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Changes of Gene Expressions in Monocrotaline induced Pulmonary Hypertension Rats after Bone Marrow Cell Transfusion

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Pulmonary artery hypertension (PAH) causes right ventricular failure and possibly even death by a progressive increase in pulmonary vascular resistance. With a progressive loss of pulmonary microvasculature, it later becomes refractory to traditional therapies. Bone marrow-derived mesenchymal stem cell therapy has provided an alternative for ailments of various organs by regeneration at the site of a lesion. The purposes of this study were to investigate changes of pulmonary pathology and investigate changes of gene expressions of ET (endothelin)-1, ET receptor A (ERA), endothelial nitric oxide synthase (eNOS), matrix metalloproteinase(MMP)2, tissue inhibitor of matrix metalloproteinase (TIMP), interleukin (IL)- 6, tumor necrosis factor (TNF) α in monocrotaline (MCT)-induced pulmonary hypertension rat models after bone marrow cell infusion.
Methods: The rats were grouped as follows: control group, subcutaneous(sc) injection of saline; MCT group, sc injection of MCT; bone marrow cell infusion (BM) group, sc injection of MCT plus bone marrow cell infusion by intravenous injection at the tail 1 week after MCT injection. Results: The average RV pressure in week 4 significantly increased in the MCT group compared with control group. It had significantly decreased in the BM group compared with the MCT group. RV weight had significantly decreased in week 4 in the BM group. The ratio of right heart / left heart+septum had significantly decreased in weeks 3 and 4 in the BM group compared with the MCT group. Medial wall thickness of pulmonary arterioles and number of muscular pulmonary arterioles had minimally decreased in the BM group compared with the MCT group. However, there was not any significant difference between the two groups. Gene expressions of ET-1, ERA, eNOS, MMP2, TIMP, IL-6 and TNF α had significantly increased in the MCT group after week 3 and significantly decreased in week 4 in the BM group compared with the MCT group.
Conclusion: There was improvement of RVH and mean RV pressure after bone marrow cell infusion. Decreases in several gene expressions were observed. Additional research on the dose and frequency of bone marrow infusion is needed to better determine the appropriate amount of bone marrow cell count required for PAH treatment.