Abstract

Background: A number of studies now suggest that endothelial progenitor cells (EPCs) may induce neovascularisation and could be a promising approach for cell based therapy for pulmonary artery hypertension (PAH).The aim of the present study was to investigate the effect of intravenous injection of bone marrow-derived endothelial progenitor cells (EPCs), alone or combined with NO inducer and HO inducer in restoring pulmonary hemodynamics and increasing microvascular perfusion in the rat monocrotaline (MCT) model of PAH so improving right ventricle performance. **Methods:** 80 Male rats were randomized to the following groups 10 rats each, **Group 1(control):** it includes 10 rats and serves as negative control group (healthy control). The other 70 rats received MCT (60 mg/kg), after 14days these rats were subdivided into the following groups **,Group 2 (PAH):** received 1 ml PBS intravenously, **Group 3 (PAH+EPCs)** received 10^6 EPCs per rat given by Intravenous infusion at the rat tail vein, **Group 4 (PAH+NO)** received NO inducer (L-Arginine was given 300mg/kg body weight intraperitoneally), **Group 5 (PAH+HO)** received intraperitoneal administration of HO-1 inducer (cobalt protoporphyrin 0.5 mg/100 gm intraperitoneally, 3 times /week for 2 weeks), **Group 6 (PAH+NO)** received I.V. administration of 10^6 EPCs plus NO inducer, **Group 7 (PAH+HO)** received I.V. administration 10^6 EPCs plus HO-1 inducer, **Group 8 (PAH+NO+HO)** received I.V. administration 10^6 EPCs plus NO and HO-1 inducers. Hemodynamic measurements, tissue examination by real time PCR and ELISA, histopathological analysis, immunohistochemical studies were done**. Results:** Heart functions showed improvement in the treated groups with better improvement in the group received EPCs combined with both NO and HO-1 inducers. Gene expression demonstrated that proANP, MMP-9 and Bax were downregulated while Bcl-2 and SDF-1 were upregulated and the level of VEGF was increased in all treated groups with more significant effect in the group treated with EPCs combined with both NO and HO-1 inducers. **Conclusion:** Combined therapy of BM-EPCs with both NO and HO-1 inducers was superior to either EPCs, NO or HO-1 alone.

Key words: Pulmonary artery hypertension, EPCs, NO, HO-1 and angiogenesis