GW23-e2470

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

doi:10.1136/heartjnl-2012-302920b.8

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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 cardioprotective effects, but the precise mechanism remains unknown. In this study, we aimed to determine the cardiovascular responses of pretreatment with a DPP4 inhibitor-Sitagliptin in 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, lavaged with double-distilled water), Sitagliptin group (n=8, lavaged with Sitagliptin, 30 mg/kg/day). After pretreated 2 weeks, rats in

Ischaemia/Reperfusion and Sitagliptin groups were subjected to 30 min of coronary artery occlusion, followed by reperfusion for 2 h, and then the effect of Sitagliptin 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) and superoxide dismutase (SOD) in plasma.

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

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

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