Reviews

Acupuncture for the Treatment of Spinal Cord Injuries

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ABSTRACT

EA

Spinal cord injuries with or without vertebral fractures cause neurological deficits associated with spinal cord concussion, compression, contusion, laceration or a combination of these. The diagnosis is based on the history, clinical signs and diagnostic imaging. The prognosis for spinal cord injuries varies with the type of injury and the severity of neurological deficits. If no radiographic evidence of vertebral fracture or luxation are present, the prognosis may be better, but the severity of the neurological deficits and improvement of these deficits over the following 1-2 months best determines the prognosis. From a tradtional Chinese Veterinary Medicine perspective, spinal cord injuries are due to Qi and Blood Stagnation with Qi Deficiency below the site of Stagnation. In experimental studies of spinal cord injury, electroacupuncture has been shown to reduce cell death, promote neuronal plasticity and enhance cellular regeneration. Clinical research has shown that electro-acupuncture and dry needle acupuncture combined with conventional treatments is significantly more effective to treat spinal cord injury from intervertebral disk herniation, than conventional therapy alone. Current acupuncture treatment recommendations for animals with spinal cord injuries have been based on the clinical experiences of different individuals. Further studies are needed to determine the most effective acupoints, acupuncture techniques and duration and frequency of acupuncture treatments to develop the optimum standards of care for acupuncture treatment of spinal cord injuries in animals.

Key words: acupuncture, electro-acupuncture, spinal cord injury, veterinary, small animals

TCVM Traditional Chinese veterinary medicine AP Acupuncture DN Dry needle acupuncture

Electro-acupuncture

The spinal cord is part of the central nervous system, located within a protective bony canal formed by the the vertebral column. Acute spinal cord injury commonly occurs in dogs and cats when the vertebral column is injured from automobile accidents, falls, fights and gunshot wounds and or when intervertebral disks protrude or herniate into the spinal canal. Chronic repeated spinal cord injury can occur from vertebral instabilty as in "Wobbler Syndrome" (cervical spondylomyelopathy). Spinal cord injury results in neurological deficits due to concussion, compression, contusion, laceration or a combination of these.

Injury to the spinal cord results in mild to severe

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neurological deficits. Vertebral fractures and luxations and acute intervertebral disk herniation occur in the cervical, thoracic and lumbar regions and often result in an immediate onset of neurological deficits. Cervical injuries may cause neck pain, ataxia, quadriparesis or quadriplegia with paralysis of the respiratory muscles and death. Thoracolumbar spinal cord injuries often cause local pain, pelvic limb proprioceptive deficits, paraparesis, paraplegia, loss of voluntary control of urination and defecation and loss of deep pain sensation from the toes. Lesions between T3-L3 commonly cause hyperactive pelvic limb spinal reflexes and lesions between L4-S2 cause depressed or absent pelvic limb spinal cord reflexes in dogs and cats.² Injury of the spinal cord at the thoracolumbar region in dogs and cats results in paraplegia and thoracic limb hyperextension (Schiff-Sherrington phenomenon). Although the Schiff-Sherrington phenomenon indicates acute severe injury, if deep pain is still present in the pelvic limb toes and remains present over the next few days, the prognosis is may still be good for recovery.

Clinical signs associated with spinal cord injury generally occur immediately after the injury and are generally non-progressive even though progressive pathophysiological changes occur locally at the site of the lesion. In some patients with spinal cord injury, an

ascending and descending myelomalacia develops from the original site of injury within 2-4 days. When this occurs, paraplegic dogs with a T3-L3 injury and intact pelvic limb spinal cord reflexes will lose the spinal cord reflexes over the next few days, as the lesion progressively descends. As the lesion progressively ascends, the spinal cord segments and nerves to intercostal and diaphragm muscles become affected and respiration function is depressed. The prognosis for ascending and descending myelomalcia is grave.¹ Hemorrhage, edema, ischemia, laceration, degeneration, necrosis, demyelination and focal and ascending and descending malacia of the neuronal tissues can be seen on histological examination of spinal cord injury of patients at necropsy. When the injury involves a fracture of the vertebral column, sequestered bone fragments may be lodged in the vertebral canal and can cause compression, inflammation and degeneration further damaging the spinal cord.

