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INTRAVENOUS DELIVERY OF BONE MARROW CELLS PROMOTES RECOVERY OF LOWER URINARY TRACT FUNCTION IN RATS WITH SPINAL CORD INJURY

Hypothesis / aims of study
Failure of axon regeneration following spinal cord injury (SCI) may lead to permanent paralysis and lower urinary tract dysfunction. Recent studies have demonstrated that systemic delivery of bone marrow cells enhances functional recovery in rodents following contusive spinal cord injury (1). The goal of the present study was to determine whether intravenous delivery of bone marrow cells can enhance recovery of lower urinary tract function in rats with spinal cord injury.

Study design, materials and methods
Ethical approval for the study was granted by the University Committee for Animal Experimentation. Twelve-week-old female Wistar rats were anesthetized by inhalation of 2% halothane. Laminectomy was performed at the Th8/Th9 level to expose the spinal cord segment. SCI was induced by placing a 40 g rod on the exposed dura for 30 minutes. Animals were allowed to recover, and the bladder was manually expressed twice daily after SCI until sacrifice. Seven days after induction of SCI, rats were anesthetized using intraperitoneal injections of ketamine (75 mg/kg) and xylazine (10 mg/kg). A micro-drill was used to create a small hole (2×2 mm) in the femur, and 2 ml of bone marrow were aspirated using a 22-gauge needle. Marrow samples were diluted in 2 ml of Ficoll. Cells were centrifuged (2,000 rpm for 15 min) and then resuspended in 2 ml of neural progenitor cell maintenance medium (NPMM). Cells from the mononuclear layer were collected and suspended in 1 ml NPMM. Next, these autologous bone marrow cells (1 ml, 1×10^7 cells) were injected into the femoral vein of SCI rats (n=10). The control group consisted of SCI rats that received intravenous injections of culture medium alone (n=10). Rats underwent assessment of voiding behaviour in a metabolic cage on day 28, and cystometry was performed on day 31. Neurologic evaluation included a modified 7-point hindlimb Tarlov scale applied weekly until the voiding behaviour study. Statistical comparison of differences between groups was performed using the Mann-Whitney U test. A p value < 0.05 was considered to indicate statistical significance.

Results
Median final Tarlov scores were significantly higher in SCI rats receiving bone marrow cells (score=9) compared to those receiving intravenous injection of medium alone (score=4). Average voided volume was significantly lower in bone marrow transplant rats than in control rats (0.85 ± 0.08 ml versus 1.45 ± 0.10 ml, respectively). Further, cystometry demonstrated that maximum pressure was significantly lower in bone marrow transplant rats than in control rats (29.2 ± 1.3 cmH_20 versus 40.5 ± 2.8 cmH_20, respectively). Post void residual was significantly lower in bone marrow transplant rats than in control rats (0.09 ± 0.04 ml versus 0.74 ± 0.08 ml, respectively).

Interpretation of results
Intravenous injection of autologous bone marrow cells into SCI rats promotes recovery of lower urinary tract and locomotor function. The significant decrease in maximum pressure and the increase in voiding efficiency suggest that bone marrow transplantation results in decreased bladder outlet resistance, likely due to amelioration of detrusor sphincter dyssynergia. Further, recovery of locomotor function correlated with recovery of lower urinary tract function.

Concluding message
This study demonstrated that intravenous administration of autologous bone marrow cells promoted recovery of lower urinary tract function in SCI rats. Further study to determine whether this technique is efficacious in human patients would be of benefit.

References

1. Spinal cord injury in rat: treatment with bone marrow stromal cell transplantation. Neuroreport. 11, 3001-3005, 2000.