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Song Y S[1], Lee H J[2], Doo S W[1], Kim J H[1], Yang W J[1], Lee S J[3], Yun J H[4], Kim S U[2]
1. *Department of Urology, Soonchunhyang University Hospital,* ***2.*** *Medical Research Institute, Chung-Ang University College of Medicine,* ***3.*** *Department of Urology, Kyunghee University Hospital,* ***4.*** *Department of Urology, Soonchunhyang University Gumi Hospital*

IMPROVED CYSTOMETRIC PARAMETERS USING TRANSPLANTATION OF MESENCHYMAL STEM CELLS INTO BLADDER IN RATS WITH SPINAL CORD INJURY

Hypothesis / aims of study
In spinalized rats, inefficient bladder function might lead to complete deterioration of bladder function. The present study was performed to investigate human mesenchymal stem cells (B10) directly transplanted to the bladder wall could improve cystometric parameters in SCI rats.

Study design, materials and methods
B10 were labeled with fluorescent silica magnetic nanoparticles (MNP) contained rhodamine B isothiocyanate (RITC) conjugated to terminal silanol groups. Forty 6-week old female Sprague-Dawley rats were divided into 4 groups (group 1: control, group 2: sham operation, group 3: SCI, group 4: SCI rats receiving B10). For SCI model, contusion was performed on the thoracic spinal cord using very severe intensity weight drop. Four weeks after the onset of SCI, B10 were injected into the bladder wall. Serial T2-weighted MR images were taken immediately B10 injection (1×10^6 cells) and at 4 weeks post-transplantation. Locomotor behavioral tests were performed using rotarod, Basso–Beattie–Bresnahan (BBB) test and voiding response was assessed at 4 weeks after transplantation and bladder was harvested. Nissl staining of spinal cord sections was performed.

Results
The hindlimbs of all the animals with SCI were completely paralyzed one day after contusion injury. Both of rotarod and BBB score were 0 and the development of SCI was confirmed and still preserved until 8 weeks after SCI. Non-recovery from SCIs was still found in Nissl staining until 8 weeks after SCI. While weight of bladder and collagen deposition increased after SCI, transplantation of B10 induced recovery to the original weights. Immunofluorescence microscopic observation of MNP-labeled B10 cells demonstrated the abundant red RITC dots in the cytoplasm of the B10 cells. MR imaging of MNP-labeled B10 cells in the bladder showed hypointense signal intensities on T2-weighted images until 4 weeks post-transplantation. B10 cells positive for human mitochondria antigen were found in the transplantation site indicating that MNP-labeled B10 cells survived in the bladder at 4 weeks after transplantation. Transplanted B10 differentiated to smooth muscle cells. The SCI group showed a higher collagen deposition than the sham operation group ($P<0.05$). The group with transplantation of B10 hMSCs after SCI showed a lower collagen deposition than the group with SCI ($P<0.05$). Intercontraction interval decreased after SCI but it recovered after B10 treatment. Maximal voiding pressure and residual urine volume increased after SCI but it recovered after B10 treatment.

Interpretation of results
Transplantation of B10 to the bladder wall showed differentiation into smooth muscle cells, a lower collagen deposition and improved dysfunction of the bladder in the rat SCI model.

Concluding message
Transplantation of mesenchymal stem cells to the bladder wall could be a novel therapeutic strategy against bladder dysfunction in patients with SCI.

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