The diagnosis of spinal cord injury is based on the history, clinical signs and diagnostic imaging. An obvious fracture or dislocation of the vertebral column may be seen on routine radiographs, but computerized axial tomography (CT) and magnetic resonance imaging (MRI) are needed to visualize spinal cord lesions. A therapeutic plan should be implemented as soon as possible. Delay of the treatment can dramatically prolong the recovery period and may decrease the success of any treatment, the long-term survival and quality of life of the animal. In quadriplegic and paraplegic animals, high dose methylprednisolone sodium succinate is recommended as soon as possible, but not after 8 hours.^{1,2} Oral analgesic drugs are also administered and surgical decompression of the spinal cord is performed as soon as the patient is stable.^{1,2} Although the prognosis is often considered poor in patients with no deep pain sensation, many animals if properly treated, show a return of sensation and improvement of function within 4-6 weeks. Improvement may continue over the next 1-2 years.

Spinal Cord Injury from a TCVM Perspective

In traditional Chinese veterinary medicine (TCVM), spinal cord injuries are due to Qi and Blood Stagnation. Paresis and paralysis are due to Qi Deficiency below the site of Stagnation. The Qi and Blood Stagnation may cause pain around the injury site. Deficiency and Stagnation of Qi depletes Blood and Gu Qi that nourish the neurons and other cells and degeneration and demyelination occurs.

Spondylosis, other forms of vertebral degeneration and intervertebral disk disease are classified as Bony Bi syndrome in TCVM.^{3,4} If left untreated, animals suffering from Wind Bi, Cold Bi, Damp Bi and Heat Bi syndromes will progress to Bony Bi syndrome. Bony Bi is most commonly associated with Kidney Yang Deficiency, Kidney Yin Deficiency or Kidney Yang or Yin Deficiency plus Kidney Qi

Deficiency. The treatment strategy for Bony *Bi* syndrome includes expelling or eliminating the pathogenic factors (Wind, Cold, Damp and/or Heat), eliminating the Stagnation of *Qi* and Blood (cause of painful sensations) and nourishing the Kidney.^{3,4}

In TCVM, the brain and spinal cord are included in the Extraordinary Fu organs and are referred to as Brain and Marrow, respectively.⁴ The Extraordinary Fu organs possess anatomical characteristics similar to those of the Fu organs (tubular in structure), but possess TCVM physiological functions similar to those of the Zang organs (store essential substances).⁴ The Extraordinary Fu organs store Kidney Jing, Marrow, Blood or Bile. The functions of the Extraordinary Fu organs are directly or indirectly related to the Kidney.

The Brain is located in the highest point of the body and is referred to as the "Sea of the Marrow", "House of the Mind" and *Shen*. Therefore, the Brain controls memory, consciousness, thought processes, the spirit of the animal and all the activities of the body. Normal functions of the Brain require nourishment from Kidney *Jing* and Heart Blood. The Marrow is the substance that can be found within the brain, spinal cord and bone marrow. The Kidney is the origin of Essence that is essential for Marrow production. The major function of Marrow is to nourish and replenish the substances in the brain, spinal cord and bone marrow.

Acupuncture (AP) treatment of spinal cord injury includes controlling pain (*Hua-tuo-jia-ji*, LI-4, LIV-3), alleviating incontinence (SP-6, BL-32, BL-39, BL-40, KID-1, CV-3, CV-4), facilitating repair of the neuronal tissues (*Bai-hui*, GV-14, GV-4, GV-1, *Wei-jian*), alleviating *Qi* and Blood Stagnation (LIV-3, BL-17, SP-10), nourishing Kidney (BL-23, KID-3, *Shen-shu, Shen-peng, Shen-jiao*) and improving the general *Qi* levels and immune function of the animal (ST-36, LI-10, LI-11). Acupoints BL-30, BL-36, BL-37, BL-40, BL-60, GB-21 and GB-34 can also be used along with others.³ Details of the anatomical locations and indications of the acupoints commonly used to treat spinal cord injuries are outlined in Table 1.

