GW23-e0344

EXOGENOUS HIGH MOBILITY GROUP BOX 1 PROTEIN IMPROVES CARDIAC FUNCTION AFTER MYOCARDIAL INFARCTION IN RATS

doi:10.1136/heartjnl-2012-302920a.79

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Objectives Exogenous high mobility group box 1 protein (HMGB1) injection could prevent left ventricular remodelling and enhance left ventricular function during myocardial infarction (MI). However, the mechanism remains unclear. This study was to investigate in the mechanism of cardioprotection of HMGB1 during MI in rats.

Methods Anesthetised male rats were treated once with HMGB1 (200 ng) 4 h after MI; and then executed after 7 and 28 days, respectively. Cardiac function was measured by echocardiography. Collagen deposition were measured by masson trichrome. Dishevelled-1 and β-catenin protein expression were measured by western blot. Dishevelled-1 mRNA expression were measured by real-time PCR.

Results After MI 7 days or 28days, the left ventricular ejection fraction (LVEF) was significantly decreased compared to that of sham operated control group ($p<0.05$). However, the LVEF of HMGB1-treated groups were significantly increased compared to those of the MI group in both 7 days and 28 days ($p<0.05$). Masson trichrome staining detected large number of collagen deposition in the peri-infarct area of MI/7days and 28 days, while it was significantly reduced in the MI-HMGB1/7days and 28 days ($p<0.05$), indicating that the collagen volume fraction was significantly reduced in the HMGB1-treated group in infarcted border zone. The expression of dishevelled-1 protein was significantly increased in both MI/7days and MI-HMGB1/7days compared to that of SO group ($p<0.05$). However, dishevelled-1 protein has a sudden drop and decreased significantly in MI/28days ($p<0.05$). Conversely, it was significantly increased in MI-HMGB1/28days ($p<0.05$). β-catenin protein expression consistent with dishevelled-1, increased significantly at MI/7days and then turn to decrease significantly in MI/28days (group 3), while it was continually

increasing from 7 to 28 days in MI-HMGB1/7 days and MI-HMGB1/28 days ($p<0.05$). Compared with sham-operated group, expression of dishevelled-1 mRNA increases both in MI/7 days and MI-HMGB1/7 days ($p<0.05$), and then the dishevelled-1 gene expression decreased abruptly in MI/28 days ($p<0.05$). While the dishevelled-1 mRNA expression has a markedly increasing in MI-HMGB1/28 days group ($p<0.05$).

Conclusions Our study suggested that exogenous high mobility group box 1 protein injection improves cardiac function after MI which may be involved in Wnt/β-catenin signalling activation.