GW23-e1210 **PROTECTIVE EFFECTS OF ERYTHROPOIETIN ON CARDIAC FUNCTION IN DIABETIC RATS**

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[1]Dai Qiming, [1]Zhang Shufeng, [1]Lu Jing, [2]Dai Qiming. *[1]Cardiology department, Zhongda Hospital, Southeast University; [2]Department, Zhongda Hospital, Southeast University*

Objectives To investigate the protective effects of erythropoietin on cardiac function of diabetic rats and its mechanism

Methods Forty-five male SD rats (180–200 g) were randomly divided into three groups: normal control (CON, n=15), STZ-induced diabetic rats (DM, n=15), and diabetic rats treated with EPO (DM+EPO, n=15). Diabetic rat model was established by intraperitoneal injection of STZ. These rats were fed under standard conditions. The rats in DM+EPO group received EPO (1000 U/kg per injection) at 7-day intervals after diabetic model was established. Rats in CON group and DM group received the same dose of saline. At the beginning of experiment and the end of the 12th week blood samples of rats were collected to analyse red blood cell count and fasting blood glucose. Echocardiography was performed to get the parameters of cardiac function in rats and blood was collected to analyse the count of endothelial progenitor cells (EPCs) at the end of the 12th week. CTGF protein expression in myocardial tissue was detected by immunohistochemical method, while VEGF protein and VEGF mRNA expressions were examined by realtime RT-PCR and western blot respectively.

Results (1) Red blood cell count and fasting blood glucose: The average red blood cell count of the CON group, DM group and DM +EPO group at the end of the 12th week was $(8.16\pm0.37)\times10^{12}$/l, $(7.68\pm0.44)\times10^{12}$/l and $(8.63\pm0.47)\times10^{12}$/l respectively. No significant difference was found between DM+EPO group and CON group, as well as between CON group and DM group ($p > 0.05$). But DM+EPO group was significantly higher than diabetic group ($p<0.01$). The average fasting blood glucose of the three groups was 4.13±0.43 mmol/l, 20.27±1.20 mmol/l and 21.37±1.53 mmol/l respectively. No significant difference was found in fasting blood glucose between DM+EPO group and DM group ($p > 0.05$), but the two groups were both higher than CON group ($p<0.01$). In DM+EPO group the fasting blood glucose at the beginning and the 12th week had no difference ($p >> 0.05$). (2) Index of cardiac function measured by echocardiography: The average of left ventricular ejection fraction (LVEF) of three groups was 79.4±8.12%, 65.7 ±5.49% and 75.6±4.87% respectively. LVEF of DM group was significantly lower than CON group, while DM+EPO group was significantly higher than DM group ($p<0.01$). But the difference between DM+EPO group and CON group was not significant ($p>0.05$). (3) The count of EPCs (%) in blood: The count of EPCs in blood for the DM+EPO group was much higher than CON group and DM group (51.75±1.91 vs 7.65±0.90 or 2.71±0.74, $p< 0.01$), and CON group was higher than DM group ($p<0.01$). (4) The expression of CTGF in myocardial tissue: Mild positive staining with VEGF was observed in CON group, while VEGF staining was strongly seen in DM group and moderate in DM+EPO group. (5) The expression of VEGF mRNA: The expression of VEGF mRNA for DM+EPO group was much higher than CON group and DM group (0.81±0.031 vs 0.65±0.040 or 0.29±0.053, $p<0.01$), and DM group was lower than CON group ($p<0.01$). (6) The expression of VEGF protein: The expression of VEGF protein for the DM+EPO group was much higher than CON group and DM group (0.59 ±0.026 vs 0.40±0.032 or 0.23±0.024, $p<0.01$), while DM group was lower than CON group ($p<0.01$).

Conclusions (1) EPO can improve the cardiac function of diabetic rats. (2) EPO can increase the count of EPCs in blood, upregulate the expression of VEGF and downregulate the expression of CTGF of myocardial tissue in diabetic rats. 3. EPO can protect cardiac function in diabetic rats probably via improving microvascular function and inhibiting fibrosis of myocardial tissue.