

Managing Acute Spinal Cord Injuries

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ABSTRACT: Acute spinal cord injuries commonly seen in veterinary patients include vascular, compressive, and concussive injuries. Vascular lesions, or infarcts, are usually caused by fibrocartilagenous emboli. Concussive and compressive injuries have a variety of pathologies, including intervertebral disk disease, fractures, and luxations (dislocations) of the vertebral column. Although considerable controversy exists over the most appropriate way to manage acute spinal cord injuries, early surgical intervention or decompression remains the best treatment option in managing acute compressive injuries in veterinary patients. High-dose methylprednisolone sodium succinate, an established treatment in human medicine, is falling out of favor because studies have shown little therapeutic benefit and severe adverse effects.

ver the past few decades, many drugs have been tested in the laboratory and clinical setting for their use in the treatment of spinal cord injuries (SCIs). Promising new treatments are continuously emerging in this field, with several showing marked benefits in the early stages of SCI. Because much of veterinary medicine is extrapolated from human studies, this article discusses pertinent information from the human as well as the veterinary literature regarding new approaches for

the treatment of acute SCI.



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INITIAL ASSESSMENT AND EMERGENCY TREATMENT

In an animal with an SCI and a history of trauma (e.g.,

motor vehicle accident, fight with another animal, falling from a height), the initial physical assessment focuses mostly on life-threatening problems. The ABCs (airway, breathing, cardiovascular assessment) of trauma management are assessed first. Maintaining oxygenation and tissue perfusion via hemodynamic support helps prevent aggravation of the secondary injury cascade and further neurologic deterioration. The maintenance of oxygenation and tissue perfusion has been shown to be the main criterion influencing the outcome in patients with head injuries. ²⁻⁴

Many animals with SCI secondary to trauma have other injuries that can alter the prognosis and course of treatment. The patient's neurologic status may improve once the state of shock is addressed. If an unstable SCI (e.g., fracture,



Figure 1. Immobilization on a backboard is imperative. This backboard is radiolucent so that the patient does not need to be moved for radiography.

luxation) is suspected, immobilization on a firm, flat surface (backboard) is imperative (Figure 1).

If an acute disk extrusion or fibrocartilagenous embolism (FCE) is suspected, the initial neurologic examination is critical to the timing of diagnostics and prognosis. A thorough neurologic examination is vital to the accurate interpretation of diagnostic test results and will help to determine the best treatment course for the patient.

PROGNOSIS

The severity of an SCI is inferred from the conducting ability of the long tracts in the spinal cord responsible for deep pain perception (DPP). DPP is tested by squeezing a digit with hemostats (or a similar tool) to the extent that pressure is applied to the periosteum, if necessary, and looking for a cerebral response. Preservation of DPP is associated with an overall good prognosis in self-limiting SCIs. Injuries with the potential for ongoing damage (e.g., instability, severe compression) may have a less positive prognosis. Varying levels of nursing care and physical therapy are necessary for optimal results.

In a recent study,⁵ 92% of dogs that had DPP after acute intervertebral disk herniation and were treated with decompression via hemilaminectomy recovered ambulatory function. This finding is consistent with past studies on intervertebral disk herniations in dogs with DPP.^{6–9} Thoracolumbar disk extrusion with lack of,

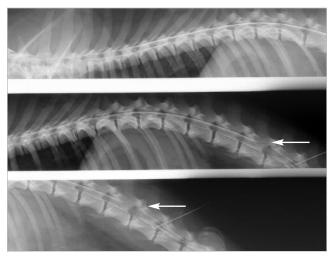


Figure 2. Lateral myelogram showing attenuation of the dorsal and ventral contrast columns over the L4-L5 intervertebral disk space (arrows). The cranial endplate of L5 is fractured and displaced dorsally. (Courtesy of Dr. Tammy Stevenson)

or questionable, DPP carries a more guarded prognosis, with up to 69% of patients becoming ambulatory.^{5,6,9-11} Traumatic spinal fractures or luxations and FCEs with intact DPP often carry a good prognosis. However, FCEs with lack of DPP carry a guarded prognosis, and spinal fractures or luxations with lack of DPP generally have a poor to grave prognosis¹⁰ for recovery.

