RENOPROTECTIVE EFFECTS OF TONSIL-DERIVED MESENCHYMAL STEM CELLS IN GENTAMICIN-INDUCED ACUTE KIDNEY INJURY

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Introduction and Aims: Gentamicin (GM)-induced acute kidney injury (AKI) occurs in 10-20% of treated patients, and even more in populations at risk. The drug is accumulated in renal epithelial cells, which causes the loss of the brush border, apoptosis, massive proteolysis and overt necrosis of renal tubules. Recent developments in stem cell research have shown a great promise for the treatment of AKI, however the mechanisms underlying the improvement in kidney function and structure provided by stem cell therapy remain unclear. Tonsil-derived mesenchymal stem cells (T-MSCs) can be isolated from the tonsillectomy of patients, and are reported to be effective in treatment of various diseases. The aim of this study is to investigate the therapeutic potential of T-MSCs in the treatment of AKI induced by GM.

Methods: Twenty male Sprague-Dawley rats were divided into four groups: Control, Gentamicin (GM, 140 mg/kg/day, ip for 10 days), GM+T-MSCs (1x10⁷ cells, intravenous injection at 1 day after the 1st GM injection) and only T-MSC group. To examine the intra-renal localization of T-MSCs, T-MSCs were labeled with PKH-26 red fluorescence before infusion. Labeling efficacy was assessed by immunocytochemistry. Measurement of BUN, Cr, proteinuria and histologic analysis including TUNEL staining for assessing cell apoptosis were performed on 16 days of GM injection.

Results: PKH-26-labeled T-MSCs were observed in renal tubular cells in GM+T-MSCs group. The infusion of T-MSCs preserved renal function, ameliorated renal tubular lesions and reduced apoptosis in the rats with GM-induced AKI. The infusion of T-MSCs also downregulated the expression of Bax, Cytochrome c, Cleaved caspase-9 and -3 and upregulated the expression of Bcl-2.

Conclusions: Our results suggest that T-MSCs may protect the kidney from GM-induced AKI, possibly via the mechanism of modulation of apoptosis. Further studies will be necessary to verify therapeutic potential of T-MSCs with an investigation of reno-protective mechanisms in various spectrum of renal disease.