

Functional outcomes after application of chitosan-gelatin hydrogel in a rat model of severe spinal cord injury

Vibhor Krishna MD; Xing Jin; Hampton Andrews; Abhay K. Varma MD; Mark Kindy; Xuejun Wen
Medical University of South Carolina, Charleston, SC



Introduction

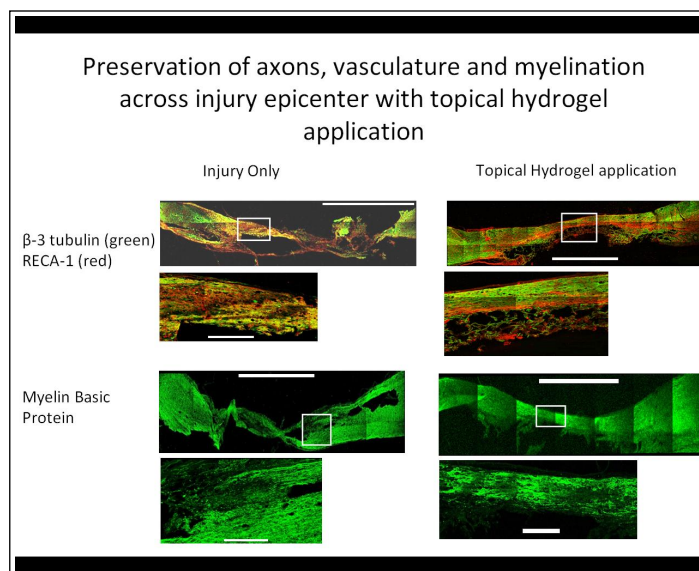
Discovery of effective therapeutics for neuroprotection after spinal cord injury (SCI) is highly desirable. Hydrogels offer advantage of targeted and sustained alterations in the microenvironment at the injury site. They can conform to the lesion volume and have a potential to permeate through the injured tissue. We designed a thermo-sensitive, biodegradable chitosan-gelatin hydrogel for neuroprotection and growth factor delivery after SCI. The functional outcomes were evaluated after topical application of this hydrogel in a rat model of severe contusive SCI.

Methods

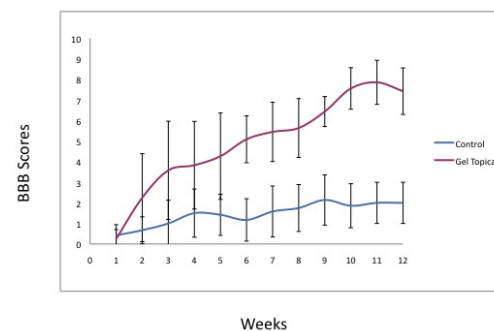
36 adult SD rats were assigned to a **control** (SCI only) and two experimental groups (topical hydrogel, and injectable hydrogel). We induced severe contusion SCI in all animals by a computer-controlled impactor. In the **topical** group, 60 μ l hydrogel solution was placed on the cord surface at the lesion epicenter. 10 μ l hydrogel was injected at 6 points (within lesion site, proximal and distal) bilaterally in the **injectable** hydrogel group. Weekly behavioral testing was performed using the BBB scale (minimum 0, maximum 21). Some animals in each group were sacrificed at 8 weeks and immunohistochemistry was performed to study scar formation, and tissue preservation. The lesion volume was assessed in 5 animals each in control and topical groups at 12 weeks.

Results

BBB scores were significantly better in the topical group as compared to the control group. (Figure 1) Immunohistochemistry revealed preservation of neuronal bridge across the injury epicenter. (Figure 2) This neuronal tissue had preserved architecture with axons traversing the lesion cavity. The mean lesion volume, as assessed by Luxol fast blue staining, was significantly less in the topical group (2.04 ± 0.5 versus 1.66 ± 0.6 , $p < 0.05$). (Figure 3)

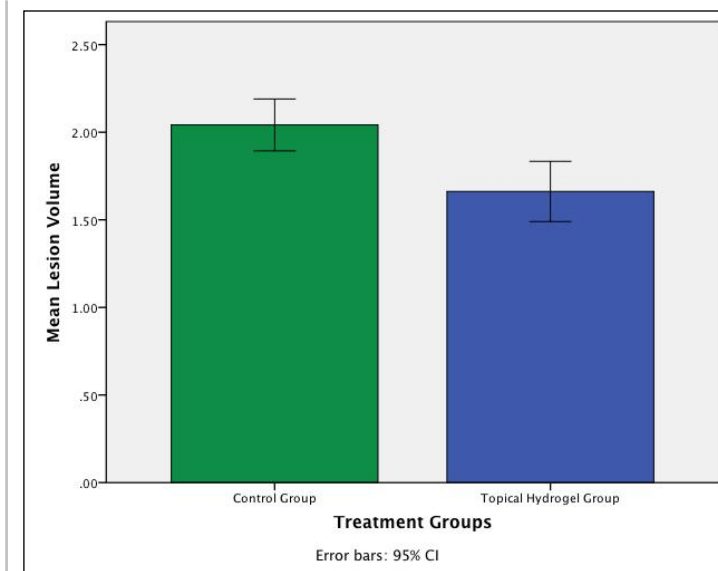


Improved BBB scores after topical hydrogel application



Learning Objectives

Topical application of chitosan-gelatin hydrogel improves functional outcomes after severe contusion spinal cord injury in rats.



Conclusions

The application of chitosan-gelatin hydrogel improves functional outcomes when combined with GDNF in a rat model of severe spinal cord injury. Further studies are warranted to evaluate its efficacy large animal model and optimize its effects.

References

- Hall ED, Springer JE. Neuroprotection and acute spinal cord injury: a reappraisal. *NeuroRx*. 2004;1(1):80-100.
- Onose G, Angheliescu A, Muresanu DF, et al. A review of published reports on neuroprotection in spinal cord injury. *Spinal Cord*. 2009;47(10):716-26.
- Nomura H, Tator CH, Shoichet MS. Bioengineered strategies for spinal cord repair. *J Neurotrauma*. 2006;23(3-4):496-507.
- Horn EM, Theodore N, Assina R, Spetzler RF, Sonntag VK, Preul MC. The effects of intrathecal hypotension on tissue perfusion and pathophysiological outcome after acute spinal cord injury. *Neurosurg Focus*. 2008;25(5):E12.
- Basso DM, Beattie MS, Bresnahan JC. A sensitive and reliable locomotor rating scale for open field testing in rats. *J Neurotrauma*. 1995;12(1):1-21.
- Basso DM, Beattie MS, Bresnahan JC. Graded histological and locomotor outcomes after spinal cord contusion using the NYU weight-drop device versus transection. *Exp Neurol*. 1996;139(2):244-56.