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EARLY BUT NOT LATE INSULIN TREATMENT IMPROVES LEFT VENTRICULAR REMODELLING AND CARDIAC FUNCTION INDUCED BY MYOCARDIAL INFARCTION IN RATS

Fu Feng, Ji Lele, Liu Wenchong, Yang Weidong, Wang Jing, Zhang Haifeng, Gao Feng *Department Of Physiology, Fourth Military Medical University, Xi´an, China*

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Objectives Insulin exerts significant cardioprotective effects in acute myocardial ischaemia/reperfusion (MI/R) through the PI3K-Akt signalling. The present study was aimed at investigating the effect of insulin treatment on the prolonged postischemic cardiac structural and functional changes.

Methods Adult male rats were subjected to left anterior descending coronary artery occlusion and were randomised to receive one of the following treatments: saline, early insulin treatment or late insulin treatment (the same dose and routine of insulin starting at 1 week after the surgery).

Results Infarct size was significantly reduced in early but not late insulin treatment group compared to control group 4 wks after MI (30.2±2.5% vs 45.2±2.6%, n=6, p<0.05). In addition, early but not late insulin treatment attenuated the increase in LV end-systole diameter (0.40±0.02 vs 0.54±0.03 cm, n=8, p<0.05) and decrease in ejection factor (65.4±3.1% vs 48.1±2.1%, n=8, p<0.01). Interstitial collagen volume fraction (6.38±0.63% vs 9.44±0.48%, n=6, p<0.05) and myocardial apoptosis index (8.24±1.29% vs 18.14±1.43%, n=6, p<0.05) in LV border regions were decreased with early but not insulin treatment. Interestingly, insulin-stimulated fluorodeoxyglucose uptake (3.48±0.79 vs 18.80±1.06, n=6, p<0.01) was significantly lower 1 wk after MI together with blunted Akt phosphorylation but increased p38 MAPK phosphorylation in non-infarcted myocardium compared with those in the normal animals.

Conclusion These data indicate that early but not late insulin treatment improves left ventricular remodelling and cardiac function in rat MI model, myocardial insulin resistance may be one possible mechanism that abolished the cardioprotective effects of late insulin treatment on cardiac structure and function.