Hindawi Publishing Corporation
Advances in Pharmacological Sciences
Article ID 9128018

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

Received 4 November 2015; Revised 6 January 2016; Accepted 13 January 2016

Academic Editor: Masahiro Oike

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