% of inactive patients, 66.4% of active patients and 23.5% of very active patients had metabolic syndrome (OR .048 CI 95% (.03-.072)), (OR .787 CI 95% (.59-1.03)) and (OR 15.9 CI 95% (11.8-21.3)) respectively. Our results showed a significant inverse association between physical activity levels and anthropometric measurements in both gender. Moreover, a significant association was found between physical activity levels and triglycerides, HDL-cholesterol and blood pressure in both sexes (P value < 0.05 for all) and diabetes complications (P value < 0.05 for all).
CONCLUSION: We conclude that low levels of physical activity are associated with increased prevalence of metabolic syndrome. Furthermore, inactive patients had a high percentage of diabetes complications among type 2 diabetes patients in Gaza Strip, Palestine.
KEYWORDS: Physical activity, metabolic syndrome, type 2 diabetes mellitus, Gaza, Palestine

DOI: http://dx.doi.org/10.4314/ejhs.v27i3.9

REVIEW

The Prevalence of Metabolic Syndrome and Its Related Factors among Adults in Palestine: A Meta-Analysis

Abdel Hamid el Bilbeisi[1], Sakineh Shab-Bidar[2], Diane Jackson[3], Kurosh Djafarian[1*]

ABSTRACT

BACKGROUND: ***Metabolic syndrome (MetS)is increasingly becoming a challenging public health issue in Palestine. The current burden of MetS in the country is unknown. There has been limited research on the prevalence of MetS. This meta-analysis is the first to estimate the population prevalence of MetS and its related factors among adults in Palestine.***

METHODS: ***A PRISMA systematic search appraisal and meta-analysis were conducted. A systematic literature search of PubMed, Scopus and Google Scholar was conducted in December 2014 up to February 2015. Generic, methodological and statistical data was extracted from the eligible studies which reported MetS prevalence. A random effect meta-analysis was conducted on crude MetS prevalence rates. Heterogeneity was assessed by Cochran's Q and I^2 tests. Subgroup analyses were also performed according to the predefined criteria.***

RESULTS: ***The literature search yielded a total of 49 studies. Eight papers were included in the final analysis with sample size ranging 163 to 992. In addition, 2937 cases with MetS among people aged 15 years or more were estimated in Palestine between 2001 and 2014. There was high heterogeneity among studies (I^2 = 95.8% p<0.001). The prevalence of MetS was 37.0% among adult Palestinians population ranging from 17 to 59.5%. Subgroup analysis did not show source of heterogeneity based on subject's health status and MetS criteria.***

CONCLUSION: ***Our meta-analysis clearly demonstrates that MetS is highly prevalent (37.0%) among Palestinian adults. The high prevalence of MetS in Palestine should be seriously considered and planners should take steps to reduce it.***

KEYWORDS: ***Prevalence, Metabolic syndrome, Meta-analysis, Palestine***

OPEN ACCESS

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Affiliation and Correspondence:
[1]Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences - International Campus IC-TUMS) Tehran, Iran
[2]Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran
[3]Public Health Nutrition Research Group, Rowett Institute of Nutrition and Health, Aberdeen University, Aberdeen, Scotland, UK
[*]Email: kdjafarian@tums.ac.ir

DOI: http://dx.doi.org/10.4314/ejhs.v27i1.10

2- Ahmed Abdurahman

First Name	Last Name	Program	Level	School
Ahmed A.	Abdurahman	Public Health Nutrition	M.Sc.	Nutrition

Published Articles:

	Title of the Article
1	Household Food Insecurity May Predict Underweight and Wasting among Children Aged 24–59 Months

ECOLOGY OF FOOD AND NUTRITION
http://dx.doi.org/10.1080/03670244.2016.1207069

Routledge
Taylor & Francis Group

Household Food Insecurity May Predict Underweight and Wasting among Children Aged 24–59 Months

Ahmed A. Abdurahman[a], Khadijeh Mirzaei[b], Ahmed Reza Dorosty[b], A. Rahimiforoushani[c], and Haji Kedir[d]

[a]Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran; [b]Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran; [c]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran; [d]College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia

ABSTRACT

The aim of this study was to examine the association between household food insecurity and nutritional status among children aged 24–59 months in Haromaya District. Children (N = 453) aged 24–59 months were recruited in a community-based cross-sectional survey with a representative sample of households selected by a multistage sampling procedure in Haromaya District. Household Food Insecurity Access Scale and anthropometry were administered. Multinomial logistic regression models were applied to select variables that are candidate for multivariable model. The prevalences of stunting, underweight, and wasting among children aged 24–59 months were 61.1%, 28.1%, and 11.8%, respectively. The mean household food insecurity access scale score was 3.34, and 39.7% of households experienced some degree of food insecurity. By logistic regression analysis and after adjusting for the confounding factors, household food insecurity was significantly predictive of underweight (AOR = 2.48, CI = 1.17–5.24, p = .05) and chronic energy deficiency (AOR = 0.47, CI = 0.23–0.97, p = .04) and marginally significant for wasting (AOR = 0.53, CI = 0.27–1.03, p = .06). It is concluded that household food security improves child growth and nutritional status.

KEYWORDS

Ethiopia; household food insecurity; preschool children; undernutrition

Undernutrition is the leading cause of child death, contributing to more than three million deaths every year (SAVE 2010). Globally, 159 million children under 5 years old were stunted (23.8%), 50 million were wasted (7.5%), and 16 million were severely wasted (2.4%) in 2014 (UNICEF, WHO, and WB 2014). A significant number of the world's undernourished children are living in countries where recurrent food insecurity and prolonged disasters occur, and these aggravate their vulnerability. In these countries, factors such as repeated occurrence of communicable diseases, inadequate caring

3- Maryam Mazaherioun

First Name	Last Name	Program	Level	School
Maryam	Mazaherioun	Nutritional Sciences	PhD	Nutritional Sciences & Dietetics

Published Articles:

	Title of the Article
1	Benefcial effects of n-3 polyunsaturated fatty acids on adiponectin levels and AdipoR gene expression in patients with type 2 diabetes mellitus: a randomized, placebo-controlled, double-blind clinical trial

Beneficial effects of n-3 polyunsaturated fatty acids on adiponectin levels and AdipoR gene expression in patients with type 2 diabetes mellitus: a randomized, placebo-controlled, double-blind clinical trial

Maryam Mazaherioun[1], Ahmad Saedisomeolia[1,2], Mohammad Hassan Javanbakht[1], Fariba Koohdani[1], Mohammad Reza Eshraghian[3], Mahmoud Djalali[1]

[1]Department of Cellular and Molecular Nutrition, School of Nutritional Sciences and Dietetics, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[2]Discipline of Nutrition and Metabolism, School of Molecular Bioscience, University of Sydney, NSW, Sydney, Australia
[3]Department of Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

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Corresponding author:
Prof. Mahmoud Djalali
Department of Cellular and Molecular Nutrition
School of Nutritional Sciences and Dietetics
International Campus
Tehran University of Medical Sciences
HojatDoost St
14155/6117 Tehran, Iran
Phone: +98 (21) 88955979
Fax: +98 (21) 88955979
E-mail: mjalali87@yahoo.com

Abstract

Introduction: There is evidence that n-3 polyunsaturated fatty acids (n-3 PUFAs) exert beneficial effects to improve type 2 diabetes mellitus (T2DM), but its complications remain poorly understood. Hypoadiponectinemia is one of the important mechanisms responsible for T2DM which necessitates developing novel therapeutic strategies. We aimed to determine the effect of n-3 PUFA supplementation on circulating adiponectin and mRNA expression of adiponectin receptors (AdipoR1, AdipoR2) and Sirt-1 in T2DM patients.
Material and methods: A randomized, double-blind, placebo-controlled trial of 10-week follow-up of n-3 PUFAs (2.7 g/day) vs. placebo in T2DM patients (n = 88) was conducted. In detail, T2DM patients (n = 44) were treated with n-3 PUFAs and the remainder received placebo. Anthropometric and metabolic characteristics were assessed in all participants. Circulating level of adiponectin and mRNA expression of AdipoR1, AdipoR2 and Sirt-1 were measured in peripheral blood mononuclear cells (PBMC) using real-time polymerase chain reaction before and after the intervention.
Results: It was found that n-3 PUFAs increased AdipoR1 gene expression (fold change = 1.321 in n-3 PUFAs vs. 1.037 in placebo) and AdipoR2 mRNA (fold change = 1.338 in n-3 PUFAs vs. 1.034 in placebo). No significant changes were observed for Sirt-1 expression. The serum level of adiponectin significantly (p = 0.035) increased in n-3 PUFAs (5.09 to 5.58 μg/ml) but remained unchanged in the placebo group.
Conclusions: Daily supplementation with n-3 PUFAs (2.7 g) was effective to significantly improve gene expression of AdipoR1 and AdipoR2 and the serum level of adiponectin in T2DM patients. Therefore, n-3 PUFAs might emerge as an adjuvant for current antidiabetic therapies. However, confirmatory long-term studies are required.

Key words: n-3 poly-unsaturated fatty acids, type 2 diabetes mellitus, randomized controlled trial, adiponectin, Sirt-1, adiponectin receptors, peripheral blood mononuclear cells.

