[gw22-e0931]

PARACRINE ACTION ACCOUNTS FOR MARKED PROTECTION OF MONOCROTALINE-INDUCED PULMONARY ARTERIAL HYPERTENSION BY BONE MARROW-DERIVED ENDOTHELIAL PROGENITOR CELLS

DongMei Jiang¹, Jie Han², JunHui Zhu¹, GuoSheng Fu¹ ¹*Department of Cardiology, Sir Run Run Shaw Hospital, Hangzhou, China;* ²*College of Medicine, The First Affiliated Hospital, Zhejiang University, Zhejiang, China*

10.1136/heartjnl-2011-300867.108

Background Endothelial dysfunction is a characteristic pathophysiology of pulmonary arterial hypertension (PAH). Some paracrine factors secreted by bone marrow-derived endothelial progenitor cells (BMDEPC) have the potential to protect endothelial integrity and function. This study investigated whether BMDEPC enhances production of vasoprotective substances through paracrine action in pulmonary arteries of monocrotaline (MCT)-induced PAH.

Methods and Results Mononuclear cells were obtained from femoral bone marrow of normal F344 rats and cultured for seven days to yield BMDEPC. Pulmonary arteries were exposed to BMDEPC (5×10^6 cells) in vitro or in vivo. Three weeks later, cyclooxygenase-2 (COX-2) expression, prostacyclin (PGI_2) and cAMP release were examined in isolated pulmonary arteries. Treatment with BMDEPC improved the pulmonary artery relaxation of MCT-induced PAH, and BMDEPC were observed in the pulmonary bed. Further analysis demonstrated increased protein expression of COX-2 in all three layers of arteries transplanted with BMDEPC. And, release of PGI_2 and content of cAMP were significantly enhanced. Moreover, the increased release of PGI_2 and cAMP were reversed only by a selective COX-2 inhibitor. Treatment with conditioned media obtained from BMDEPC exerted the same effect of BMDEPC on pulmonary artery in vitro or in vivo.

Conclusions Transplantation of BMDEPC effectively ameliorates MCT-induced PAH. Growth factors secreted in a paracrine manner by BMDEPC promotes vasoprotection by increasing the release of PGI_2 and content of cAMP. Furthermore, the COX-2/ PGI_2 synthase pathway appears to take a major responsibility for this effect.