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The efficacy of MSC-HGF in treating pulmonary arterial hypertension (PAH) and connexin remodelling

Research Article

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Abstract: Background: This study investigated whether the hepatocyte growth factor (HGF) genetically modified marrow-mesenchymal stem cells (MSCs) transplantation could offer a therapeutic benefit for pulmonary arterial hypertension (PAH). Methodology: Three weeks after monocrotaline administration, Sprague–Dawley rats were randomly divided into the following groups: PAH (n=10), MSCs (5×10^6 MSCs injected into the jugular veins, n=10), HGF (5×10^6 MSCs transfected with Ad-HGF into the jugular veins, n=10). Another three weeks later, hemodynamic changes and histomorphology were observed. Electron microscopy and immunofluorescence were also used to observe changes in the gap junctions of the heart. Results: Compared with the PAH and MSC groups, hemodynamic parameters improved significantly in the MSC-HGF group. Right ventricular hypertrophy was improved as measured by the RV/LV weight and thickness ratios. Histologically, cardiac myocytes and cell nuclei recovered and interstitial fibrosis decreased in the MSC and MSC-HGF groups. Under electron microscopy, the gap junctions exhibited a disorganised morphology in the PAH group and the number of gap junctions was lower in this group than in the other groups. The distribution of connexins 43 and 40 were improved in the MSC-HGF group. Conclusions: MCT-induced PAH can be treated and improved by HGF genetically modified MSCs, which may occur *via* connexin remodeling.

Keywords: *Pulmonary arterial hypertension • Marrow-mesenchymal stem cells • Hepatocyte growth factor • Connexin*

1. Introduction

Pulmonary arterial hypertension (PAH) is characterised by pulmonary arterial vasospasm, intimal hyperplasia, vascular smooth muscle cell (VSMC) proliferation, *in situ* thrombosis, and vascular remodeling, which may ultimately lead to heart failure and even death [1-3]. Despite significant advances in mechanistic research and drug development for PAH over the last several decades, treatment for PAH is limited and exhibits poor efficacy. Although the etiology and pathogenesis of PAH remain highly complex and unclear [4], most patients eventually die from refractory right heart failure. Gaine, *et al*. [1] reported that pulmonary artery pressure has little effect on the prognosis of patients with PAH. Chin, *et al*. [5] revealed that the right ventricular function under a high-pressure load determined PAH severity and patient survival. Based on the above theory, it is critical to find

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