

INTRAVENOUSLY TRANSPLANTED BONE MARROW STROMAL CELLS PROMOTE RECOVERY OF LOWER URINARY TRACT FUNCTION IN RATS WITH COMPLETE SPINAL CORD INJURY

Hypothesis / aims of study

Lower urinary tract dysfunction is a serious consequence of spinal cord injury. Recent studies have demonstrated that directly injected bone marrow cells^[1] and intravenously administered neural progenitor cells^[2] promote locomotor recovery in rodents following contusive spinal cord injury. The goal of the present study was to determine whether intravenously transplanted bone marrow stromal cells can promote recovery of lower urinary tract function in rats with spinal cord transection.

Study design, materials and methods

Twenty two male Sprague-Dawley rats (200-250g) were included in this study. Sixteen rats received a spinal cord transection and a transplant of cell culture medium (OP-controls, n=8) or bone marrow stromal cells (BMSCs, n=8). Spinal cord transection was performed under chloral hydrate (360 mg/kg, i.p.) anesthesia. After a Th8/Th9 laminectomy, the dura matter and spinal cord were cut with a scalpel blade and a section of spinal cord (2mm) was removed. Gelfoam was placed between the severed ends of the spinal cord. The animals were allowed to recover, and the bladder was manually expressed every 8-12h after injury until spontaneous micturition reestablished. Transplanted bone marrow stromal cells were obtained from donor adult male Sprague-Dawley rats. BMSCs were plastic-adhered grown at 37°C in a 5%CO₂ water-jacketed incubator for five passages. At 9 d after SCI, cultured bone marrow stromal cells (3×10⁶ in 300 μl culture medium) or cell culture medium (300 μl) were slowly injected with a 1ml syringe into the tail vein of SCI rats. Six laminectomy-only rats served as age-matched controls with an intact spinal cord (CNS-intact). Rats were performed urodynamic tests including cystometry combined with external urethral sphincter (EUS) electromyogram (EMG) record at 4 weeks after transplantation. At the time of sacrifice, bladders were removed, blotted dried, and weighted. Statistical comparison of differences between groups was performed using one-way ANOVA test. P<0.05 was selected for statistical significance.

Results

Urodynamics demonstrated that leak point pressure was significantly lower in BMSCs rats than in OP-control rats (33.8±3.8 mmHg versus 40.7±4.0 mmHg, respectively, p<0.01). BMSCs rats showed significant decrease in residual urine volume (RUV) (0.89±0.17 ml versus 1.53±0.68 ml, respectively, p<0.05) and increase in voiding efficiency (26.25±6.93% versus 2.78±1.46%, respectively, p<0.01) compared to OP-control rats. The episodes of detrusor overactivity (DO) was also fewer in BMSCs rats than in OP-control rats (2.1±1.1 versus 8.9±4.1, respectively p<0.01) and absent in CNS-intact rats. Bladder weight was significantly increased in BMSCs rats (0.56±0.09 g, p<0.01) and OP-control rats (0.50±0.11 g, p<0.05) compared to CNS-intact rats (0.36±0.08 g), but it wasn't significantly different between BMSCs rats and OP-control rats. EUS-EMG record showed that two types of EUS-EMG activity (tonic and bursting) were detected during cystometry in all CNS-intact rats. However, in 4 of 8 BMSCs rats and 7 of 8 OP-control rats only tonic EUS activity was remained and bursting EUS activity was abolished during bladder filling. Otherwise, the silent period between EUS bursts was shorter in BMSCs rats (69.0±13.74 ms, p<0.05) and OP-control (32.5 ms) rats compared to CNS-intact rats (131.78±17.07 ms) .

Interpretation of results

These results indicate that intravenous injection of bone marrow cells into SCI rats promotes recovery of lower urinary tract function. The significant decrease in leak point pressure, RUV, episodes of DO and the increase in voiding efficiency suggest that bone marrow stromal cells transplantation results in decreased bladder outlet resistance, likely due to amelioration of detrusor-sphincter dyssynergia. In addition, bursting EUS-EMG activity is commonly observed during voiding in BMSCs rats compared to OP-control rats, which is consistent with the significant increase of voiding efficiency in BMSCs rats. This may be relate to reduce capsaicin-sensitive C-fiber bladder afferent input, which contributes to DO and DSD in deeply anesthetized SCI rats^[3].

Concluding message

This study demonstrated that intravenously transplanted bone marrow stromal cells promoted recovery of lower urinary tract function in rats with spinal cord transection. Further studies are needed to determine the mechanism of this transplantation improving lower urinary tract function and the efficacy of this technique in human beings.

References

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Is this a clinical trial?

No

What were the subjects in the study?

ANIMAL

Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?

Yes

Name of ethics committee

Ethics committee of China Rehabilitation Research Center

