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Possible Role of Fenofibrate and Clofibrate in Attenuated Cardioprotective Effect of Ischemic Preconditioning in Hyperlipidemic Rat Hearts

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Abstract : Objective: The present study has been designed to investigate the beneficial role of Fenofibrate & Clofibrate in attenuated the cardioprotective effect of ischemic preconditioning (IPC) in hyperlipidemic rat hearts. Materials & Methods: Experimental hyperlipidemia was produced by feeding high fat diet to rats for a period of 28 days. Isolated langendorff's perfused normal and hyperlipidemic rat hearts were subjected to global ischemia for 30 min followed by reperfusion for 120 min. The myocardial infarct size was assessed macroscopically using triphenyltetrazolium chloride staining. Coronary effluent was analyzed for lactate dehydrogenase (LDH) and creatine kinase-MB release to assess the extent of cardiac injury. Moreover, the oxidative stress in heart was assessed by measuring thiobarbituric acid reactive substance, superoxide anion generation and reduced form of glutathione. Results: The ischemia-reperfusion (I/R) has been noted to induce oxidative stress by increasing TBARS, superoxide anion generation and decreasing reduced form of glutathione in normal and hyperlipidemic rat hearts. Moreover, I/R produced myocardial injury, which was assessed in terms of increase in myocardial infarct size, LDH and CK-MB release in coronary effluent and decrease in coronary flow rate in normal and hyperlipidemic rat hearts. In addition, the hyperlipidemic rat hearts showed enhanced I/R-induced myocardial injury with high degree of oxidative stress as compared with normal rat hearts subjected to I/R. Four episodes of IPC (5 min each) afforded cardioprotection against I/R-induced myocardial injury in normal rat hearts as assessed in terms of improvement in coronary flow rate and reduction in myocardial infarct size, LDH, CK-MB and oxidative stress. On the other hand, IPC mediated myocardial protection against I/R-injury was abolished in hyperlipidemic rat hearts. However, Treatment with Fenofibrate (100 mg/kg/day, i.p.), Clofibrate (300mg/kg/day, i.p.) as a agonists of PPAR-α have not affected the cardioprotective effect of IPC in normal rat hearts, but its treatment markedly restored the cardioprotective potentials of IPC in hyperlipidemic rat hearts. Conclusion: It is noted that the high degree of oxidative stress produced in hyperlipidemic rat heart during reperfusion and consequent down regulation of PPAR-α may be responsible to abolish the cardioprotective potentials of IPC.

Keywords : Hyperlipidemia, ischemia-reperfusion injury, ischemic preconditioning, PPAR-α
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