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NEW CELL-MEDIATED GENE THERAPY FOR THE RECOVERY OF NEUROGENIC BLADDER INDUCED BY SPINAL CORD INJURY

Hypothesis / aims of study

Neurogenic bladder induced by spinal cord injury (SCI) is a serious public health issue because it causes severe morbidity and mortality in the patients with SCI; however, there has been no effective treatment, yet. Therefore, in this study, we evaluated the effect of TGN (cell-mediated gene therapy employed for the regeneration of nerve tissue; TissueGene, Inc.) on the recovery of voiding dysfunction in the rat of SCI.

Study design, materials and methods

SCI was made at T10 by contusion injury in rats. Three types of TGN (TGN-01, TGN-02, TGN-S1) were injected to the injured spinal cord. After injection with TGN, BBB scale test (7th, 11th, 15th day after injury), Ladder walking test (15th day after injury), and Treadmill walking test (17th day after injury) were conducted to evaluate motor recovery. Cystometric study (18th day after injury) was done to evaluate the voiding function on the 18th day after injury. Histologic evaluation and western blot analyses of BDNF, NGF, and VEGF of the injured spinal cord were done.

Results

After SCI, motor dysfunction and decreased basal pressure and duration of bladder contraction were noted. Moreover, injured spinal cord tissue and the overexpression of BDNF, NGF, and VEGF induced by SCI were noticed. The rats administered with 3 types of TGN showed improved motor function by the BBB scale test, Ladder walking test, and Treadmill test. The increased basal pressure and duration of bladder contraction in the rats administered with TGN-01, -02, and -S1 were observed compared with the rats with SCI from the cystometry. Significant recovery of injured spinal cord was observed by H&E. TGN-01, -02, and -S1 significantly inhibited the overexpression of BDNF, NGF, and VEGF.

Interpretation of results

After SCI, we observed decreased detrusor contractility from the cystometric finding of decreased basal contraction pressure. Increased basal contraction pressure was noted after administration with 3 types of TGN. The result meant that the neural recovery. Moreover, the rats administered with TGN- 01 and -S1 showed urinary leakage similar with the normal voiding pattern. In addition, improved motor function, histologic and molecular findings supported the recovery of detrusor function.

Concluding message

From the results about the recovery of injured spinal cord in both histologic and functional aspects, we suggest the possible role of TGN in the neurogenic bladder induced by SCI. However, the effect of TGN on the improvement of voiding impairment seemed not to be sufficient due to the relatively short evaluation period in this study. Therefore, the effect of TGN will be determined by the further long-term study.

Disclosures

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