DIAGNOSTICS

Complete vertebral column radiographs, taken with the patient on a backboard, are recommended in cases of suspected trauma to identify any obvious vertebral fractures or luxations. Lateral views are taken first to identify major fractures and luxations while minimizing the potential for further trauma to the spinal cord. However, orthogonal views are also needed. If available, horizontal-beam radiography can be used to get a ventrodorsal view to avoid moving an animal with an unstable vertebral fracture. Myelography may be conducted to help determine whether decompression is necessary (Figure 2), although computed tomography (CT) and magnetic resonance imaging (MRI) are more useful in providing additional information and are often less traumatic. If the neurologic signs can be associated with the site of a radiographically identified vertebral fracture, CT or MRI is appropriate. If they cannot, myelography or MRI can be conducted. MRI is preferable to other imaging modalities because of the additional information that can be acquired regarding the extent of injury

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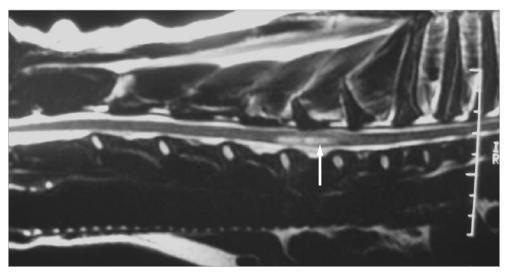


Figure 3. A T2-weighted magnetic resonance image of the lateral cervical spine. Note the hyperintensity (*arrow*), consistent with edema, in the parenchyma over the body of C6. This is consistent with an FCE.



Figure 4. Postsurgical ventrodorsal radiograph of a plate used to stabilize L4-L5 subluxation.

to the spinal cord. In dogs with suspected FCE, the preferred imaging modality is MRI. Usually, the infarct is clearly visible, especially on T2-weighted and fluid-attenuated inversion recovery images (Figure 3).

PATHOPHYSIOLOGY

SCI comprises primary and secondary mechanisms of injury, as well as sustained compression. Primary injury occurs at impact. The parenchyma and vasculature of the spinal cord are directly damaged by compression, contusion, shearing, laceration, or stretching. The primary mechanical trauma, along with subsequent persistent compression and changes in vascularity, triggers a secondary cascade of pathologic events. These events include depletion of the neuronal ATP level, intracellular accumulation of calcium and sodium, formation of oxygen free radicals, and increases in cytokine production and extracellular levels of glutamate, lactic acid, and nitric oxide. 12-14

SCI also causes systemic and local vascular abnormalities. ¹² Systemic hypotension with a loss of autoregulation within the spinal cord can result in significant changes in spinal cord blood flow ¹² and subsequently exacerbate the secondary cascade of events.

Medical therapy is aimed at minimizing the progression of the secondary injury pathways by improving local blood flow, free radical scavenging, and antiinflammatory activity. However, no effective medical therapy has been proven in dogs.

CURRENT TREATMENT OPTIONS AND RECOMMENDATIONS

Early Surgical Intervention and Decompression

Early surgical intervention is the best treatment option available in veterinary medicine for compressive or unstable lesions. Early decompression has been shown to enhance neurologic recovery in several animal studies¹⁵⁻¹⁷ and to be beneficial in reducing complications, length of stay, and hospital costs for humans with traumatic injuries. 18-21 A retrospective, multicenter trial confirmed that there is little agreement on the optimum timing of surgical treatment for spinal fractures or subluxations in human trauma victims²²; however, despite the lack of current standards, recommendations in the human literature stress urgent decompression in acute SCI.20,21 Early decompression or stabilization (Figure 4) removes the source of continued compression or contusion and subsequently decreases the cascade of secondary events.