4- Sajjad Moradi

First Name	Last Name	Program	Level	School
Sajjad	Moradi	Nutritional Sciences	M.Sc.	Nutritional Sciences & Dietetics

Published Articles:

	Title of the Article
1	Adipokines may mediate the relationship between resting metabolic rates and bone mineral densities in obese women

Osteoporos Int (2017) 28:1619–1629
DOI 10.1007/s00198-017-3914-6

ORIGINAL ARTICLE

Adipokines may mediate the relationship between resting metabolic rates and bone mineral densities in obese women

S. Moradi[1,2] · K. Mirzaei[3] · A. A. Abdurahman[2] · S. A. Keshavarz[4]

Received: 12 May 2016 / Accepted: 4 January 2017 / Published online: 23 January 2017

Abstract
Summary The researchers sought to test the possible link between resting metabolic rate and bone mineral density through four adipokines. Participants with lower resting metabolic rate (RMR) per kilogram demonstrated higher total bone mineral density (BMD), total T-score, and total Z-score. Omentin-1 had a mediatory effect on the relationship between RMR/kg of body weight and bone parameters.
Introduction The previous results of studies regarding the links between obesity and bone health are controversial. For this reason, the researchers sought to test the possible link between RMR and BMD through the following four adipokines: vaspin, retinol binding protein 4, angiopoietin-like 6 (ANGPL6), and omentin-1.
Methods We enrolled 312 obese Iranian women (30 ≤ body mass index <40) in this cross-sectional study. In order to examine the association of serum adipokine levels with RMR and BMD, the participants were grouped based on RMR per body weight. Body composition, dietary intake, bone mineral density, and resting metabolic rate were assessed in all participants. Serum adipokine levels were quantified by the enzyme-linked immunosorbent assay (ELISA) method.
Results Low levels of RMR/kg were strongly associated with higher weight, body mass index, fat mass, and visceral fat levels. In fact, participants with an RMR/kg of body weight <20 kcal/24 h/kg were more obese ($p < 0.05$). Another noteworthy finding was that participants with lower RMR/kg demonstrated higher total BMD, total T-score, and total Z-score. Our results showed that omentin-1 had a mediatory effect on the relationship between RMR per kilogram of body weight and bone parameters ($p < 0.05$). Nevertheless, other adipokines such as vaspin, retinol-binding protein 4 (RBP4), and ANGPL6 did not affect the relationship between RMR and BMD ($p > 0.05$).
Conclusions The inhibitory effect of omentin-1 on TNF-alpha seems to be able to reduce the amount of circulating leptin as adipokine, affecting energy expenditure and improving bone loss induced by estrogen deficiency and controlled effect of RMR on BMD.

Keywords Adipokine · Bone mineral density · Obesity · Omentin-1 · Resting metabolic rate

Abbreviations

BH	Body height
BMI	Body mass index
BIA	Bioelectrical impedance analysis
BMD	Bone mineral density
BW	Body weight
RMR	Resting metabolic rate
DXA	Dual-energy X-ray absorptiometry
EDTA	Ethylenediaminetetraacetic acid

✉ K. Mirzaei
mirzaei_kh@tums.ac.ir

1 Osteoporosis Research Center, Endocrine Diseases and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran

2 Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences International Campus (TUMS-IC), Tehran, Iran

3 Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), P.O.Box:14155-6117, Tehran, Iran

4 Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran

5- Farzaneh Rezagholizadeh

First Name	Last Name	Program	Level	School
Farzaneh	Rezagholizadeh	Nutritional Sciences	M.Sc.	Nutritional Sciences & Dietetics

Published Articles:

	Title of the Article
1	A posteriori healthy dietary patterns may decrease the risk of central obesity: findings from a systematic review and meta-analysis
2	Association between the prevalence of obstructive sleep apnoea and the severity of keratoconus

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Review Article

A posteriori healthy dietary patterns may decrease the risk of central obesity: findings from a systematic review and meta-analysis

Farzaneh Rezagholizadeh[a], Kurosh Djafarian[b], Samaneh Khosravi[c], Sakineh Shab-Bidar[d,*]

[a] Department of Community Nutrition, School of Nutritional Sciences and Dietetics, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[d] Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Central obesity is a pivotal component of metabolic syndrome, and several studies have investigated the association of dietary patterns and central obesity. However, findings of studies are inconclusive. Therefore, we aimed to conduct the present study to summarize the available data regarding the association of a posteriori dietary patterns and central obesity in adults to test the hypothesis of whether a highly healthy dietary pattern is associated with decreased risk of central obesity. We searched all published English studies to identify related articles in MEDLINE, EMBASE, and Google Scholar databases up to December 2015. The meta-analysis was conducted on 13 studies including 12 cross-sectional studies and 1 case-control study that reported odds ratios (ORs), relative risks, or hazard ratios for risk of central obesity. The between-study variance was assessed using Cochran Q test and I^2. Subgroup analysis was applied to define possible sources of heterogeneity. The highest category of healthy/prudent patterns compared with those in the lowest category resulted in significant decrease in the risk of central obesity (pooled OR was 0.81 [95% confidence interval 0.66-0.96]). Pooled results indicated a higher nonsignificant increase in the risk of central obesity (OR was 1.16 [95% confidence interval 0.96-1.35]) in the highest category of Unhealthy/Western pattern compared with those in the lowest category. There was also a significant heterogeneity in the observed associations. We found that sex, country, and continent were the potential sources of heterogeneity. The results of the present meta-analysis showed that a posteriori healthy dietary patterns may decrease the risk of central obesity, whereas no significant association was found between unhealthy dietary patterns and central obesity. Together, the results highlight the need for well-designed and carefully carried out clinical trials based on dietary patterns in future research.

Abbreviations: BMI, body mass index; CI, confidence interval; FFQ, food frequency questionnaire; MetS, metabolic syndrome; OR, odds ratio; PCA, principle component analysis; WC, waist circumference.

* Corresponding author. Tel.: +98 2188955979.
E-mail addresses: farzaneh_rezagholizadeh@yahoo.com (F. Rezagholizadeh), kdjafarian@tums.ac.ir (K. Djafarian), s.khosravi86@ymail.com (S. Khosravi), s_shabbidar@tums.ac.ir (S. Shab-Bidar).

Association between the prevalence of obstructive sleep apnoea and the severity of keratoconus

Mohammad Naderan,[1] Farzaneh Rezagholizadeh,[2] Masoome Zolfaghari,[1] Morteza Naderan,[1] Mohammad Taher Rajabi,[3] Mohammad Amin Kamaleddin[4]

[1]School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[2]School of Nutritional Sciences and Dietetics, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[3]Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences,Tehran, Iran
[4]Department of Biotechnology, College of Science, University of Tehran, Tehran, Iran

Correspondence to
Dr Mohammad Naderan, School of Medicine, Tehran University of Medical Sciences, Keshavarz Boulevard, Tehran, Iran; moh@naderan.com

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ABSTRACT

Aim The purpose of this study was to determine the association between prevalence of obstructive sleep apnoea (OSA) in patients with keratoconus (KC) and the severity of KC.

Methods Six-hundred and sixteen patients with KC and 616 patients without KC in the control group were enrolled in this prospective case–control study. Both groups were matched by age, gender, and body mass index (BMI). The Berlin Questionnaire was administered in both groups. Keratometric and topographic measurements of the KC eyes were recorded.

Results Seventy-six (12.3%) and 40 (6.5%) patients were identified as high risk for developing OSA in KC and control groups, respectively ($p<0.001$). Family history of OSA and BMI were the risk factors for OSA in the KC group, while in the control group the only risk factor for OSA was the patient's gender. Patients with KC with a high risk of OSA had a significantly higher mean K, flat K, steep K ($p<0.05$), and a thinner corneal thickness ($p<0.05$). The severity of KC decreased in both OSA groups except for the grade 4 of high risk group which was the second most frequent group after grade 1 ($p=0.005$).

Conclusions Our study revealed that patients with KC are at increased risk of developing OSA, and patients with KC who are at higher risk of developing OSA may have more severe KC.

INTRODUCTION

Keratoconus (KC) is a chronic bilateral non-inflammatory ectatic disorder of the cornea, and is described as a progressive frontal protrusion and thinning of the cornea.[1] In a series of 50 patients, Pihlblad and Schaefer[2] found that the prevalence of obstructive sleep apnoea (OSA) in the patients with KC was 24%. However, in similar studies, Gupta *et al*[3] and Saidel *et al*[4] found the frequency of OSA among patients with KC to be 18% and 19.6%, respectively.

OSA has remarkably been connected with some ophthalmological disorders, including KC[5] and floppy eyelid syndrome (FES).[6] OSA is a sleep disorder defined by various repetitive episodes of apnoea and hypopnoea for at least 10 s, and is noticeable by reduced oxygen saturation in the patient.[7] Recurrent episodes of OSA lead to fragmented sleep, hypoxia, fatigue, excessive daytime sleepiness and motor accidents.[7] Untreated OSA is connected with an elevated risk of all-cause mortality and can be central to premature death and increased mortality rate.[8] The occurrence of OSA in the western adult population is approximately 1–5%.[9] An epidemiological study on the Iranian population showed the prevalence of sleep apnoea syndrome and high-risk sleep apnoea was found to be nearly 5%.[10] The incidence of OSA differs according to age and gender, with the highest frequency of nearly 5% between 45 and 65 years of age.[11] This figure has been reported as 2% in men, which is slightly higher than in women.[12]

Suitable intervention can reduce the morbidity and mortality associated with OSA. Identifying the risk factors connected with the progress of OSA can help address public and primary healthcare services concerned about OSA. With this in mind, the aim of this study was to determine the prevalence and risk factors associated with the development of OSA in patients with KC and to compare them with patients without KC to ascertain whether patients with KC are at higher risk of developing OSA. Finally, to determine if there is an association between the prevalence of OSA and the severity of KC.

MATERIALS AND METHOD

Study populations

A prospective case–control study in patients with KC was conducted from January 2012 to January 2014 at the Zarrinbakhsh Eye Clinic, Tehran University of Medical Sciences, Tehran, Iran. The institutional ethics committee at Tehran University of Medical Sciences approved the study design and protocol. After explanation of the nature of the study, informed consent was obtained and all participants agreed to enter the study.

