NEUROPROTECTION FOR SPINAL CORD INJURY
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Key Points
- Neuroprotective treatments for spinal cord injury mitigate acute secondary mechanisms.
- Few – if any – rigorously evaluated neuroprotectives are effective in the clinical setting
- The lack of clinically effective neuroprotective agents may reflect a need for better pre-clinical models, multi-species validation, replication studies, and stronger study design.1

Glucocorticoids such as MPSS act by non-genomic mechanisms (eg, membrane stabilization and anti-oxidant) to provide neuroprotection. While there are data from the 1990s showing that MPSS marginally improved functional outcome in people with SCI, other studies have not replicated these findings. In dogs with naturally occurring SCI, glucocorticoids have not been shown to have positive outcome effects; on the contrary, retrospective studies indicate higher rates of adverse effects and potentially worsened clinical outcome following glucocorticoid delivery.

Polyethylene glycol (PEG) is a surfactant that has been shown to anatomically and physiologically fuse spinal cord axons in injury models. Additionally, PEG may facilitate physiologic repair of compressed spinal cord parenchyma. In 2004, an open label phase I/II study examined PEG in dogs lacking deep nociception due to thoracolumbar disk herniation and compared outcomes to historical controls.2 The drug appeared to be safe when delivered IV and in 17/19 dogs recovery of pelvic limb nociception occurred within 2 days of PEG administration. Given the open label nature of the design and the use of historical controls, these data have been questioned. Additionally, some rodent models have not shown a consistent, robust benefit associated with PEG treatment.1 Currently, PEG is being investigated in a phase III study in dogs with SCI -early reports suggest limited-no outcome effect.

Matrix Metalloproteinases (MMPs) appear to be important in facilitating leukocyte infiltration into the spinal cord and initiating parenchymal necrosis. Expression of MMP-9 is associated with more severe SCI in dogs with disk herniation and has been linked to poor functional outcomes in rodent models.3,4 Illomostat (GM 6001) is a non-specific MMP blocker that penetrates the spinal cord and improves recovery across rodent injury models. A phase I/II study using this drug in dogs with disk herniation has been completed at Texas A&M University.

Manipulation of immune response, via cellular or antibody strategies, is another means of neuroprotection. Activated macrophages have been shown to produce nerve growth factor and facilitate regeneration. Delivery appears safe in humans. Monoclonal antibodies can be directed against integrins, p-selectin, or other targets to reduce white blood cell infiltration. Currently, antibody delivery is primarily limited to rodent model investigations.