Corticosteroids

In the 1970s and 1980s, dexamethasone was the recommended initial treatment for acute SCI. The aim was to limit the inflammatory response incited by the injury. However, laboratory studies failed to demonstrate efficacy.²³ Moreover, dexamethasone has very little ability to inhibit oxygen radical damage in central nervous system tissue.²⁴



By contrast, methylprednisolone sodium succinate (MPSS) has been proposed in experimental studies to have neuroprotective mechanisms via its improvement of local blood flow and free-radical scavenging and antiinflammatory properties.^{24,25} The antioxidant efficacy of MPSS has been found to be unrelated to its glucocorticoid steroid receptor activity.²⁴

Multiple experimental models have showed a significant improvement with MPSS administration; however, MPSS has been shown in humans and animals to be of little clinical therapeutic benefit. Although initial results in human clinical trials were encouraging, subsequent analyses of the data failed to verify statistically significant improvement.^{25–27} The marginal improvement reported consisted of an overall improvement in motor score of three points divided between 14 muscle groups (one point equaled a flicker of movement).²⁸ At best, this combined score may be the movement of a finger. Studies in dogs have also failed to establish the clinical efficacy of MPSS, although no blinded clinical trial has been done. 5,29

A thorough neurologic examination is vital to the accurate interpretation of diagnostic test results.

MPSS has been shown to cause significant adverse effects. Reviews of cases in which dogs received high doses of MPSS showed that between 33% and 90% of dogs exhibited severe adverse effects such as diarrhea, melena, vomiting, hematochezia, hematemesis, gastrointestinal hemorrhage, and anorexia. 30,31 Other documented effects in humans include acute adrenal insufficiency,³² acute corticosteroid myopathy,³³ significant splenic lymphocyte depletion,³⁴ pulmonary eosinophilic infiltrates,³⁴ gastric hemorrhage,³⁵ and intestinal mucosal edema and necrosis.³⁴ MPSS may also have additional detrimental effects on neuronal regeneration and axonal sprouting.³⁶

Based on a consensus meeting of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons, MPSS has not been recommended as a standard of treatment nor as a guideline. It is considered to be an option, with the acknowledgment that adverse effects are more consistent than clinical benefits.³⁷

POTENTIAL NEW THERAPIES

Within the past decade, a number of drugs have been investigated in the laboratory and clinical setting and passed over in human medicine. However, some of these drugs are still being considered in veterinary medicine.

The practical application of new treatment strategies focuses on three lines of approach: acute neuroprotection to limit secondary damage, enhancement of axonal regeneration and plasticity, and treatment of demyelination.³⁸ It is critical that ongoing studies use appropriate experimental models and look for functionally relevant outcomes. Spontaneous SCIs in dogs have been proposed as a useful experimental model and are being used to assess several potential therapies.^{39–42}

Thyrotropin-Releasing Hormone

Thyrotropin-releasing hormone (TRH) is a tripeptide that has numerous physiologic and biochemical actions in addition to its effect on thyroxine. Administration of TRH once daily for 7 days, starting 24 hours or 7 days after experimental SCI, has demonstrated improved neurologic

neurons.⁴⁵ Bone marrow stromal cells are thought to have advantages over other stem cells because they secrete cytokines such as colony-stimulating factor, interleukins, stem cell factor, nerve growth factor, brain-derived neurotrophic factor, and vascular endothelial growth factor.⁴⁶ The aim of stem cell therapy is to replace, repair, or enhance the biologic function of damaged cells.⁴⁵

Both bone marrow stromal cells and freshly collected bone marrow have been shown in human clinical trials to be safe and to show partial improvement of function in patients with SCI.⁴⁶ Intravenous injections of these cell cultures or granulocyte colony-stimulating factor have been shown to significantly improve pelvic limb motor function recovery in rats with compressive SCI,^{45,46} with the most apparent and rapid recovery in animals that received bone marrow stromal cells.⁴⁶

Stem cells show a great deal of potential and are a

Early surgical intervention and decompression are the best treatment options available in veterinary medicine.

function in a dose-related manner.^{23,43} TRH has several adverse effects, but studies on derivatives are ongoing, and one derivative was shown to be safe in dogs.⁴⁴

Polyethylene Glycol

Polyethylene glycol (PEG) is a hydrophilic polymer that interacts with and repairs damaged axonal membranes. There is evidence that PEG may interfere with secondary oxidative injury processes by interacting with mitochondria. Dogs without DPP that received MPSS, decompressive surgery, and PEG or P188 (a similar polymer) regained the ability to ambulate (some were considered to be spinal walking) in one study. However, this was not a placebo-controlled trial, and the recovery rate was similar to that of other reported studies in which surgery alone was used. 6,10,11

This study showed that no adverse effects were associated with PEG administration; unfortunately, it did not prove efficacy. Larger studies to evaluate the efficacy of PEG as a potential treatment in the management of acute SCI are ongoing.