All patients over 18 years of age who were diagnosed with KC were enrolled in the study. The diagnosis of KC was based on clinical diagnostic signs of KC found by using scanning-slit biomicroscopy, such as the Fleischer ring, corneal tilting, Vogt's striae, corneal stromal thinning, or scissoring reflex on retinoscopy, and corneal topography mapping, and anterior or posterior elevation mapping (mean simulated keratometry >45.2 dioptres (D), central corneal power >47.2 D or inferior–superior asymmetry >1.4 D) by Pentacam (OCULUS Optikgerate GmbH, Wetzlar, Germany). Based on the inclusion criteria, 616 patients were diagnosed and enrolled in the study. The same number of patients attending the cornea clinic for refractive errors, who were matched by age, gender and body mass index (BMI) with the patients with KC, were selected as the control group. The control group was matched with the KC group by the 'frequency matching' method in which the overall age and BMI of the control group matched with the overall age and BMI of the KC group. In the control group, the inclusion criteria were

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6- Mohammad Reza Shiri-Shahsavar

First Name	Last Name	Program	Level	School
Muhammad Reza	Shiri-Shahsavar	Nutritional Sciences	PhD	Nutritional Sciences & Dietetics

Published Articles:

	Published Articles:Published Articles:Title of the Article
1	A Novel Combination of Docosahexaenoic Acid, All-Trans Retinoic Acid, and 1, 25-Dihydroxyvitamin D3 Reduces T-Bet Gene Expression, Serum Interferon Gamma, and Clinical Scores but Promotes PPARγ Gene Expression in Experimental Autoimmune Encephalomyelitis

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A Novel Combination of Docosahexaenoic Acid, All-Trans Retinoic Acid, and 1, 25-Dihydroxyvitamin D_3 Reduces T-Bet Gene Expression, Serum Interferon Gamma, and Clinical Scores but Promotes PPARγ Gene Expression in Experimental Autoimmune Encephalomyelitis

Mohammad Reza Shiri-Shahsavar[1] · Abbas Mirshafiee[2] · Karim Parastouei[3] · Abbas Ebrahimi-Kalan[4] · Saeed Yekaninejad[5] · Farid Soleymani[2] · Reza Chahardoli[3] · Ramin Mazaheri Nezhad Fard[6] · Ali Akbar Saboor-Yaraghi[1,2]

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Abstract Vitamins are immunologically interesting due to their significant immunomodulatory activities. Experimental autoimmune encephalomyelitis (EAE) is one of the most commonly used experimental models for studying autoimmune disorder in multiple sclerosis (MS). The aim of this study was to evaluate the protective and ameliorative effects of novel combination of all-trans retinoic acid (ATRA), 1,25-dihydroxyvitamin D_3 (D_3), and docosahexaenoic acid (DHA) on EAE-specific determinants and target gene expressions. Mice were randomly categorized into three groups before EAE induction [non-treated EAE (Group E), treated EAE (Group T), and healthy mice (Group H)]. Encephalomyelitis was induced in female C57BL/6 mice by subcutaneous immunization using commercial kits. Preceding day of EAE induction, combination of ATRA, D_3, and DHA was administered with a single IP injection every 48 h and continued until day 26. Findings of present study showed that administration of vitamins A, D, and DHA significantly decreased average clinical scores, cumulative EAE score, and EAE incidence in Group T, compared to Group E (p values <0.001). Interferon γ secretion in serum and T-bet mRNA expression in splenocytes were significantly reduced ($p = 0.004$, $p = 0.029$, respectively) while PPARγ mRNA expression was significantly increased in Group T compared to Group E ($p = 0.021$). These findings highlighted that ATRA, D_3, and DHA combination modulated PPARγ and T-bet gene expression and resulted in decrease in Th1 response and lymphocyte invasion into the central nervous system (CNS) and resultant inflammation. In conclusion, the results of this study suggested the potential use of this intervention in treatment and/or prevention of EAE/MS and probably other Th1 cell-mediated autoimmune diseases.

Keywords Multiple sclerosis (MS) · Experimental autoimmune encephalomyelitis (EAE) · Peroxisome proliferator-activated receptor gamma (PPARγ) · Vitamins · T-bet · ATRA, D_3 and DHA combination therapy

✉ Ali Akbar Saboor-Yaraghi
asaboor@tums.ac.ir

1 Department of Cellular and Molecular Nutrition, School of Nutritional Sciences and Dietetics, International Campus, Tehran University of Medical Sciences, Tehran, Iran

2 Department of Immunology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

3 Department of Cellular and Molecular Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran

4 Neuroscience Department, School of Advanced Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran

5 Department of Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

6 Department of Pathobiology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Introduction

Multiple sclerosis (MS) is an immune-mediated, neurodegenerative disease which affects the central nervous system (CNS) (Compston and Coles 2008). It is a chronic progressive, potentially debilitating disorder with considerable social impact and economic consequences (Heydarpour et al. 2015).

Chapter Eight

School of Pharmacy

1- Maher Darwish

First Name	Last Name	Program	Level	School
Maher	Darwish	Drug control analysis	PhD	Pharmacy

Published Articles:

	Title of the Article
1	Partially decomposed PVP as a surface modification of ZnO, CdO, ZnS and CdS nanostructures for enhanced stability and catalytic activity towards sulphamethoxazole degradation.
2	Shape-controlled ZnO nanocrystals synthesized via auto combustion.
3	Integration of nickel doping with loading on graphene for enhanced adsorptive and catalytic properties of CdS nanoparticles towards visible light degradation of some antibiotics.
4	Photocatalytic activity of ZnO nanoparticles prepared by a microwave method in ethylene glycol and polyethylene glycol media: A comparative study.
5	Microwave-assisted polyol synthesis and characterization of pvp-capped cds nanoparticles for the photocatalytic degradation of tartrazine and possible involved mechanisms.

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Partially decomposed PVP as a surface modification of ZnO, CdO, ZnS and CdS nanostructures for enhanced stability and catalytic activity towards sulphamethoxazole degradation

MAHER DARWISH[1], ALI MOHAMMADI[1,2,*] and NAVID ASSI[1]
[1]Department of Drug and Food Control, Faculty of Pharmacy, International Campus, Tehran University of Medical Sciences, Tehran 14155-6451, Iran
[2]Nanotechnology Research Centre, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran 14155-6451, Iran
*Author for correspondence (alimohammadi@tums.ac.ir)

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Abstract. In order to prepare stable and efficient photocatalysts, a microwave-furnace-assisted method using ethylene glycol (EG) as a solvent has been employed to obtain metal oxides and metal sulphides nanocatalysts with partial decomposition of the polyvinylpyrrolidone (PVP) cap (P-ZnO, P-CdO, P-ZnS and P-CdS); this associates the protective functionality of PVP with enhanced catalytic activity due to effective carriers transfer. The as-produced catalysts characterization revealed an extended growth of metal oxides compared with metal sulphides, which is attributed to the competition of EG as the source of oxygen with PVP to capsulate metal oxides during the synthesis. Infrared spectra confirmed the PVP–metal complexation and partial decomposition of the polymer. Metal sulphides exhibited a better catalytic activity compared with metal oxides for sulphamethoxazole degradation in UVC light owing to their size and morphology impact; further, P-CdS induced 71% antibiotic degradation after 10 h of illumination with visible light compared with only 48% for P-ZnS, 29% for P-ZdO and 20% for P-CdO due to improved light absorption. Interestingly, around 86% degradation was induced by mixing P-CdS with P-ZnS in 80:20% ratio, indicating an enhanced visible light activity due to improved electron–hole pair separation and high redox potential of P-ZnS.

Keywords. Polyvinylpyrrolidone; sulphamethoxazole; photocatalyst; metal sulphide; microwave-assisted; nanostructure.

1. Introduction

In recent years, antibiotics have occupied an advanced position among environmental pollutants due to their pharmaceutical characteristics and extensive consumption that has consequently led to the presence of their residues in environmental water. This presence has been evidenced to incite mutations in the aquatic microorganisms with continuous exposure and may further induce new strains to exist [1]. A more complicated issue is the possibility of developing an antibiotic resistance among aquatic bacteria and the transfer of resistant genes to pathogenic bacteria, which pose a great risk to human health [2,3]. Sulphamethoxazole (SMX) is among the most commonly used antibiotics for human and livestock treatment. This compound is highly resistant to conventional and biological treatments owing to its antibacterial nature, and it can persist in the environment for more than 1 year, leading to the aforementioned risks [4,5]. Hence, greater consideration must be given to eliminating such an agent from domestic and industrial effluents before discharging into the environment.

In this regard, advanced oxidation procedures (AOPs) have been devised as effective methods, which involve the generation of highly reactive species such as hydroxyl ($OH^{\bullet}$) and superoxide ($O_2^{-\bullet}$) radicals for the oxidation and destruction of organic pollutants [6]. Among these, nanosized heterogeneous semiconductors have gained an increasing attention and are now considered as a convenient candidate to substitute conventional methods for wastewater treatment. The advantages of these photocatalysts are their possible ability to completely degrade the organic pollutants; this results from their amazing electronic and optical properties arising from quantum confinement effects and increased surface area-to-volume; in addition to being environment friendly, they may operate in solar light and diminish the cost of treatment [7,8]. There has been an exponential growth in the number of reports concerning the synthesis and applications of metal oxides and metal chalcogenides nanocatalysts of II–VI semiconductor group, such as ZnO, ZnS, CdS, CdSe, etc. Among the various methods for synthesis, the polyol-mediated method has been reported to be suitable for preparing such nanoparticles. This method involves heating the precursors in a polyalcohol medium that plays multiple roles such as a solvent, reductant, complexant and surfactant [9]. Broadly speaking, using the polyol method can give amazing characteristics for the synthesized nanoparticles, including a uniform shape, narrow size distribution and small degree of aggregation [10]. Moreover, it was confirmed that polyol method is highly

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Shape-controlled ZnO nanocrystals synthesized via auto combustion method and enhancement of the visible light catalytic activity by decoration on graphene

Maher Darwish [a], Ali Mohammadi [a, b, *], Navid Assi [a], Qazale Sadr Manuchehri [a], Youssef Alahmad [c], Samer Abuzerr [d]

[a] Department of Drug and Food Control, Faculty of Pharmacy, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[b] Pharmaceutical Quality Assurance Research Centre, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Pharmaceutical Chemistry and Drug Control, Faculty of Pharmacy, Albaath University, Homs, Syria
[d] Department of Environmental Health Engineering, Faculty of Public Health, International Campus, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Several shapes of ZnO nanocatalysts have been acquired by the alteration of auto combustion method parameters in order to obtain the most efficient catalyst towards 2-nitrophenol degradation under UV-C. Thereafter, the procedure with tuned parameters was employed to decorate ZnO on graphene nanosheets to improve its visible light driven catalytic performance. Characterization results of the as-prepared nanocatalysts revealed that initial pH, fuel to metal ratio, and calcination temperature have influenced different growth and agglomeration directions. However, XRD patterns indicated the monocrystalline hexagonal phase of all tested products. Furthermore, UV–Vis and FTIR spectra exhibited the red-shift of ZnO absorption towards the visible light region upon loading on graphene and confirmed the successful reduction of graphene oxide by the subsequent preparation steps. Indeed, 2-nitrophenol degradation under visible light irradiation has shown a considerable enhancement with all graphene oxide weights utilized. Moreover, the kinetics of the reaction that fitted to the pseudo first-order kinetic and Langmuir-Hinshelwood models elaborated the dominance of pollutant catalytic degradation over its adsorption despite the improved adsorption in the presence of graphene. Finally, the degradation mechanism we suggested involves mainly the surface complexation of 2-NP on the catalyst surface to enable the absorption of visible light through ligand-to-metal charge transfer.