In spinal cord injuries with severe neurological deficits and spinal cord compression, surgical decompression and stabilization of the fractured vertebrae (when present) should be performed as soon as the patient is stable. After the surgery, a combination of electro-acupuncture (EA) and dry needle acupuncture (DN) should also be initiated as soon as possible. Acupoints on the incision site are not used. Electroacupuncture of Governing Vessel, Hua-tuo-jia-ji or Bladder Channel acupoints above and below the lesion site is recommended and EA and DN of other acupoints may also be performed (Table 1). Local EA at 2-4 milliampere and 2-20 Hertz for 30 minutes is usually recommended.³ Acupuncture may be administered two to three times per week for several weeks initially for animals with severe neurological deficits, but the

Table 1: The location, attributes, indications of actions of acupuncture points suggested to treat spinal cord injuries³

Acupoint	Anatomical location	Attributes, Indications, and Actions
Bai-hui	Dorsal midline between L7-S1	Pelvic limb paresis or paralysis, lumbosacral pain, intervertebral disk disease over lumbosacral region
Hua-tuo-jia-ji	On dorsolateral region of back, 0.5 <i>cun</i> lateral to dorsal spinous process of each vertebra from T1 to L7	Thoracic and lumbar pain, intervertebral disk disease
Wei-jian	At tip of tail	Paralysis of the tail, pelvic limb weakness
Shen-shu	On dorsolateral caudal lumbar region, 1.5 <i>cun</i> lateral to <i>Bai-hui</i>	Kidney <i>Yin/Qi</i> Deficiency, urinary incontinence, thoracolumbar pain
Shen-peng	On dorsolateral caudal lumbar region, 1.5 cun cranial to Shen-shu	Pelvic limb paresis or paralysis, lumbosacral pain, lumbosacral intervetebral disk disease
BL-17	On dorsolateral aspect of spine, 1.5 <i>cun</i> lateral to caudal border of dorsal spinous process of T7	Influential point for Blood
BL-23	On dorsolateral aspect of spine, 1.5 <i>cun</i> lateral to caudal border of dorsal spinous process of L2	Kidney <i>Yin</i> and <i>Qi</i> Deficiency, urinary incontinence, thoracolumbar intervertebral disk disease, pelvic limb weakness
BL-36	Ventral to lateral border of tuber ischii in groove between biceps femoris and semitendinosus muscles	Lumbosacral pain, pelvic limb paresis or paralysis
BL-39	On lateral end of popliteal crease, on medial border of biceps femoris muscle tendon	Urinary incontinence, thoracolumbar intervertebral disk disease
BL-40	In center of popliteal crease	Master point of the caudal back and coxofemoral joint, urinary incontinence, and pelvic limb paresis or paralysis
CV-3	Ventral midline 4 cun caudal to umbilicus	Urinary incontinence
CV-4	Ventral midline 3 cun caudal to umbilicus	Urine retention, urinary incontinence, dysuria
GV-14	Dorsal midline in intervertebral space of C7-T1	Yin Deficiency, cervical pain, intervertebral disk disease
GV-4	Dorsal midline in intervertebral space of L2-L3	Thoracolumbar pain, intervertebral disk disease
LIV-3	Proximal to metatarsopharyngeal joint between second and third metatarsal bones	Qi Stagnation, pelvic limb paresis or paralysis
SP-10	When stifle is flexed, SP10 is located 2 <i>cun</i> proximal and medial to patella, in depression cranial to sartorius muscle	Blood Deficiency, pelvic limb paresis or paralysis
KID-1	On volar side of pelvic limb between third and fourth metatarsals underneath central pad	Dysuria and urinary incontinence
KID-3	On caudomedial aspect of pelvic limb in thin fleshy tissue between medial maleolus of tibia and calcaneus level with tip of medial maleolus	Thoracolumbar intervertebral disk disease

