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Protective effect of diltiazem and fenofibrate against ischemia-reperfusion induced cardiac arrhythmias in isolated rat hearts

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Fenofibrate is a peroxisome proliferator-activated receptor (PPAR)-α activator, that lowers triglycerides, but it also influences cytochrome P 450 (CYP-450) dependent arachidonic acid metabolism. CYP-450 metabolizes arachidonic acid to epoxyeicosatrienoic acids (EETs). EETs have diverse cardiovascular functions including coronary dilator antihypertensive, anti platelet and protective effects against ischemia reperfusion induced injury in the heart and kidneys. The beneficial cardiovascular effects of fibrates are linked to its CYP-450 inducing properties that in turns increases the endogenous production of EETs. Diliazem, a standard calcium channel blockers was used as a reference drug. The aim of this study was to find out whether fenofibrate can provide protection against ischemia and re-perfusion (I/R)-induced cardiac arrthymias in isolated rat hearts. Male Wistar rats were used in the study; fenofibrate was administered 100 mg/kg orally for five days. One hour after the administration of the last dose, the animals were sacrificed and hearts were isolated, mounted on Langendorff apparatus and perfused with Krebs solution with constant flow (10 ml/min). 15 min after stabilization, hearts were subjected to ischemia by ligating the left coronary artery with a suture for 10 min. Reperfusion was initiated by releasing the ligature and continued monitoring of hearts for 30 min for ventricular premature counts (VPC), ventricular tachycardia (VT) and ventricular fibrillation (VF) via ECG lead and force transducers connected to power lab. Fenofibrate pre-treatment caused a significant decrease in the incidence of VF from 80% (control) to 33% (fibrate treated animals), ($P<0.05$). VPC were also markedly decreased from 1497±105 (control) to 1094±135 (fibrate treated). Significant protective effect of fenofibrate was evident against ischemia-reperfusion induced VT, reducing the total duration of VT to 13±4 seconds in fibrate treated animals compared to 147±38 seconds in vehicle treated group. Diltiazem (1 µml/ml) completely protected the hearts against I/R-induced arrhythmia. These finding indicate that fenofibrate suppresses arrhythmia in isolated rat heart subjected to ischemia-reperfusion induced injury. Further studies are underway to elucidate the possible role of EETs in the observed cardioprotective effects of fenofibrate and other possible cardiovascular effects.

Biography

Ishfaq A Bukhari is an assistant professor at King Saud University, Saudi Arabia. Previously he worked as a Post-Doctoral Fellow in the Department of Pharmacology, Medical College of Wisconsin, USA during 2009-2010. His current research area is Regulation of vascular tone in the heart by novel endothelial products. He got his PhD from Department of Pharmacology, Faculty of Pharmacy, University of Karachi, Pakistan and Department of Biological and Biomedical Sciences Aga Khan University Medical College, Karachi and M.Phil from University of Karachi, Pakistan. He has published more than 20 article in various national and international journals.

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