1. Introduction

Synthetic phenols arising from industries such as petrochemicals, pesticides, dyes, pharmaceuticals, etc. were subjected to intense research regarding their toxicity and ecological impacts. The toxic effects of these compounds on aquatic life have been proven for over fifty years now [1]. More seriously, their verified carcinogenic and mutagenic effects have urged the United States Environmental Protection Agency (US EPA) to consider them as priority pollutants [2].

Photocatalytic degradation using nanostructures is one of the most promising techniques to tackle the water contamination problem effectively in order to diminish the potential risks of such pollutants on human and environment. The pros of such technique include the use of environmentally friendly oxidants, complete mineralization of pollutants under mild temperature and pressure conditions, and the absence of waste disposal problem [3].

The design of controlled size and morphology of photocatalysts plays a pivotal role in developing their chemical and physical properties and influences their catalytic potency largely. Therefore, more effort has been given for the preparation of nanostructures with controlled morphologies and crystal evolution [4,5]. Among the various photocatalysts being used nowadays, ZnO semiconductor has been recognized for its high capability to form in

* Corresponding author. Department of Drug & Food Control, Pharmaceutical Quality Assurance Research Centre, Faculty of Pharmacy, Tehran University of Medical Sciences, P.O. Box: 14155-6451, Tehran, Iran.
E-mail addresses: m-darwish@razi.tums.ac.ir (M. Darwish), alimohammadi@tums.ac.ir (A. Mohammadi), navid_a30@yahoo.com (N. Assi), gmanuchehri@yahoo.com (Q.S. Manuchehri), youssef.alahmad@yahoo.fr, yalahmad@albaath-univ.edu.sy (Y. Alahmad), samer_516@hotmail.com (S. Abuzerr).

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Integration of nickel doping with loading on graphene for enhanced adsorptive and catalytic properties of CdS nanoparticles towards visible light degradation of some antibiotics

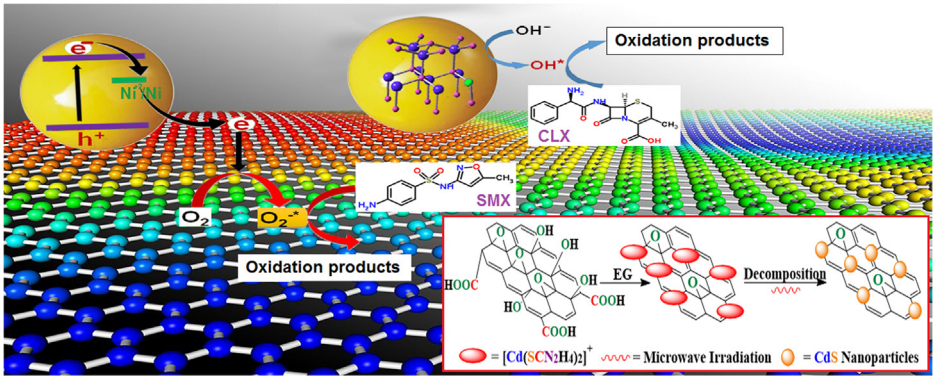
Maher Darwish (M.Sc, Ph.D Student)[a], Ali Mohammadi (Pharm.D, Ph.D)[a,b,*], Navid Assi (Analytical chemistry, Ph.D Student)[a]

[a] Department of Drug and Food Control, Faculty of Pharmacy, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[b] Nanotechnology Research Centre, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

HIGHLIGHTS

- Simultaneous Ni doping and loading on graphene was achieved to modify CdS catalyst.
- Both doping and compositing extended the absorption into visible light region.
- A mechanism was proposed to explain the roles of Ni dopant and graphene matrix.
- Photostability and reusability of G-NiCdS composite were investigated and confirmed.
- Reasons behind superior catalytic activity of G-NiCdS composite were summarized.

GRAPHICAL ABSTRACT



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ABSTRACT

Water dispersible, highly efficient nickel doped CdS nanoparticles anchored on graphene nanosheets as a photocatalyst for cephalexin and sulfamethoxazole photodegradation have been prepared in a facile microwave-furnace assisted method. Each one of the two modifications has played a critical role in nanocomposite functioning. Defects originated by dopant boosted the lifetime of carriers and thereupon graphene matrix transferred them to contribute effectively the photocatalytic process. Characterization results revealed the formation of monocrystalline hexagonal phase of all products and that both doping and loading on graphene have red-shifted the absorption edge of CdS towards the visible light region. Furthermore, FTIR confirmed the successful reduction of graphene oxide by the subsequent preparation steps. Adsorption isotherms revealed the role of graphene in enhancing substrate adsorption. Nevertheless, dissimilar pathways of catalytic degradation were observed on the doped composite as cephalexin

* Corresponding author. Associate Professor of Pharmaceutical Analysis, Department of Drug & Food Control and Nanotechnology Research Centre, Faculty of Pharmacy, Tehran University of Medical Sciences, P.O. Box: 14155–6451, Tehran, Iran.
E-mail addresses: m-darwish@razi.tums.ac.ir (M. Darwish), alimohammadi@tums.ac.ir (A. Mohammadi), navid_a30@yahoo.com (N. Assi).

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Photocatalytic activity of ZnO nanoparticles prepared by a microwave method in ethylene glycol and polyethylene glycol media: A comparative study

Qazale Sadr Manuchehri[1, a], Navid Assi[2, b*], Sanaz Pourmand[3, c], Maher Darwish[4, d] and Amir Pakzad[2, e]

[1]Young Researchers Club, Pharmaceutical Sciences Branch, Islamic Azad University, Tehran, Iran

[2]Department of Chemistry, Tehran Science and Research branch, Azad University, Tehran, Iran

[3]Department of Chemistry, Amirkabir University of Technology (AUT), Tehran, Iran

[4]Department of Food and Drug Control, Faculty of Pharmacy, International Campus, Tehran University of Medical Sciences, Tehran, Iran

[a]gmanuchehri@yahoo.com, [b*]navid_a30@yahoo.com, [c]pourmand_s@yahoo.com, [d]m-darwish@razi.tums.ac.ir, [e]amir.pakzad.85@yahoo.com

Keywords: Microwave assisted; Sol-gel; Zinc oxide; Nanoparticle; 2-nitrophenol; Photocatalysis

Abstract. Zinc oxide nanoparticles have been synthesized by a sol-gel microwave assisted method using either ethylene glycol (ZnO-EG) or poly ethylene glycol ethanolic solution (ZnO-PEG) as dispersing media. The nanoparticles were characterized by X-ray diffraction, field emission scanning electron microscopy, energy dispersive X-ray spectroscopy, and Fourier transform infrared. X-ray analysis revealed a hexagonal phase structure of both zinc oxides. The average crystallite size calculated from Scherrer equation was 27 nm and 53 nm in good agreement with 24 nm and 55 nm microscopic results for ZnO-EG and ZnO-PEG, respectively. The catalytic activity of the as-prepared nanoparticles was compared by the photodegradation of 2-nitrophenol under UVC. The effect of various parameters such as pH, catalyst weight, and pollutant concentration on the percent degradation was investigated. Best optimization was pH=7, 0.06g of nanoparticles weight, and 10 $mg.L^{-1}$ pollutant concentration. Furthermore, pseudo first order kinetic based on Langmuir–Hinshelwood (L–H) model was proposed for degradation reactions and experimental data were in good agreement with this model.

1. Introduction

Among the various problems threatening human life quality nowadays, shortage of water and water pollution are considered of the most challenging. Hence, the requirement of purifying and decontaminating water resources is of a great importance. Nitrophenolic compounds represent a class of widely discharged water pollutants. They are of synthetic origin and used in wide range of versatile industries such as pharmaceuticals, pesticides, explosives, and as intermediates for the synthesis of many other chemicals [1]. Due to their high toxicity, weak biodegradability, and large accumulation in the environment, these compounds can pose a great danger on human health [2]. Consequently, they have been listed as “priority pollutants” by U.S. Environmental Protection Agency's (USEPA) and their concentration was suggested to be monitored to less than 10 $ng.L^{-1}$ in environmental water [3, 4]. The main reason behind the difficult biodegradation of these compounds is the presence of the strong electron withdrawing group (NO_2) which reinforces the stability of the aromatic ring [5].

Over the past two decades, enormous efforts have been devoted to the destruction of phenolic pollutants from aqueous solutions. In this connection, advanced oxidation procedures (AOPs) seem to be the most promising technologies to destroy wide range of organic pollutants in a highly efficient unselective manner [6]. Among those, photocatalysts have gained a great attention due to their ability to oxidize and afterward, mineralize organics into nontoxic products [7]. Photocatalysis

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Microwave-assisted polyol synthesis and characterization of pvp-capped cds nanoparticles for the photocatalytic degradation of tartrazine

Maher Darwish[a], Ali Mohammadi[a,b,*], Navid Assi[a]

[a] Department of Drug and Food Control, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[b] Nanotechnology Research Centre, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Polyvinylpyrrolidone capped cadmium sulfide nanoparticles have been successfully synthesized by a facile polyol method with ethylene glycol. Microwave irradiation and calcination were used to control the size and shape of nanoparticles. Characterization with scanning electron microscopy revealed a restricted nanoparticles growth comparing with the uncapped product, hexagonal phase and 48 nm average particle size were confirmed by X-ray diffraction, and finally mechanism of passivation was suggested depending on Fourier transform infrared spectra.

The efficiency of nanoparticles was evaluated by the photocatalytic degradation of tartrazine in aqueous solution under UVC and visible light irradiation. Complete degradation of the dye was observed after 90 min of UVC irradiation under optimized conditions. Kinetic of reaction fitted well to the pseudo-first-order kinetic and Langmuir–Hinshelwood models. Furthermore, 85% degradation of the dye in 9 h under visible light suggests that cadmium sulfide is a promising tool to work under visible light for environmental remediation.

