

Changes of pulmonary pathology and genes according to dose of umbilical cord blood derived mesenchymal stem cells in monocrotaline-induced pulmonary artery hypertension rat

*Hong Y.M.(1), Bae H.K.(1), Lee H. R.(1), Kim K. C.(2), Yang Y. S. (3), Oh W. I.(3), Choi S. J.(3)
Department of Pediatrics, Ewha Womans University School of Medicine(1); Department of Thoracic and Cardiovascular Surgery, Ewha Womans University School of Medicine(2); Biomedical Research Institute, MEDIPOST, Co., Seoul, Korea (3)*

Introduction: Pulmonary arterial hypertension (PAH) causes right ventricular failure and possibly even death due to a progressive increase in pulmonary vascular resistance. Human umbilical cord blood derived mesenchymal stem cells (hUCB-MSCs) transfusion have recently been studied to evaluate their potential as a source of cell therapy. The purposes of this study are to investigate changes of hemodynamics, pulmonary pathology and ten gene expressions such as ET (endothelin)-1, ET receptor A (ERA), endothelial nitric oxide synthase (eNOS), matrix metalloproteinase (MMP)-2, tissue inhibitor of MMP (TIMP)-1, interleukin (IL)-6, tumor necrosis factor (TNF)- α , Bcl (B cell leukemia/lymphoma)-2, caspase-3, vascular endothelial growth factor (VEGF) according to dose in monocrotaline (MCT)-induced PAH rat models after hUCB-MSCs transfusion.

Methods: The rats were divided into four groups as follows: the control (C) group (subcutaneous injection of saline 0.1 mL/kg), M group (subcutaneous injection of MCT 60 mg/kg), the UA group (hUCB-MSCs transfusion 1.5×10^6 /mL/cm²), the UB group (hUCB-MSCs transfusion 3×10^5 /mL/cm²). They received transfusion through the internal jugular vein 1 week after MCT injection.

Results: The mean right ventricular pressure (RVP) significantly decreased in the UA and the UB group compared with the M group in weeks 2 and 4. Right ventricle (RV) weight and the ratio of RV/left ventricle (LV)+septum significantly decreased in the UA and the UB group compared with the M group in week 2. Medial wall thickness of the pulmonary arteriols was significantly decreased in the UA group compared with the UB group in week 4. The number of intra-acinar arteriols was significantly decreased in the UB group compared with the UA group in week 4. Gene expressions of ET-1, ERA, eNOS, MMP-2, TIMP-1, IL-6, TNF- α , Bcl-2, caspase-3 and VEGF significantly decreased in the UA and the UB group compared with the M group.

Conclusion: After a transfusion of the UB dosage of hUCB-MSCs, there was also a similar improvement of RVH and mean RVP compared with UA dosage. Decreases in several gene expressions were also observed. Additional research on determining the optimal dose of hUCB-MSCs infusion is needed in PAH treatment.