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Tonsil-derived Mesenchymal Stem Cells Attenuate Peritoneal Epithelial-to-Mesenchymal Transition and Fibrosis by Reducing Oxidative Stress

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Objectives : Mesenchymal stem cells (MSCs) are multipotent adult stem cells with regenerative potential and paracrine effects on damaged tissues. Epithelial-to-mesenchymal transition (EMT) of mesothelial cells (MCs) is a key contributor to peritoneal dysfunction in peritoneal dialysis (PD). Recent studies suggest that MSCs can mitigate organ fibrosis by inhibiting EMT. This study explores the effects of tonsil-derived MSCs (T-MSCs) in TGF-β-induced EMT of human peritoneal mesothelial cells (HPMCs) and peritoneal fibrosis.
Methods : A PD-induced peritoneal fibrosis model was established in Sprague-Dawley rats via daily intraperitoneal infusion of glucose-based dialysate containing methylglyoxal for three weeks. T-MSCs (5×10^6 cells) were administered intraperitoneally on day 14. Peritoneal thickening and function were assessed by histology and the peritoneal equilibrium test (PET). In in-vitro experiment, HPMCs were co-cultured with T-MSCs or T-MSC-conditioned medium (T-MSC-CM) using a transwell system to assess EMT and reactive oxygen species (ROS) production, The effects of T-MSC on the expression of antioxidant enzymes and anti-fibrotic proteins were compared with adipose-derived MSCs (AD-MSCs) and bone marrow-derived MSCs (BM-MSCs).
Results : In PD+T-MSC group, peritoneal function was improved as indicated by enhanced D2/D0 glucose and D/P creatinine compared to PD group. Anti-human nuclei staining confirmed T-MSC engraftment along the mesothelial layer. T-MSCs alleviated EMT and peritoneal fibrosis with an amelioration of oxidative stress, as evidenced by decreased expression of 8-OHdG, nitrotyrosine, and 4-HNE, along with increased glutathione and superoxide dismutase 2 (SOD2). T-MSCs and T-MSC-CM inhibited TGF-β-induced EMT and ROS production in HPMCs. Compared to AD-MSCs and BM-MSCs, T-MSCs exhibited higher expression of antioxidant enzymes (catalase, GPx, and SOD) and anti-fibrotic proteins (HGF and BMP-7). T-MSC-CM also restored TGF-β-induced suppression of antioxidant enzymes and anti-fibrotic factors in HPMCs.
Conclusions : T-MSCs exert potent anti-fibrotic and antioxidant effects, which result in reducing EMT and peritoneal fibrosis. These findings suggest the therapeutic potential of T-MSCs in preventing peritoneal dysfunction in PD patients.