1. Introduction

During the last two decades, photocatalytic materials received a large quantity of research interest as they have a great potential to be applied in detoxification of environmental organic pollutants and as a clean energy source [1]. Semiconductor heterogeneous photocatalysts such as TiO_2, ZnO, SnO_2, WO_3, Fe_2O_3, and CdS have been intensively investigated in the area of water and air purification and in remediation reactions [2].

Like other advanced oxidation procedures (AOPs), the common characteristic of photocatalytic materials is the generation of very reactive species such as, principally but not exclusively, hydroxyl radicals ($HO^{\bullet}$), which initiate a series of reactions leading eventually to the destruction of the target pollutant [3]. Recently, nanostructures of these photocatalysts have attracted more consideration as they are expected to have higher photocatalytic activity than their bulk counterparts due to their smaller size, higher surface area-to-volume ratio, and increased band-gab energy which in turn lead to higher redox potentials [4].

Cadmium sulfide (CdS), a typical metal chalcogenide semiconductor with a direct band gap $E_g \approx 2.43$ eV at room temperature [5], has become one of the most considerable materials in research communities due to its diverse promising applications in the field of solar cells, photoelectronic devices and photocatalysis [6]. This material has shown better catalytic functions compared to those of TiO_2 due to the rapid generation of electron–hole pairs by photoexcitation [7]. Nevertheless, CdS has the fatal photocorrosion problem due to the self-oxidation by the generated hole [8]. To overcome such a problem, an effective approach is to cover the nanoparticle core surface with a polymeric capping agent which might also help to stabilize the surface, control the growth, and prevent agglomeration of the nanoparticles [9–11].

Many methods have been utilized for the synthesis of CdS nanostructures such as co-precipitation [7,12], polyol [13], solvothermal [14,15], hydrothermal [16], non-aqueous chemical method [17], and chemical bath deposition [18]. Among these different processes, the polyol method appears as an easy to carry out with many other advantages: a uniform shape, a narrow size distribution, and a low degree of agglomeration [19]. This method generally uses poly-alcohol like ethylene glycol (EG), diethylene

* Corresponding author art: Department of Drug & Food Control and Nanotechnology Research Centre, Faculty of Pharmacy, Tehran University of Medical Sciences, P.O. Box 14155-6451, Tehran, Iran. Fax: +98 21 88358801.
E-mail addresses: m-darwish@razi.tums.ac.ir (M. Darwish), alimohammadi@tums.ac.ir (A. Mohammadi), navid_a30@yahoo.com (N. Assi).

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2- Legese Chelkeba

First Name	Last Name	Program	Level	School
Legese	Chelkeba	Pharmacotherapy	Ph.D	Pharmacy

Published Articles:

	Title of the Article
1	The effect of parenteral selenium on outcomes of mechanically ventilated patients following sepsis: a prospective randomized clinical trial
2	The effect of high-dose Parenteral Sodium Selenite in Critically Ill Patients following Sepsis: A Clinical and Mechanistic Study

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RESEARCH

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The effect of parenteral selenium on outcomes of mechanically ventilated patients following sepsis: a prospective randomized clinical trial

Legese Chelkeba[1,2,3,4], Arezoo Ahmadi[2], Mohammad Abdollahi[3], Atabak Najafi[2], Mohammad Hosein Ghadimi[3], Reza Mosaed[3] and Mojtaba Mojtahedzadeh[1,2,3*]

Abstract

Background: Sepsis and septic shock is characterized by oxidative stress that mainly promotes systemic inflammation and organ failure due to excessive free radical production and depletion of antioxidant defenses. Therefore, we investigated the effect of selenium administration on antioxidant status, levels of cytokines and clinical outcomes.

Methodology: This study was a prospective randomized control trial (RCT) whereby patients received selenium as sodium selenite (2 mg IV bolus followed by 1.5 mg continuous infusion for 14 days) plus standard therapy. The control group received standard therapy without selenium. The primary endpoint was 28-day mortality. The changes in the mean levels of glutathione peroxidase (GPX) activity, IL-6, IL-8 and IL-10, the incidence of ventilator-associated pneumonia (VAP) and other secondary endpoints were also recorded. VAP was broken down into early VAP and late VAP to see the clinical significance of each. We also recorded any adverse outcomes from selenium infusion.

Results: Over 24-month period, 54 patients were recruited and randomized and an intention to treat (ITT) principle was applied (selenium, $n = 29$; control, $n = 25$) in the final analysis. There was no statistically significant difference between the two groups in 28-day mortality although it was lower in the selenium group compared with the control group: 9 (31 %) in the selenium versus 10 (40 %) in the control groups ($p = 0.49$). At day 0, GPX activity was 0.185 ± 0.3 versus 0.19 ± 0.3 U/mL ($p = 0.9$), day 3, GPX activity was 0.52 ± 0.5 versus 0.17 ± 0.2 U/mL ($p = 0.02$), at day 7 it was 0.55 ± 0.5 versus 0.24 ± 0.3 U/mL ($p = 0.032$), at day 10 it was 0.62 ± 0.7 versus 0.33 ± 0.4 U/mL ($p = 0.048$) and at day 14 it was 1.1 ± 1 versus 0.89 ± 1 U/mL ($p = 0.70$) for the selenium versus control groups, respectively. However, there were no significant differences between the mean plasma levels of all the three inflammatory cytokines at any point in time between the two groups. There was a significant reduction in occurrence of VAP in the selenium group compared with the control group (55.2 versus 84 %, $p = 0.023$), respectively.

Conclusion: High-dose selenium administration within the time frame of early goal-directed therapy was not resulted in reduction of 28-day mortality, but increased the activity of glutathione peroxidase with no effect on the levels of inflammatory cytokines at any point in time in mechanically ventilated septic patients. However, selenium supplementation in mechanically ventilated patients following sepsis was associated with reduced occurrence of VAP.

Trial registration: IRCT201212082887N4 at WHO Clinical Trial Registry, August 29, 2014

Keywords: Severe sepsis, Septic shock, Selenium, Ventilator-associated pneumonia

*Correspondence: mojtahed@tums.ac.ir
[1] Department of Clinical Pharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, International campus (TUMS-IC), Tehran, Iran
Full list of author information is available at the end of the article

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Research Article

The Effect of High-dose Parenteral Sodium Selenite in Critically Ill Patients following Sepsis: A Clinical and Mechanistic Study

Legese Chelkeba[1,2,3,4], **Arezoo Ahmadi**[2], **Mohammad Abdollahi**[3], **Atabak Najafi**[2], **Mohammad Hosein Ghadimi**[3], **Reza Mosaed**[3], **Mojtaba Mojtahedzadeh**[1,2,3]

[1]Department of Clinical Pharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, International Campus, [2]Department of Anesthesiology and Critical Care Medicine, Sina Hospital, Faculty of Medicine, Tehran University of Medical Sciences, [3]Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran, [4]Department of Clinical Pharmacy, Faculty of Health Sciences, Jimma University, Jimma, Ethiopia

Abstract

Introduction: Severe sepsis and septic shock is characterized by inflammation and oxidative stress. Selenium levels have been reported to be low due to loss or increased requirements during severe sepsis and septic shock. We investigated the effect of high-dose parenteral selenium administration in septic patients. **Methods:** A prospective, randomized control clinical trial was performed in septic patients. After randomization, patients in selenium group received high-dose parenteral sodium selenite (2 mg intravenous [IV] bolus followed by 1.5 mg IV continuous infusion daily for 14 days) plus standard therapy and the control group received standard therapy. The primary endpoint was mortality at 28 days. Changes in the mean levels of high mobility group box-1 (HMGB-1) protein and superoxide dismutase (SOD), duration of vasopressor therapy, incidence of acute renal failure, and 60 days' mortality were secondary endpoints. **Results:** Fifty-four patients were randomized into selenium group ($n = 29$) and control group ($n = 25$). There was no significant difference in 28-day mortality. No significant difference between the two groups with respect to the average levels of HMGB-1 protein and SOD at any point in time over the course of 14 days had observed. **Conclusion:** In early administration within the first 6 h of sepsis diagnosis, our study demonstrated that high-dose parenteral selenium administration had no significant effect either on 28-day mortality or the mean levels of HMGB-1 and SOD (Trial Registration: IRCT201212082887N4 at WHO Clinical Trial Registry, August 29, 2014).

Keywords: High mobility group box-1 protein, mortality, selenium, sepsis, septic shock, severe sepsis, superoxide dismutase

Introduction

The incidence of sepsis was high and in the United States it is estimated to be 300/100,000 population per year.[1] The spectrum of disease is a major cause of morbidity and mortality globally, with mortality in severe sepsis ≥5-fold higher than that for acute coronary syndrome or stroke.[2] With advances in health-care services and technology, appropriate organ support, and treatment of the underlying inciting pathogens, the mortality rate is still 20%–50%.[3]

During infection, pathogens or cellular components are recognized by receptors expressed on the surface of the innate immune cells known as pattern recognition receptors. The same receptors often recognize damage-associated molecular patterns (DAMPs) indicating that the similarities between pathogen-induced and inflammatory responses to cellular stress, injury, or necrosis.[4] Trauma or injury generates danger-associated molecular patterns (i.e., high mobility group box-1 [HMGB-1], heat shock proteins, and S100 proteins) that augment toll-like receptors expressions such as pathogen-associated molecular patterns.[5] HMGB-1, one of the most extensively studied DAMPs, is a protein involving in nuclear stabilization and gene transcription which, if released in large quantities into the extracellular environment, becomes a lethal mediator of systemic inflammation.[6,7] A significant amount of HMGB-1 levels have observed in majority of patients up to a week after the diagnosis of sepsis or septic shock and are correlated with the degree of organ dysfunction.[6]

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Address for correspondence: Dr. Legese Chelkeba, Department of Clinical Pharmacy, Faculty of Health Sciences, Jimma University, Jimma, Ethiopia.
E-mail: legese.chelkeba@gmail.com

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Chapter Nine

School of Advanced Technologies in Medicine

1- Amjad Hayat Khan

First Name	Last Name	Program	Level	School
Amjad	Hayat Khan	Biotechnology	Ph.D	Advanced Technologies

Published Articles:

	Title of the Article
1	Humanizing glycosylation pathways in eukaryotic expression systems
2	Application of immuno-PCR assay for the detection of serum IgE specific to Bermuda allergen
3	Application of immuno-PCR for the detection of early stage cancer
4	Licensed monoclonal antibodies and associated challenges

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REVIEW

Humanizing glycosylation pathways in eukaryotic expression systems

Amjad Hayat Khan[1] · **Hadi Bayat**[2,3] · **Masoumeh Rajabibazl**[4,5] · **Suriana Sabri**[6] · **Azam Rahimpour**[2,3]

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Abstract Glycosylation represents the most widespread posttranslational modifications, found in a broad spectrum of natural and therapeutic recombinant proteins. It highly affects bioactivity, site-specificity, stability, solubility, immunogenicity, and serum half-life of glycoproteins. Numerous expression hosts including yeasts, insect cells, transgenic plants, and mammalian cells have been explored for synthesizing therapeutic glycoproteins. However, glycosylation profile of eukaryotic expression systems differs from human. Glycosylation strategies have been proposed for humanizing the glycosylation pathways in expression hosts which is the main theme of this review. Besides, we also highlighted the glycosylation potential of protozoan parasites by emphasizing on the mammalian-like glycosylation potential of *Leishmania tarentolae* known as *Leishmania* expression system.

