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PROTECTIVE EFFECTS OF SITAGLIPTION PRETREATMENT ON MYOCARDIAL ISCHAEMIA/ REPERFUSION INJURY IN RATS

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Objectives DPP4 inhibitors have been approved for antihyperglycemic agents. In addition to the insulinotropic effect, GLP-1 signalling was reported to have cardioprotectiveeffects, but the precise mechanism remains unknown. In this study, we aimed to determine the cardiovascular responses of pretreatment with a DPP4 inhibitor-Sitagliptionin ischaemia/reperfusion rats and investigate its underlying mechanism.

Methods Twenty-four Male Sprague-Dawley rats were randomly divided into 3 groups: Sham group (n=8, lavaged with double-distilled water), Ischaemia/Reperfusion group (n=8, lavagedwith double-distilled water), Sitagliption group (n=8, lavaged with Sitagliption, 30 mg/kg/day). After pretreated 2 weeks, rats in

Ischaemia/Reperfusionand Sitagliptionn groups were subjected to30 min of coronary artery occlusion, followed by reperfusion for 2 h, and then the effect of Sitagliptionn on the cardiovascular responses were evaluated by detecting changes of left ventricular weight index (LVWI), myocardial cell apoptosis by flow cytometry (FCM), the levels of blood glucose, creatine kinase-MB (CK-MB), lactate dehydrogenase (LDH), malondialdehyde (MDA), glutathione peroxidase (GSH-Px) andsuperoxide dismutase (SOD) in plasma.

Results TheLVWI and the blood glucose level in three groups were nonsignificant differences. The CK-MB, LDH, MDA level and cell apoptosis rate in Sitagliptionn group were significant lower than I/R group (CK-MB: 776.4±44.0 μ/l vs 1359.2±187.2 u/l, p<0.05; LDH: 1326.9±166.8 nmol/ml vs 2131.1±303.8 nmol/ml, p<0.01; MDA: 39.5±6.3 vs 55.2±3.5 nmol/ml, p<0.01; rate: (20.3±3.1)% vs (28.1 ±3.3)%, p<0.01), but still higher than those in Sham group (CK-MB: 776.4±44.0 μ/l vs 578.8±60.0 μ/l, p<0.01; LDH: 1326.9 ±166.8 vs 503.8±188.5 nmol/ml, p<0.01; MDA : 39.5±6.3 vs 26.45 ±1.9 nmol/ml, p<0.01; rate: (20.3±3.1)% vs (11.7±1.9)%, p<0.01).

Compared with I/R group, the GSH-Px and SOD level in Sitagliptionn group were significantly increased (GSH-Px: 241.8 ±12.9 u/ml vs 189.7±19.9 u/ml, p<0.01; SOD: 234.7±13.1 nmol/ml vs 163.3±23.2 nmol/ml, p<0.01), but still lower than those in Sham group (GSH-Px: 241.8±12.9 u/ml vs 282.6±15.6 u/ml, p<0.01; SOD: 234.71±13.1 nmol/ml vs 288.7±20.2 nmol/ml, p<0.01).

Conclusions Our results suggested sitagliptionn pretreatment could provide significantly cardio protective effects against ischaemia/reperfusion injury in rats. The mechanisms might be attributed to scavenging lipid peroxidation products, increasing antioxidantdefense enzymes and preventing myocardial cell apoptosis.