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POSTCONDITIONING ATTENUATES THE MYOCARDIAL INJURY INDUCED BY ISCHAEMIA/REPERFUSION IN THE HYPERLIPIDEMIC RATS

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Objectives To investigate the effects of postconditioning (PostC) on the myocardial ischaemia/reperfusion injury in the hyperlipidemic rats.

Methods 60 Sprague-Dawley (SD) rats were randomly divided into Sham, I/R+normal diet, I/R+Vehicle+HC diet, I/R+PostC+HC diet groups. The levels of plasma lipid was examined by chromatometry, and the area at risk (AAR) and infarct size were evaluated by TTC staining, the AAR was expressed as a percentage of the left ventricular area (AAR/LV). The plasma creatine kinase (CK) activity was also measured. Myocardial apoptosis examined by Caspase-3 activity assay; the mRNA and the protein expression of HIF-1 α and iNOS were assessed by RT-PCR and Western blot.

Results The infarct size in Control group was greatly increased than that in Sham group both in normal diet and hyperlipidaemia ($33.38 \pm 1.4\%$ vs $39.54 \pm 1.16\%$, $p < 0.01$). Hyperlipidaemia reinforced the increase of plasma creatine kinase (CK) activity by I/R. (0.56 ± 0.06 vs 0.47 ± 0.04 , $p < 0.01$), and further augmented myocardial apoptosis induced by I/R. The activity of Caspase-3 significantly increased in Control group compared to Sham group. However, hyperlipidaemia further augmented the increase of Caspase-3 activity induced by I/R (4.63 ± 0.42 vs 2.31 ± 0.27 , $p < 0.01$). Postconditioning attenuated the myocardial infarct size in I/R rats by decreasing plasma CK activity (0.38 ± 0.06 vs 0.43 ± 0.05 , $p < 0.05$), and ameliorated Caspase-3 activity (1.72 ± 0.16 vs 2.43 ± 0.25 , $p < 0.01$). In normal diet rats, I/R extremely increased the HIF-1 α protein level, while postconditioning further enhanced the increase of HIF-1 α protein expression induced by I/R. But under the hyperlipidemic condition, HIF-1 α protein level was much higher than that in normal diet groups. While postconditioning also markedly increased HIF-1 α level. The mRNA level of HIF-1 α were no significant changes in all groups. But the iNOS expression both in mRNA and in protein level were increased in hyperlipidemic rats.

Conclusions Postconditioning attenuates the myocardial injury induced by ischaemia/reperfusion in hyperlipidemic rats by increasing the expression of HIF-1 α , which may be related to iNOS-cGMP signalling pathway.