Bone Marrow Stem Cells

Studies have shown that embryonic stem cells can survive and differentiate into astrocytes, oligodendrocytes, and "buzzword" for the 21st century. It is extremely important, however, that the safety characteristics (tumorigenicity, viability, sterility, and antigenic compatibility) of the donor cells be determined before clinical use is attempted.⁴⁵

Transplantation Strategies

Transplantation strategies are being evaluated in dogs with SCI.⁴¹ Transplantation of olfactory ensheathing cells derived from the olfactory bulb into the spinal cord has been shown to promote regeneration of injured axons and recovery of lost function in rats.^{41,47–49} In dogs, transplantation of autologous olfactory ensheathing cells from the olfactory bulb to the canine spinal cord has been shown to be safe.^{47,50} More recently, it has been shown that olfactory ensheathing cells can be harvested from the olfactory mucosa in dogs and are accessible from the nasal cavity and frontal sinus.⁵¹ This would alleviate the need to take cells from the olfactory bulb and increases the likelihood of such autologous transplantation becoming a viable treatment option.

Minocycline

Minocycline, a highly lipophilic, semisynthetic derivative of tetracycline, can cross the blood-brain barrier



and exert antiinflammatory and neuroprotective effects.⁵² It has been shown to inhibit excitotoxicity, oxidative stress, and the proinflammatory mediators released by activated microglia.⁵² Rats administered systemic minocycline showed a decreased recovery time and reduced lesion size 14 days after SCI.53

Erythropoietin

Erythropoietin is a locally produced cytokine with neuroprotective and antiinflammatory properties.⁵⁴ It has been shown to play an important role in the early stages following primary ischemic and concussive SCIs. 54,55

Oscillating Field Stimulation

An electrical field cathode has both trophic and tropic effects on injured spinal cord tissue. 42,56 In one placebocontrolled trial, an electric field in which the polarity oscillated every 15 minutes was applied to dogs with severe SCIs and no DPP. 42,56 This trial showed the safety of the procedure and a trend toward improvement, although statistical significance was not achieved. 42,56 A phase I clinical trial was subsequently approved and successfully completed in humans. 42,56 As with other promising therapies, this approach needs to be investigated further in more standardized studies.

Experimental Treatments

Many treatment strategies have shown promise in experimental trials but have not yet been studied in clinical trials. Notable examples include nimodipine,36 riluzole, 57,58 monoclonal antibodies, 59,60 and vaccination with dendritic cells pulsed with myelin basic protein.⁶⁰

Other emerging treatments for SCI that are being investigated include hyperbaric oxygen,61 autologous macrophages,62 mild hypothermia,63 Raffinee,64 edaravone,65 atorvastatin,66 nicotinamide,67 melatonin,68 and resveratrol.69

PAIN MANAGEMENT

Pain should be managed appropriately for all patients with SCI. Pain should be anticipated and treated before the patient exhibits behavior associated with pain.

Pain is managed with NSAIDs, narcotics, or a combination of both; however, there are potential problems with both classes of drugs. If opioids are used to treat pain, fluid therapy and blood pressure monitoring is indicated. There are reports in the literature that naloxone (an opioid antagonist) increases spinal cord blood flow and pressure and, hence, spinal cord perfusion. 23,36,70



Figure 5. Canine rehabilitation. Swimming a dachshund 3 weeks after surgery to help maintain and improve muscle mass and pelvic limb range of motion.

These findings implicate endorphins in the pathophysiology of SCI.^{23,36,70} However, human clinical trials did not show a significant improvement in outcome with naloxone treatment, and the reported effects are likely secondary to the improvement in spinal cord blood flow.²⁴ This further accentuates the importance of maintaining blood pressure to support the recovery of the spinal cord.

