GW23-e0308

MENSTRUAL BLOOD STEM CELLS IMPROVED MYOCARDIAL SURVIVAL AFTER RAT MYOCARDIAL INFARCTION BY PARACRINE

doi:10.1136/heartjnl-2012-302920j.31

Zhi Jiang, Jian an Wang. *Department of Cardiology, Second Affiliated Hospital, Zhejiang University College of Medicine, Administration Building, Rm. 1601, 88 Jiefang Road, Hangzhou, Zhejiang Province, P. R. China 310009*

Objectives In the study, we hypothesised menstrual blood stem cells (MBSCs) protect ischaemic myocardium through paracrine effect.

Methods MBSCs were isolated and expanded from human female menstrual blood. Then we infused the MBSCs intramyocardially in a rat acute myocardial infarction model, and cocultured MBSCs with neonatal rat cardiomyocytes (NRCs).

Results In vitro experiments, the apoptosis ratio of NRCs underwent hypoxia/reoxygenation in coculture group was lower than the control group (8.95±1.32% vs 18.42±1.80%, $p<0.01$), and intracellular ROS generation was also lower (change fold, 27.8 ±4.1% vs 80.0±12.7%, $p<0.01$). The medium of normoxia and hypoxia cultured MBSCs was determined the secreted EGF, VEGF and TGF-β (559±21, 0, 635±59 ng/ml in normoxia culture respectively, 582±19, 198±6, 664±102 ng/ml in hypoxia culture respectively). The RNA was also extracted and reverse transcriptional PCR showed that MBSCs expressed multiple cytokines. The MBSCs were transplanted intramyocardially after ligation of the left anterior descending (LAD) in rats. After 48 h, less apoptotic cardiomyocytes were detected in the transplant group (infarct, 54.24±2.10% vs 67.97±3.28%, $p<0.01$; peri-infarct, 6.93±1.05% vs 11.88 ±1.47%, $p<0.05$) and western blot showed higher level of AKT phosphorylation and upregulation of BAX, as well as the decreased expression of cleaved caspase 9. 4 weeks later, 18-fluorodeoxyglucose microPET images indicated more viable cardiomyocytes in the scar area of transplant group than those of saline group (0.357 ±0.067 vs 0.275±0.053, $p<0.01$ in transverse section, 0.333±0.046 vs 0.267±0.045, $p<0.01$ in coronal section). The infarct size of transplant group was less than saline group in Masson's trichrome stain (33.6±2.9% vs 41.6±4.9%, $p<0.05$). Immunofluorescence of the peri-infarct and infarct region by vWF and α-SMA staining showed obviously higher vessel density in the transplant group (vWF positive microvessels, 186±16/field vs 118±12/field, $p<0.05$; α-SMA positive arteriole, 35±7/field vs 21±6/field, $p<0.05$). Few differentiation of MBSCs toward endotheliocyte, smooth muscle cell and cardiomyocytes were found and no specific immune cell infiltration were observed around the MBSCs in vivo.

Conclusions MBSCs paracrined multiple cytokines to protect cardiomyocytes from apoptosis and stimulate angiogenesis, which rescued the myocardium in the infarct region and finally resulted in a better cardiac function.