Keywords Glycosylation pattern · Glycoengineering · LEXSY · Eukaryotic expression systems

✉ Azam Rahimpour
rahimpour@sbmu.ac.ir

Amjad Hayat Khan
a-hayatkhan@razi.tums.ac.ir

1 Department of Medical Biotechnology, School of Advanced Technologies in Medicine, International Campus, Tehran University of Medical Sciences, Tehran, Iran

2 Medical Nano-Technology and Tissue Engineering Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3 Department of Tissue Engineering and Regenerative Medicine, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

4 Department of Clinical Biochemistry, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

5 Department of Biotechnology, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

6 Department of Microbiology, Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia (UPM), 43400 Serdang, Selangor, Malaysia

Introduction

Among posttranslational modifications (PTMs), glycosylation is the most common and complex modification of many cell surface and secreted eukaryotic proteins. Glycosylation is the enzymatic addition of oligosaccharides to nascent polypeptide chains in the endoplasmic reticulum (ER). Attached oligosaccharide structure is further modified by an array of glycosidases and glycosyltransferases inside ER and Golgi complex. The modification reactions occurring in ER are highly conserved between lower and higher eukaryotes. While reactions taking place inside Golgi complex varies among species and cell types (Jacobs and Callewaert 2009). Due to non-template based biosynthesis of glycans, glycoproteins typically occur as a mixture of glycoforms. Consequently, making the field of glycoproteomics more complex compared to other omics (Zoldoš et al. 2013). Approximately, 50% of the human native proteins including immunoglobulin are glycoproteins. The glycan residues greatly influence the physical and chemical properties of proteins i.e. folding, site specificity, cellular homeostasis, and immune regulation (Dalziel et al. 2014). Nonhuman glycans make recombinant proteins immunogenic (Li and d'Anjou 2009). That's why several academic and industrial laboratories have focused on engineering the glycosylation pathways of expression systems for humanizing the glycosylation reactions and eliminating immunogenic epitopes.

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Application of immuno-PCR assay for the detection of serum IgE specific to Bermuda allergen

Samine Rahmatpour [a, i, 1], Amjad Hayat Khan [b, 1], Rasoul Nasiri Kalmarzi [c], Masoumeh Rajabibazl [d, e], Gholamreza Tavoosidana [f], Elahe Motevaseli [f], Nosratollah Zarghami [a, g, h, **], Esmaeil Sadroddiny [i, *]

[a] Department of Medical Biotechnology, Faculty of Advanced Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran
[b] Department of Medical Biotechnology, School of Advanced Technologies in Medicine, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[c] Cellular and Molecular Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran
[d] Department of Clinical Biochemistry, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[e] School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[f] Department of Molecular Medicine, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran
[g] Department of Clinical Biochemistry and Laboratory Medicine, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
[h] Tuberculosis and Lung Disease Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[i] Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

In vivo and *in vitro* tests are the two major ways of identifying the triggering allergens in sensitized individuals with allergic symptoms. Both methods are equally significant in terms of sensitivity and specificity. However, in certain circumstances, *in vitro* methods are highly preferred because they circumvent the use of sensitizing drugs in patients. In current study, we described a highly sensitive immuno-PCR (iPCR) assay for serum IgE specific to Bermuda allergens. Using oligonucleotide-labelled antibody, we used iPCR for the sensitive detection of serum IgE. The nucleotide sequence was amplified using conventional PCR and the bands were visualized on 2.5% agarose gel. Results demonstrated a 100-fold enhancement in sensitivity of iPCR over commercially available enzyme-linked immunosorbent assay (ELISA) kit. Our iPCR method was highly sensitive for Bermuda-specific serum IgE and could be beneficial in allergy clinics.

1. Introduction

Immunoglobulin E (IgE) is the least abundant and fifth class of immunoglobulins, providing first line of defense against parasitic infestation. Besides, IgE is one of the major mediators of immediate hypersensitivity reactions that underlie atopic conditions such as, urticaria, seasonal allergy, asthma, and anaphylaxis [1,2]. The growing prevalence of allergies particularly, asthma [3] has motivated the research community to understand the structure as well as the interaction of IgE with other proteins. The interaction between IgE and effector cells takes place through a network of receptor proteins: FcεRI (high-affinity receptors) and FcεRII (low-affinity receptors) [4,5]. Two major tests: skin testing and serum assays for allergen-specific IgE have been employed in allergy diagnostic clinics. In former approach, a small amount of diluted allergen is delivered to the body through pricking or scratching the skin, or intradermal injection, and the skin is used as a mirror of cells present in nose or lungs [6,7]. This method is rapid, sensitive, inexpensive, and the best available option employed in allergy clinics. Unfortunately, due to associated adverse events skin testing is impractical to perform in patients with a risk of anaphylaxis, who cannot discontinue interfering medications, or suffering from skin diseases. In contrast, *in vitro* tests are safe and could be used as substitutes [8,9]. In addition, *in vitro* allergy testing also provides the opportunity to monitor the clinical efficacy of commercially

* Corresponding author.
** Corresponding author. Department of Medical Biotechnology, Faculty of Advanced Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran.
E-mail addresses: zarghami@tbzmed.ac.ir (N. Zarghami), sadroddiny@sina.tums.ac.ir (E. Sadroddiny).
[1] Equally contributed.

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Review

Application of immuno-PCR for the detection of early stage cancer

Amjad Hayat Khan, Esmaeil Sadroddiny*

Department of Medical Biotechnology, School of Advanced Technologies in Medicine, International Campus, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Cancer detection in premalignant stage is directly related with increase survival rate. Several biomarkers have been investigated and characterized for monitoring changes inside the cancerous cells. Although enzyme-linked immunosorbent assay (ELISA) is the method of choice in clinical practice for detecting biomarkers in serum/urine samples. However, in certain malignancies the amount of biomarkers before reaching metastasis, are too low to be detected by conventional ELISA. The seminal work of Sano et al. led to the development of highly sensitive and powerful detection method, the immuno-PCR (iPCR), which can detect very small amount of antigens/biomarkers. In spite of, several publications on iPCR sensitivity, it has not been recommended for clinical use and is limited to the scientific community only. In order to evaluate the importance of iPCR, we have made an effort to collect published studies, supporting the use of iPCR in detecting premalignant cancer.

Contents

1. Introduction

According to the National Cancer Institute, North American Association of Central Cancer Registries, and National Centre for Health Statistics, cancer is the leading cause of death throughout the world [1]. Cell division, growth, and differentiation get out of control in malignancy, resulting in the development of mass of cells called tumor, except in some types of leukemia. Sometime cancerous cells disseminate from the neoplasm and spread in blood stream, thereby, leading to the formation of secondary tumors, known as metastasis. Numerous FDA approved therapeutic antibodies are available on the market for addressing diverse

* Corresponding author. Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, No 88 Italia st., PO Box. 1417755469, Tehran, Iran.
E-mail address: sadroddiny@sina.tums.ac.ir (E. Sadroddiny).

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Licensed monoclonal antibodies and associated challenges

Amjad Hayat Khan and Esmaeil Sadroddiny*
Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, International Campus (TUMS-IC), Tehran, Iran

Abstract.
Monoclonal antibodies (mAbs) are the leading class of targeted therapeutics and remarkably effective in addressing autoimmune diseases, inflammations, infections, and various types of cancer. Several mAbs approved by US food and drug administration (FDA), are available on the market and a number are pending for approval. Luckily, FDA approved mAbs have played a pivotal role in the treatment and prevention of lethal diseases. However, claiming that licensed mAbs are 100% safe is still debatable, because infections, malignancies, anaphylactoid, and anaphylactic reactions are the more frequently associated adverse events. To evaluate benefit to risk ratio of mAbs, it is important for the clinical research staff or physicians to monitor and follow-up the patients who are receiving mAbs dozes. It is recommended that patients, physicians, biopharmaceutical companies, and researchers should keep in touch to highlight and resolve antibody-based adverse events. In this review we underscore the associated challenges of mAbs, approved by FDA from 2007–2014.

Keywords: FDA approved mAbs, adverse events of mAbs, antibody-based therapeutics, safety and risks of mAbs, licensed mAbs and associated challenges

1. Introduction

Kohler and Milstein have inaugurated monoclonal antibodies (mAbs) production technology with their seminal work on hybridoma [1]. Further advancement in the field of genomics and proteomics enabled the researchers to develop mouse, chimeric, humanized, and ultimately fully human mAbs. Variable regions of chimeric and complementarity determining regions (CDRs) of humanized mAbs are derived from murine origin. On the other hand, fully human mAbs are derived purely from human sequences. International nonproprietary (INN) names of mAbs ends with suffixes -ximab, -zumab, and -mumab respectively. Table 1 enlist some of the mAbs approved by US food and drug administration (FDA) from 2007–2014.

*Corresponding author: Esmaeil Sadroddiny, Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, No 88 Italia st., Tehran, Iran. PO Box. 1417755469, Tel.: +98 21 88991118 24; Fax: +98 21 88991117; E-mail: sadroddiny@sina.tums.ac.ir.