ST-36	On craniolateral aspect of pelvic limb 3 <i>cun</i> distal to ST-35 and 0.5 <i>cun</i> lateral to cranial aspect of tibial crest, in cranial tibialis muscle	General <i>Qi</i> tonic, generalized weakness, hind limb weakness
LI-10	On craniolateral aspect of thoracic limb, 2 <i>cun</i> distal to LI-11, in groove between extensor carpi radialis and common digital extensor muscles.	Generalized or hind limb weakness, lameness or paresis or paralysis of thoracic limb
LI-11	On lateral side of thoracic limb at lateral end of cubital crease, halfway between lateral epicondyle of the humerus and biceps tendon with elbow flexed	Paresis or paralysis of thoracic limb
GB-34	On lateral side of pelvic limb at stifle, in a small depression cranial and distal to head of fibula	Influential point for tendon and ligaments, weakness, paresis and paralysis

treatment interval can be increased to once or twice a month for four to six months depending on the neurological status of the patient.

Acupuncture Mechanisms of Action for Spinal Cord Injuries

Acupuncture has been used extensively for pain management and is a useful adjunct for pain associated with vertebral and spinal cord injuries. 4,5 Endogenous opioids such as endorphin have been showed to be involved in acupuncture analgesia at both peripheral and central nervous system levels. 5-7 Dynorphin, an important endogenous opioid, acts at the spinal cord level and is another important mechanism of acupuncture analgesia. 8 Acupuncture modulation of pain is complex and involves many ascending and descending spinal cord and brainstem pathways. 5

The benefit of EA has been studied in rats after partial surgical removal of the dorsal root ganglia. In this animal model, EA significantly promoted collateral sprouting of the spared nerve fibers and neuronal plasticity. It was shown, using microarray analysis, that EA modulated the expression of several genes. For example, the ciliary neurotrophic factor was upregulated at 1 day after injury, the fibroblast growth factor (FGF)-1, insulin-like growth factor (IGF) 1 receptor, neuropeptide Y and FGF-13 were upregulated at 7 days after injury and the calcitonin gene related peptide was upregulated at 14 days after injury.

In another experimental study of spinal cord injury in rats, five 30-minute DN sessions using acupoints GV-26 and GB-34 were performed beginning immediately after the injury and then once a day for 4 days. Rats were then euthanitized and tissues collected for analysis. Acupuncture at the two acupoints significantly reduced spinal cord ventral motor neuron loss compared to the sham acupuncture control group. The combination of acupoints GV-26 and GB-34 resulted in less neuronal loss compared to rats receiving DN at only one of the acupoints. The group receiving the

two point acupuncture had significantly reduced death of neurons and oligodendrocytes associated with reduced caspase-3 activation as compared to a sham acupuncture treated control group. Rats receiving acupuncture at GV-26 and GB-34 also had significantly reduced expressions of the pro-inflammatory cytokines and inflammatory mediators, tumor necrosis factor-a (TNF- α), interleukin-1 β (IL-1 β), interleukin-6 (IL-6), nitric oxide (NO) synthase, cyclooxygenase-2 (COX-2) and metric metalloproteases-9 (MMP9) levels compared to the control group. ¹⁰

Traumatic injury to the spinal cord causes not only the immediate mechanical damage, but a cascade of secondary degenerative processes over the following days that greatly impact functional recovery. In another group of rats, the extent of spinal cord tissue loss was compared 38 days after injury in rats receiving DN and those receiving sham acupuncture. The total lesion volume was significantly less in the DN treated group. Functional recovery of rats with and without AP following spinal cord injury was also compared in rats that were maintained for 35 days. Rats receiving AP had a significantly improved function on day 35 post-injury compared to the sham AP control group. In

In another experiment of spinal cord injury in specific proteins associated with EA rats, neural treatment of acupoints on the Governing Vessel above and below the lesion were studied. 11 A pair of 0.35 mm diameter stainless steel acupuncutre needles were inserted into acupoints GV-6 (midline between T11-12 in rats) and GV-9 (midline between T7-T8 in rats) and the spinal cord injury lesion was at T10. Connected together to a standard EA machine, a dense and disperse technique was used that provided ≤ 1 milliampere, 60 Hz alternating for 1.05 and 2.8 seconds for 20 minutes. Most groups of rats were treated with EA beginning on the 7th day after injury when they were stable and then were treated daily for 7 days. The neural specific proteins Annexin-A5 (ANXA5) and collapsing response mediator proteins-2 (CRMP2), known to be beneficial to

