INTRODUCTION:

The cauda equina syndrome typically results following injury to the lumbar spine. Approximately 10-20% of all traumatic spinal cord injury (SCI) affects this region. Lumbar SCI involves a crush injury to the spinal nerve roots of the cauda equina resulting in flaccid paralysis of lower motor neurons. Thus, the pathophysiology involves anterograde Wallerian nerve degeneration of peripheral nerves, as well as retrograde degeneration producing chromatolysis and cell death of motor neurons. Previously, locomotor function of a rat was characterized after compression injury of lower motor neurons. Brain-Derived Neurotrophic Factor (BDNF), a member of the neurotrophin family, has been implicated in the maintenance and synapses of neurons and prevention of cell death. The purpose of this study was to compare locomotor recovery after intrathecal treatment with a neurotrophic factor, BDNF, to saline and compression injury only in a rat model.

METHODS:

**Experimental Design.** Continuous infusion of BDNF, saline, or compression injury only were randomly assigned to 51 Sprague-Dawley rats (240 – 260 gm) undergoing compression injury. Investigators performing surgery or conducting evaluations were blinded to the assigned treatments. Rats were evaluated weekly for 10 weeks.

**Concentric Compression Procedure.** A laminectomy at L2 was performed and a silk suture was passed around the conus medullaris, cauda equina, and nerve roots. The suture was tied in a simple knot and 200g weights were applied to the two ends for 20 minutes.

**Intrathecal Catheter & Pump.** A second laminectomy was completed at L6. An intrathecal catheter was threaded through a small needle puncture in the dura and attached to a microosmotic pump (ALZET®) implanted subcutaneously—allowing continuous infusion for 28 days of either BDNF or saline solution.

**Functional Evaluation.** Locomotor function outcome measures were recorded by investigators blinded to the treatments once a week over a 10 week observation period using the BBB 21 point locomotor scale (Basso, Beattie, and Bresnahan, 1995).

**Analysis.** Mean functional score and standard deviations were computed by treatment and week. Differences in mean recovery between treatments with a repeated measure of time were assessed by Analysis of Variance (ANOVA).

RESULTS:

Concentric compression with 200g weights applied for 20 minutes resulted in severe neurologic dysfunction affecting lower extremities and the bladder. There was no significant difference in the attrition rate among the treatments: 25% (4/16) for BDNF, 19% (3/16) for saline, and 26% (5/19) for crush only. Rats surviving throughout the 10 week observation period (n=12 BDNF, n=13 saline, n=14 crush only) never regained full function. As injury persisted throughout the 10 weeks, greatest recovery occurred within the initial weeks after compression. (β=8.54, BDNF; β=7.23, saline; β=7.29, crush only)

The mean recovery was not significantly greater for rats treated with BDNF than those treated with saline or compression only at any time interval. However, rats treated with BDNF tended to have higher recovery than others, especially during the initial 2-3 weeks post injury and until week 5 (greatest difference between groups at week 3, p=0.06). The range of standard deviations over the days are: saline(1.22-2.78), crush only (1.50-2.65), BDNF (2.71-4.57).

DISCUSSION:

Lumbar compression using 200g weights for 20 minutes resulted in substantial locomotor injury persisting over the 10-week period of observation. The recovery curve of the BDNF treated rats was slightly steeper initially than for rats with saline or crush only. Although, the greatest variability was noted among BDNF treated rats, BDNF rats had the highest average locomotor scores during the first 5 weeks after which all treatments were comparable. Of interest, the pumps infused a solution up until four weeks which may correspond to the higher recovery noted for BDNF treated rats during that same period. This simple, reproducible, and cost-efficient rat model of lumbar SCI is currently being used to screen the effectiveness of various neurotrophic factors.

REFERENCES:


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