Target specificity and low toxicity have made mAbs fast and growing class of therapeutics and preventive agents. Amino acid sequences of mAbs have been tailored to reduce the antigenicity and enhance the specificity and functionality. Majority of the mAbs available on the market of US and Europe have been produced in murine myeloma cell lines (e.g. SP2/0, NS0), Chinese hamster ovary (CHO) cells, phage display, and *E. coli* cells [2]. Unfortunately, mAbs derived from mammalian cell lines are expensive, which is the remaining foremost obstacle in the development of new biopharmaceuticals. However, fragment antibodies such as scFv, Fab, and diabodies have been easily produced in yeast, phage display, and *E. coli* at reduced cost [3]. Luckily, antibody-based therapeutics, including, conjugated antibodies, intact antibodies and fragment antibodies have also been licensed for marketing [4].

Mechanism of action of mAbs include, antigen crosslinking, activation of apoptosis, and blockade of ligand-receptors interaction or signalling pathways (Fig. 1). Several mAbs, for instance, eculizumab,

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2- Hammed Aiyelabegan

First Name	Last Name	Program	Level	School
Hammed	Aiyelabegan	Biotechnology	Ph.D	Advanced Technologies

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Biocompatibility and nanostructured materials: applications in nanomedicine

Mahdi Adabi[a], Majid Naghibzadeh[b], Mohsen Adabi[c], Mohammad Ali Zarrinfard[a], Seyedeh Sara Esnaashari[a], Alexander M. Seifalian[d], Reza Faridi-Majidi[a], Hammed Tanimowo Aiyelabegan[e] and Hossein Ghanbari[a]

[a]Department of Medical Nanotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran; [b]Department of Nanotechnology, Research and Clinical Center for Infertility, Shahid Sadoughi University of Medical Sciences, Yazd, Iran; [c]Department of Metallurgy and Materials Engineering, Faculty of Engineering, Roudehen Branch, Islamic Azad University, Roudehen, Tehran, Iran; [d]Centre for Nanotechnology and Regenerative Medicine, University College London, London, United Kingdom; [e]Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

There has been huge interest in applications of nanomaterials in biomedical science, including diagnosis, drug delivery, and development of human organs. Number of these nanomaterials has been already studied in human or at pre-clinical trial. There is a growing concern on potential toxicity and adverse effects of nanomaterials on human health, including lack of standard method of assessment of toxicology of these materials. Our investigation indicated that the bare and small nanoparticle have higher toxicity than modified and bulk materials, respectively. In addition, spherical nanoparticles have less toxicity than rod nanoparticles due to immune response of body.

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Introduction

Nanotechnology is an emerging field involving manipulation of the matter at nanometer scale, which results in a novel class of materials with improved properties for a wide range of applications. Nanomaterials are defined as substances with one or more dimensions in the size range of 1–100 nanometers (Bleeker et al. 2012). Their use in diverse areas has been vastly explored in recent years, offering great advantages over conventional materials. In particular, the engineered nanomaterials have been widely investigated for the biomedical applications, including development of new diagnostic tools such as nanobiosensors and precise imaging modalities, novel therapeutics based on targeted drug delivery systems, and scaffolds for tissue engineering (Chang 2014, Karimi et al. 2015, Ketabchi et al. 2016, Naghibzadeh and Adabi 2014). Due to the increasing usage of nanomaterials in various fields of science and technology, the concerns have been emerged about their safety, biocompatibility, and toxicity.

Nanotoxicology as a branch of toxicology has been attracted researchers attention to specifically investigate potential toxic effects of nanomaterials. Nanotoxicology is an interdisciplinary field dealing with different aspects of the potential toxicity of nanomaterials. While there is a growing interest in the use of nanomaterials in different fields, the safety concerns about their use is also on the rise. Hence, there is an urgent need to address these concerns and expand our knowledge on the safety, biocompatibility, and toxicity of nanomaterials. In biomedical applications, in particular, there are serious concerns on the safety and biocompatibility of nanomaterials, considering the possibility of greater interactions between nanomaterials and biological system.

According to a consensus conference of the European Society for biomaterials in 1986, the biocompatibility is defined as the ability of a substance to present an appropriate host response in a particular application (Duncan and Izzo 2005, Williams 1989). It is worth noting that the interactions between a material and a host are influenced by several factors including the host factors and the properties of the material and the site and duration of the exposure. To understand the type and scale of these interactions, nanomaterials should be tested for potential toxicity in a variety of *in vitro* and *in vivo* settings. However, there is no harmonized standards for evaluating toxicity and biocompatibility of nanomaterials in biological systems and the rules are still being investigated (Dobrovolskaia and McNeil 2007). The aim of this research was to critically review the biocompatibility and toxicology of nanomaterials.

Several nanostructured materials have been explored for the biomedical applications. The most commonly studied materials are based on carbon, silica, and metals in different shapes (i.e., spheres, tubes, and rods) (Adabi et al. 2011, Ketabchi et al. 2016, Shakoori et al. 2015, Tavakol et al. 2014). The toxicity and biocompatibility of these materials depends on several factors such as the size, surface area, functional

CONTACT Hossein Ghanbari, MD, PhD hghanbari@tums.ac.ir Assistant Professor of Nanotechnology & Regenerative Medicine, School of Advanced

Chapter Ten

School of Dentistry

1- Raja Al-Mussawi

First Name	Last Name	Program	Level	School
Raja	Al-Mussawi	Prosthetic Dental Technology	PhD	Dentistry

Published Articles:

	Title of the Article
1	Computer-Based Technologies in Dentistry: Types and Applications
2	Prosthodontic using Rapid Prototyping

Review Article

Computer-Based Technologies in Dentistry: Types and Applications

Raja'a M. Albuha Al-Mussawi [1,2], Farzaneh Farid [3]

[1] Assistant Professor, Department of Prosthodontic, College of Dentistry, Kufa University, Najaf, Iraq
[2] PhD Student, Department of Prosthodontic Technology, School of Dentistry, International Campus, Tehran University of Medical Sciences, Tehran, Iran
[3] Assistant Professor, Department of Prosthodontics, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

Abstract

During dental education, dental students learn how to examine patients, make diagnosis, plan treatment and perform dental procedures perfectly and efficiently. However, progresses in computer-based technologies including virtual reality (VR) simulators, augmented reality (AR) and computer aided design/computer aided manufacturing (CAD/CAM) systems have resulted in new modalities for instruction and practice of dentistry. Virtual reality dental simulators enable repeated, objective and assessable practice in various controlled situations. Superimposition of three-dimensional (3D) virtual images on actual images in AR allows surgeons to simultaneously visualize the surgical site and superimpose informative 3D images of invisible regions on the surgical site to serve as a guide. The use of CAD/CAM systems for designing and manufacturing of dental appliances and prostheses has been well established.

This article reviews computer-based technologies, their application in dentistry and their potentials and limitations in promoting dental education, training and practice. Practitioners will be able to choose from a broader spectrum of options in their field of practice by becoming familiar with new modalities of training and practice.

Keywords: Virtual Reality Exposure Therapy; Immersion; Computer-Aided Design; Dentistry; Education

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Corresponding author:
F. Farid, Department of Prosthodontics, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

f.farid@yahoo.com

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INTRODUCTION

Computer-based technologies play an important role in all aspects of our daily life as well as in dentistry. Simplified interactions between human and computer have caused a profound progress in virtual reality (VR)-based dental training. On the other hand, computer-aided design/computer aided manufacturing (CAD/CAM) of dental appliances and prostheses is now widely used around the globe [1]. Although many dentists have become familiar with CAD/CAM subgroup of computer-based technologies in the recent years, VR and augmented reality (AR) techniques, which are going to find their place in learning and instruction of dental skills, are not as much known [2].

In this article, different types of computer-based technologies including VR and AR simulators, CAD/CAM systems and their applications in dentistry are reviewed.

Virtual Reality Technology

Virtual reality technology is defined as a method by which, an environment is three dimensionally simulated or replicated, giving the user a sense of being inside it, controlling it, and personally interacting with it [3,4]. The virtual environments are almost completely generated by computers [5]. Technology has a wide range of probable benefits in many aspects of life like construction of a building by providing a highly detailed virtual three-dimensional (3D) model of the building to verify each part of the plan, the cost and layout [6]. Similarly, in designing a new product, the virtual prototype can be used instead of physical prototypes to evaluate the design from different aspects [6]. In the medical field, VR is used for instruction of surgical procedures [7,8], education of patients and training students [9-12]. It also helps in treatment of psychological disorders by providing a valid controlled virtual

Prosthodontic using Rapid Prototyping

Raja'a M. Albuha Al- Mussawi[a], Farzaneh Farid[b*], Mohammed T. Alkhafagy[c], Farhad Shafiei[d]

[a]*B.Sc, Tech. Master, PhD Student, Department of Prosthodontic Technology, School of Dentistry, International Campus, Tehran University of Medical Sciences, Tehran, IRAN.*

[a]*Assistant Professor, Prosthodontic Department, College of Dentistry, University of Kufa, Najaf, IRAQ.*

[b]*Assistant Professor, Department of Prosthodontic, School of Dentistry, Tehran University of Medical Sciences, Tehran, IRAN.*

[c]*Assistant Professor, Head of Prosthodontic Department, College of Dentistry, University of Kufa,, Najaf, IRAQ.*

[d]*Assistant professor, Department of Dental Materials, School of Dentistry, Tehran University of Medical Sciences, Tehran, IRAN.*

Abstract

Rapid prototyping is a set of technicality which applied to create a scale model of a physical part or assembly rapidly utilizing three-dimensional computer aided design (CAD) data. 3D printing or "additive layer manufacturing" technology was used to Develop the part or assembly. It is a CAD/CAM technology which was created initially to manufacture prototypes for industrial purposes. RP technology encouraged the configuration and quick generation of mass quantities of precise parts by the industrial manufacturing in a convenient time with exactness and pace. In the previous two decades this technology was utilized efficiently in the medical field with a promising results. In this review the technique, methods and various uses of this fast emerging technology regarding prosthodontic will be discussed.

Keywords: Dentistry; Prosthodontics; Rapid prototyping; Computer-aided design.

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* Corresponding author.

