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Poster Presentations

P-135

Mesenchymal stem cells suppress the c-FOS expression in spinal cord injury induced neurogenic bladder: A preclinical study in rat model

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Background: The normal function of filling and emptying of the lower urinary tract depends on a healthy and intact nerve axis. Spinal cord injury (SCI) blocks signals from the brain micturition center to the urinary sphincters, and lead to the dysfunction of the lower urinary tract. The consequences of the neurogenic bladder (NGB) include kidney failure, urinary tract infections, and urinary incontinence. The current therapies are usually palliative and there is no definitive cure for this disorder. In recent years, the use of stem cells, especially mesenchymal cells, has become a promising therapeutic method for SCI-induced NGB. The *c-Fos* transcription factor is encoded by the primary immediate *c-Fos* genes. *c-Fos* is a proto-oncogene that encodes the Fos protein in the central nervous system and has been identified as an indicator for postsynaptic activation of spinal neurons that receive afferent input from the lower urinary tract. Bladder stimulation increases the number of *c-Fos*-immunoreactive neurons in the periaqueductal gray matter, pontine micturition center and spinal cord. Later to SCI, neuronal activity in urinary neurons increases. Increased expression of *c-Fos* in the bladder indicates neuronal activation in the bladder. Previous experiments show that bladder dilatation or chemical stimulation of the lower urinary tract in rats increases the number and the altered distribution pattern of Fos-IR cells is in the L6-S1 discrete regions, including the lateral and medial dorsal horns (LDH and MDH, respectively), the dorsal commissure (DCM), and the SPN regions.

Objective: To determine the effect of intravesical Bone Marrow Mesenchymal Stem Cells (BM-MSCs) transplantation on *c-FOS* expression in SCI-induced neurogenic bladder.

Materials and Methods: Twenty-four female Wistar rats were randomly divided into 4 groups (each group consisted of 6 rats): the control group which did not receive any intervention. The sham group which underwent laminectomy at the level of T9-T10 vertebrae without any spinal cord damage. Two groups with complete SCI that were dissected on the level of T9-T10 vertebrae after laminectomy using a sterile razor blade. Four weeks after injury, BM-MSCs (1×106/120 µl) were injected into six areas of bladder muscle using a 500 µl insulin syringe. In the negative control group, normal saline with the same volume was injected instead of BM-MSC. Four weeks after cell transplantation, rats were examined for molecular and histological evaluation.

Results: In the present study, a relatively new model of intravesical injection of BM-MSCs was introduced as a minimally invasive method for SCI-induced NGB management in female Wistar rats. The results of Western blot showed that after SCI, *c-Fos* expression in bladder and spinal cord increased, compared to control and sham groups ($p < 0.001$). Following treatment, its expression was decreased significantly. The results of Tukey –post hoc test show that this reduction is statistically significant in Western blot samples of bladder in BM-MSCs group compared to the SCI group ($p < 0.001$).

Conclusion: It can be concluded that the neural communication disorder caused by SCI may severely stimulate the centers which are associated with normal urinary excretion in the brain. *C-Fos* expression was suppressed after transplantation of BM-MSCs.

Key words: *Lower urinary tract, Bladder, Rats, Spinal cord injury, Mesenchymal stem cells.*