NSAIDs may be beneficial in analgesia alone or in combination with opioids or opioid derivatives. However, if the patient has evidence of gastrointestinal bleeding associated with either corticosteroid administration or stress, NSAIDs should be avoided and gastrointestinal protectants started.

Nontraditional medications (ketamine, lidocaine, and gabapentin) and adjunctive therapies (acupuncture and ice packs) should also be considered.

SUPPORTIVE CARE

Nursing care for patients with SCIs is extremely important and can be very time consuming. This supportive care may extend long past the hospital stay, and owners need to be forewarned of the time and effort needed to care appropriately for these patients.

Management of a nonambulatory animal consists of regular turning, appropriate bedding to prevent development of decubital ulcers, and cleaning to prevent urine scald. The patient's bladder should be managed appropriately. If the animal is nonambulatory, an indwelling

bladder catheter is ideal. Otherwise, the bladder should be manually evacuated three or four times/day. It is important that the urine be monitored for infection and that infections be treated promptly with antibiotics selected based on the results of urine culture.

Physical therapy is an important aspect of managing an SCI patient. Massage, passive range of motion, and stimulation of the limbs in different positions to build or maintain muscle mass, strength, balance, and coordination are ideal therapies (Figure 5).

If surgery is not an option because of financial constraints or the underlying condition, medical therapy should consist of confinement, regular physical therapy, and management of pain and urination until there is a treatment option for which the evidence of beneficial effects outweighs the detrimental effects.

CONCLUSION

Accurate diagnosis, surgical decompression as indicated, pain management, and supportive care are the foundations of managing and treating an acute SCI in veterinary medicine. At this point, there is no proven treatment for acute SCI other than decompressive or stabilization surgery when indicated. Ongoing laboratory and clinical trials are assessing different treatment options to find which have the most benefits with the fewest adverse effects. A wide range of different therapies are also being assessed in dogs with spontaneous injuries. Hopefully, this research will soon translate into viable treatment options for veterinary SCI patients.

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I. Which of the following is imperative for patients with a suspected unstable SCI?

- a. immobilization on a firm, flat surface
- b. evaluation of gait
- c. evaluation of posture
- d. administration of high doses of corticosteroids

2. Primary injury consists of

- a. direct damage to the spinal cord parenchyma via compression, contusion, shearing, laceration, or stretching.
- b. depletion of the neuronal ATP level.
- c. intracellular accumulation of calcium and sodium.
- d. oxygen free radical formation and increased cytokine production.

3. Management of an SCI should include

- a. appropriate diagnostics and surgical stabilization or decompression if needed.
- b. high doses of MPSS.
- c. dexamethasone.
- d. PEG.

4. The preferred imaging modality for evaluation of patients with a suspected FCE is

- a. plain film radiography.
- b. MRI.
- c. myelography.
- d. CT.

5. The antibiotic _____ has potential for use in the treatment of SCI.

- a. penicillin
- b. enrofloxacin
- c. minocycline
- d. amoxicillin-clavulanic acid

6. If surgery is cost prohibitive, recommendations for managing patients with SCIs include

- a. high doses of MPSS.
- b. dexamethasone.
- c. leash walking for at least 15 minutes three times/day.
- d. strict cage rest, pain management, and physical therapy.

7. Which carries a grave prognosis?

- a. absent superficial pain perception with a suspected disk extrusion
- b. absent DPP within 24 to 48 hours with a suspected disk extrusion
- c. superficial pain and absent voluntary motor function with a suspected FCE
- d. absent DPP after trauma causing a fracture/luxation of the vertebral column

8. _____ do(es) not have potential as a future therapy for SCI.

- a. Olfactory ensheathing cells
- b. Oscillating field units
- c. PEG
- d. Naloxone

9. Management of a nonambulatory animal consists of

- a. regular turning.
- b. appropriate bedding to prevent decubital ulcers.
- c. appropriate bladder management.
- d. all of the above

10. In patients with SCI secondary to trauma, the initial assessment should focus on

- a. a thorough neurologic examination.
- b. obtaining lateral radiographs.
- c. airway, breathing, and cardiovascular assessment.
- d. obtaining MRI images.