2- Fatemeh Dibaji

First Name	Last Name	Program	Level	School
Fatemeh	Dibaji	Endodontics	Ph.D	Dentistry

Published Articles:

	Title of the Article
1	Fracture Resistance of Roots after Application of Different Sealers

IEJ
Iranian Endodontic Journal

Fracture Resistance of Roots after Application of Different Sealers

Fatemeh Dibaji [a], **Farzaneh Afkhami** [a*], **Babak Bidkhori** [b], **Mohammad Javad Kharazifard** [c]

a Department of Endodontics, Dental School, Tehran University of Medical Sciences, International Campus, Tehran, Iran; b General Dentist, Tehran, Iran; c Statistical Consultant, Dental Research Center, Tehran University of Medical Sciences, Tehran, Iran

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**Corresponding author*: Farzaneh Afkhami, Department of Endodontics, Dental School, Tehran University of Medical Sciences, International Campus, Tehran, Iran.

***Tel*:** +98-21 55851151
***E-mail*:** farzaneh_afkhami@yahoo.com

ABSTRACT

Introduction: Vertical root fracture inevitably leads to tooth extraction. Thus, root filling with obturating materials and sealers that can reinforce the tooth would be an ideal way to reduce fracture in root treated teeth. This study aimed to assess the fracture resistance of roots following the application of different sealers including Epiphany, iRoot sealer and AH-plus. **Methods and Materials:** Fifty extracted human single-canal premolars without caries, curvature or cracks were used in this study. Tooth crowns were cut to yield 13-mm-long roots. Five roots were put in the negative control group and were left unprepared. Forty-five canals were prepared using ProTaper rotary files up to F3 and were then randomly divided into three groups based on the sealer type (n=15). The root canals were filled using cold lateral condensation technique with gutta-percha and AH-Plus sealer, gutta-percha and iRoot sealer and Resilon and Epiphany sealer, in groups one to three, respectively. The roots were then mounted in acrylic molds for fracture resistance testing and subjected to compressive load at a crosshead speed of 1mm/min until fracture. Data were analyzed using the one-way ANOVA. **Results:** The mean fracture resistance was 673.38±170.42 N in AH-Plus, 562.00±184.68 N in iRoot, 708.03±228.05 N in Resilon and 592.59±117.29 N in the control group. No statistically significant difference was found between the experimental groups and the negative control group (P=0.26). **Conclusion:** Application of AH-Plus, bioceramic and Resilon sealers did not change the fracture resistance of roots compared to that of unprepared root canals.

Keywords: AH-Plus; Bioceramic; Epiphany; Fracture Resistance; iRoot; Resilon; Sealer

Introduction

At present, gutta-percha along with sealer is the gold standard of root canal filling [1]. Sealers are capable of filling the voids between gutta-percha cones and the gaps between gutta-percha and dentinal canal walls [2]. Sealing of apical and lateral gaps in the root canal system and adaptation to the dentinal canal walls are the favorable characteristics of ideal sealers [3]. On the other hand, thinning and weakening of root canal walls may occur due to excessive pressure during root canal cleaning and shaping, over-instrumentation, removal of intracanal post, previous endodontic treatment, internal root resorption or dehydration due to the application of irrigating solutions. As a result, the resistance of root canals to functional loads may decrease and the roots become more susceptible to fracture. Therefore, standard principles must be thoroughly followed when filling the root canals [4, 5].

It is believed that root canal sealers that are capable of bonding to root dentin can increase the fracture resistance of endodontically treated teeth [6]. However, studies have yielded

3- Monir Moradzadeh Khiavi

First Name	Last Name	Program	Level	School
Monir	Khiavi	Oral Pathology	Ph.D	Dentistry

Published Articles:

	Title of the Article
1	Therapeutic Efficacy of Orally Delivered Doxorubicin Nanoparticles in Rat Tongue Cancer Induced by 4-Nitroquinoline 1-Oxide

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Research Article

Therapeutic Efficacy of Orally Delivered Doxorubicin Nanoparticles in Rat Tongue Cancer Induced by 4-Nitroquinoline 1-Oxide

Monir Moradzadeh Khiavi[1], Ahamd Rostami[2], Hamed Hamishekar[3], Mehran Mesgari Abassi[3], Amirala Aghbali[2], Roya Salehi[3], Bita Abdollahi[3], Soheila Fotoohi[3], Mahmud Sina[2]*

[1] *Department of Oral and Maxillofacial Pathology, School of Dentistry, Tehran University of Medical Sciences, International campus, Tehran, Iran.*
[2] *Department of Oral and Maxillofacial Pathology, School of Dentistry, Tabriz University of Medical Sciences, Tabriz, Iran.*
[3] *Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.*

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· 4-NQO
· Rats
· Nanoparticles

Abstract
Purpose: Oral cancer is one of the most significant cancers in the world, and squamous cell carcinoma makes up about 94% of oral malignancies. The aim of the present study was to compare the efficacy of doxorubicin plus methotrexate - loaded nanoparticles on tongue squamous cell carcinoma induced by 4NQO and compare it with the commercial doxorubicin and methotrexate delivered orally on seventy SD male rats.
Methods: 70 rats were divided into five groups. During the study, the animals were weighed by a digital scale once a week. Number of mortalities was recorded in the data collection forms. At the end of the treatment, biopsy samples were taken from rat tongues in order to evaluate the severity of dysplasia and the extent of cell proliferation. The results were analyzed using ANOVA, descriptive statistics and chi-square test.
Results: No statistically significant difference was found in the mean weight of five groups ($p>0.05$). No significant relationship was found between groups and mortality rate ($P = 0.39$). In addition, there was a significant relationship between groups and the degree of dysplasia ($P <0.001$). The statistical analysis showed a significant relationship between groups and the rate of cell proliferation ($p <0.001$).
Conclusion: The results of the present study showed that the use of doxorubicin plus methotrexate - loaded nanoparticles orally had more therapeutic effects than commercial doxorubicin plus methotrexate.

Introduction

Head and neck tumors include a major group of neoplasms in worldwide, and are on the rise in many parts of the world. The most common of this disease, is cancer of the mouth approximately 90% are squamous cell carcinoma (SCC).[1] Based on the reports of the World Health Organization, oral cavity carcinoma is the sixth most common cancer after lung, prostate, colorectal, stomach and bladder cancers in men and is the tenth most common, colorectal, cancer in women.[1] Most of the invasive oral carcinomas originate from altered oral pre-cancerous lesions and have a likelihood of progressing to SCC. Tumor progression in epithelial cells is classified into normal epithelium, hyperplasic (non-dysplastic), carcinoma in situ and invasive carcinomas.[1]

Squamous cell carcinoma is a multi-factorial disease. These factors are divided into two groups of internal and external factors. External factors, which include; smoking, alcoholism, syphilis and solar radiation (Vermilion lip cancer), and the internal factors, include systemic or the generalized conditions such as general malnutrition or iron deficiency anemia.[2,3] Developing this type of cancer results in changes of the patient's appearance, decreased quality of life, and most importantly decreased eating ability.[4]

Various treatments have been carried out on squamous cell carcinoma. The standard treatments for this disease include surgery, chemotherapy and radiation, each of which has its own complications. The side effects of chemotherapy include soreness of the mouth, throat, weight loss, thrombocytopenia, vomiting, anorexia, diarrhea, and constipation. The surgical patients in the more advanced stages of this disease may face dysphagia and dysphonia, and most likely deformity of the face.[5] The side effects of radiation therapy include, dry mouth, sensitive teeth/ mucosa with extensive dental caries and dysphagia.[6]

Doxorubicin is one of the most effective anti-cancer drugs. It is prescribed often in combination with other anti-cancer drugs for the treatment of the various cancers. Doxorubicin is a subgroup of anthracycline, which is a branch of antibiotics produced by Streptomyces Peucetius and a variety Cassius.[7]

***Corresponding author:** Mahmud Sina, Tel: 0098 914 1168681, Email: sinam@tbzmed.ac.ir

Chapter Eleven

School of Allied Medical Sciences

1- Amos Otieno Olwendo

First Name	Last Name	Program	Level	School
Amos	Otieno Olwendo	Medical Informatics	M.Sc.	Allied Medical Sciences

Published Articles:

	Title of the Article
1	A probabilistic Model for COPD Diagnosis and Phenotyping Using Bayesian Networks

A probabilistic Model for COPD Diagnosis and Phenotyping Using Bayesian Networks

Leila Shahmoradi [1], Amos Otieno Olwendo [1], Hussein Arab-Alibeik [1], Khosrow Agin [1], Sougand Setareh [*2]

1. Tehran University of Medical Sciences-International Campus (TUMS-IC), Tehran, Iran.
2. Department of Medical Informatics, Tarbiat Modares University of Medical Science, Tehran, Iran.

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Corresponding Author:
Sougand Setareh
Sougand.setareh@gmail.com

ABSTRACT

Introduction: This research was meant to provide a model for COPD diagnosis and to classify the cases into phenotypes; General COPD, Chronic bronchitis, Emphysema, and the Asthmatic COPD using a Bayesian Network (BN).

Methods: The model was constructed through developing the Bayesian Network structure and instantiating the parameters for each of the variables. In order to validate the achieved results, the same data set was applied to a neural network application using the Levenberge- Marquardt algorithm. Furthermore, a card Diag, a C++ application that enables graphical classification of COPD into phenotypes and depicts the relationships of COPD phenotypes was developed.

Results: The results showed that a Bayesian Network can be successfully applied to develop a probabilistic model for diagnosis and classification of COPD cases into the corresponding phenotypes.

Conclusions: A model that classifies COPD cases into phenotypes of general COPD, Chronic bronchitis, Emphysema, and Asthmatic COPD was successfully developed. Moreover, the achieved results also helped to represent graphical representations of COPD phenotypes and explained how the phenotypes relate to each other. It was also observed that COPD is mostly associated with people aged 40 years or older. Overall, smoking is the major cause of COPD.

Keywords: Bayesian networks, COPD Diagnosis, COPD Phenotypes, Noisy-OR CPD

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معاونت بین الملل

فعالیتهای پژوهشی پردیس بین الملل

(مقالات علمی)

از مهر ۱۳۹۳ تا مرداد ۱۳۹۶

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معاونت پژوهشی پردیس بین الملل

مرداد ۱۳۹۶