Serum Vitamin B12 and Methyl-malonic Acid Status in a group of Migraine Patients Compared to Healthy Controls: A Case-Control Study

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Abstract

Background

Vitamin B12 is involved in scavenging against NO and prevention of hyperhomocysteinemia, the two factors which are proposed to be probably implicated in migraine pathogenesis. Thus, in the current study we aimed at evaluating the serum vitamin B12 and its most sensitive and specific biomarker, methyl-malonic acid (MMA) status in a group of migraine patients compared to healthy controls.

Methods

Seventy migraine patients (34 chronic and 36 episodic migraineurs) and 70 sex- age matched control subjects were enrolled in this case control study from April to September 2017. Patients were diagnosed based on an expert headache specialist-neurologist examination according to the International Headache Society criteria (ICHD-IIIβ). Migraine characteristics include the number of headache attacks, severity of headaches (from 0 to 10), and duration of each attack in hours were recorded based on a 30-day headache diary. The serum vitamin B12 and MMA levels were measured with ELISA and using commercially available test kits. The study protocol was approved by the ethics committee of the Tehran University of Medical Sciences (ethics board approval code= IR.TUMS.IKHC.REC.1396.2468).

Results

The serum levels of B12 were found to be significantly lower in migraine patients than in control subjects(584.08± 300.20 vs. 750± 350.91pg/ml;P=0.007); whereas migraineurs had higher levels of MMA than control participants(2.171± 1.90 vs. 2.07± 2.05µg/dL;P=0.02). In the fully adjusted regression models, those in the highest vs. the lowest serum B12 quartile had 80% decrease in the odds of having migraine(OR= 0.20, 95% CI= 0.05-0.73;P for trend= 0.008)]; while, patients in the highest quartile of MMA had more than 5 times increased risk of developing migraine(OR= 5.44, 95%CI= 1.49-19.87;P for trend= 0.002). There was no association between serum B12 levels and headache characteristics.

Conclusion

Taken together, these results suggest that increasing level of serum B12 was accompanied by roughly 80% decrease in the odds of developing migraine. In addition, it was shown that participants with higher MMA levels, that considered as lower functional activity of B12, had about 4-to-5 fold higher odds of having migraine.

The Association Between Low Carbohydrate Diet Score and Migraine

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Introduction

The high fat, high protein and low carbohydrate diet (LCD) is widely used for seizure and epilepsy treatment. Due to the suggested underlying relationship between migraine and epilepsy, LCD might have some effects on migraine headache too. But to date, there are a few researches that have addressed the association between LCD and migraine. Thus, we aimed to investigate the relationship between total and animal or plant based LCD scores and migraine.

Methods

The case group were 534 migraineurs who were diagnosed based on ICHD III criteria. Control subjects consisted of 741 healthy individuals who were randomly selected from general population. After obtaining demographic and anthropometric data, a validated 168-item semi-quantitative food frequency questionnaire (FFQ) was applied for assessing dietary intakes. The total LCD score calculated according to dietary macronutrients intakes including carbohydrate, protein, fat and also animal fat, animal protein, vegetable plant and plant protein intake, expressed as a percentage of energy. The LCD scores increase with higher intakes of macronutrients, except for carbohydrate.

Results

Overall, about 62.1% of healthy subjects (mean age=43.66 years) and 92.5% of migraineurs(mean age=36.27 years) were women. Multiple regression models adjusted for age, gender, BMI and energy intake revealed a marginally significant 35% reduced odds of migraine for the subjects in the second quintile relative to those in the lowest quintile of total LCD score whereas the odds of migraine for those in the 4^{th} and 5^{th} quintiles increased significantly [(OR=0.65,95%CI=0.42-1.00 for the 2^{nd}quintile); (OR=0.95,95%CI=0.63-1.44 for the 3^{rd}quintile); (OR=2.04,95%CI=1.34-3.12 for the 4^{th}quintile);(OR=3.32,95%CI=2.15-5.13 for the 5^{th}quintile); compared to the lowest quintile as reference; P-for-trend=0.00].

Regarding animal based LCD score, the mentioned regression models resulted in roughly 2-7 fold higher odds of developing migraine for subjects in the fourth and fifth quintile of this score than those in the first quintile [(OR=2.67,95%CI=1.75-4.08 for the 4^{th}quintile);(OR=7.19,95%CI=4.61-11.21 for the 5^{th}quintile); P-for-trend=0.00]. In contrast, it was highlighted that the participants who had higher scores of plant based LCD had lower risk for migraine [(OR=0.44,95%CI=0.30-0.65 for the 2^{nd}quintile);(OR=0.59,95%CI=0.40-0.86 for the 3^{rd}quintile); (OR=0.83,95%CI=0.54-

1.28 for the 4thquintile);(OR=0.67, 95%CI=0.45-1.01 for the 5thquintile); compared to the lowest quintile as reference; P-for-trend=0.001]

Conclusion

These findings highlight the protective role of a low carbohydrate diet based on plant sources of fat and protein on migraine headache. Conversely, it was shown that consuming a low carbohydrate diet, but rich in animal fat and animal protein could highly increase the risk of migraine in susceptible subjects.

The Association Between Dietary Tryptophan Intake and Migraine

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Background

Migraineurs have been identified to have chronically decreased serotonin levels which markedly increases during ictal periods. Also, increased sensitivity to serotonin agonists might occur during attacks probably due to a defect in serotonin metabolism. Tryptophan is a precursor of serotonin. Once tryptophan concentrations diminished, it results in a short-term drop in neural serotonin level. However, much uncertainty still exists about the association between tryptophan and migraine. Regarding the importance of adequate tryptophan intake in regulating serotonin hemostasis and subsequent effects on migraine attacks, we designed the current study to assess the relationship between dietary tryptophan intake and migraine headache risk.

Methods

The migraine group (n=550, diagnosed according to the ICHDIII criteria) were recruited from a tertiary headache clinic. The control subjects consisted of 741 healthy volunteers who were randomly selected from general population. After collecting demographic and anthropometric data, a validated 168-item semi-quantitative food frequency questionnaire (FFQ) was used for dietary intake assessments. Multiple regression models were applied in order to explore the relationship between migraine and dietary tryptophan intake.

Results

The mean(SD) of the age of participants in the controls and migraine group was 43.83(14.50) and 36.21(9.85) years, respectively. Also, the mean(SD) BMI of controls and cases were about 27.71(4.57) and 25.99(4.79) kg/m^2, respectively. The multiple regression models were adjusted for age, sex, BMI and dietary intakes of energy, food groups(g/d) such as total grains, vegetables, fruits, fish and poultry, red and processed meat and nuts groups and also intake of a number of nutrients including animal based protein(g/d), plant based protein(g/d), total fat(g/d), saturated fat(g/d), unsaturated fat(g/d), and cholesterol(mg/d). the models showed significant inverse association between tryptophan intake and migraine risk [(OR in the 3^{rd} quartile=0.31;95%CI= 0.13- 0.72) (OR in the 4^{th} quartile= 0.19;95%CI=0.05-0.66) with the first quartile as reference;p-for-trend=0.001].

Conclusion

To the best of our knowledge, this is the first relatively large population based investigation of the migraine headache risk according to dietary tryptophan intake. Our results showed that subjects who had a median intake of 0.90-1.15 grams of tryptophan per day had a reduced odds of developing migraine by approximately 69-81%, relative to those consumed ≤0.57 g/d. These findings therefore highlighted that considering enough intake of tryptophan rich foods such as milk, poultry, egg, seafood, soybeans, salmon within a healthy diet could lead to attenuating the odds of migraine among susceptible subjects.