neuronal survival and axonal regeneration, were increased in the group receiving EA at GV-6 and GV-9 compared to the control non-acupoint electrical stimulation group. Besides these proteins, other proteins in the spinal cord associated with inflammation, cell adhesion, cell migration, signal transduction and cell apoptosis were also altered significantly to favor neuroprotection and regeneneration in the group receiving EA at GV-6 and GV-9. In another group Huatuo-jia-ji acupoints lateral to GV-6 and GV-9 were stimulated with EA. The amount of ANXA5 and CRMP was higher in rats receiving EA at GV-6 and GV-9 than those receiving EA at *Hua-tuo-jia-ji*, indicating that in this parameter of neuroprotection, EA of GV acupoints may be superior to EA of *Hua-tuo-jia-ji* acupoints.

The effects of EA on the survival of transplanted bone marrow mesenchymal stem cells (MSCs) into the transected spinal cord of rats were studied in another experiment. Electro-acupuncture was administered at GV-6, GV-9, GV-1 and GV-2 in rats with a T10 spinal cord lesion once every other day for 7 weeks using the same dense and disperse ≤ 1 milliampere, 60 Hz technique described above. 12 After EA treatment for 2-8 weeks, increased levels of neurotrophin-3 (NT-3), cyclic adenosine monophosphate (cAMP), differentiated MSCs and 5-hydroxytryptamine (5-HT) positive and calcitonin related peptide (CGRP) positive nerve fibers were increased in the lesion and nearby tissues compared to the untreated control groups. 12 In a subsequent study by the same group, the same protocol for EA and transplantation of MSCs resulted in significant improvements in pelvic limb function using a standard scoring system compared to a non-treated group, one receiving only transplantation of MSCs and another receiving only EA treatment without MSCs.¹³ Although further studies are needed for confirmation, EA plus transplantation of MSCs may improve the prognosis for recovery of function in severe spinal cord injuries in other species.

Aquaporin-4 (AQP4) is an integral membrane protein that transports water through the cell membrane. In the central nervous system, it is found in astrocytes and is increased by insults to central nervous system tissues. ¹⁴ Electro-acupuncture of GV-4 and GV-14 with 20 Hz significantly reduced the expression of AQP4 in rats with experimental spinal cord injury compared to controls. ¹⁵ The reduction in AQP4 expression was in conjunction with improvement of neurological function. It was suggested that the mechanism of action of low frequency EA may be due partly to a reduction of spinal cord edema, alleviating secondary spinal cord injury. ^{14,15}

In an experimental spinal cord compression study in dogs, the recovery time was compared in dogs receiving corticosteroids alone, EA alone, coricosteroids plus EA or no treatment. Acupoints GV-4, GV-3, BL-23, BL-24, GB-30, GB-34, ST-36, ST-40 and ST-41 were electrically stimulated with 2 volts, 25 Hz for 20 minutes every other day. Dogs that received either

corticosteroids or EA treatment alone had shorter recovery times (21.2 and 19.8 days, respectively) compared to untreated dogs (46.6 days), but dogs receiving a combination of corticosteroids and EA treatment had significantly shorter recovery times (8.2 days) than all other groups. If In another experimental study in dogs with spinal cord compression, the recovery time of dogs receiving decompression surgery alone was compared to those receiving decompression plus EA treatment. Dogs receiving decompression plus EA recovered significantly faster than those receiving decompression alone. If

In an experimental study where the dorsal root ganglia at L1-L5 and L7-S2 was removed, cats receiving 98 Hz of EA at ST-32, ST-36, GB-39 and SP-6 showed a significant increase in the number of cells expressing nerve growth factor (NGF), neurotrophin-3 (NT-3) and a brain derived neurotrophic factor (BDNF) in the the spared L6 dorsal root ganglia ipsilateral to the treatment side. Similar EA stimulation in a normal cat showed significantly increased expressions of mRNA of these neurotrophic factors in a dorsal root ganglia ipsilateral to the treatment side as compared to the non-treatment side providing further evidence for the promotion of nerve regeneration by EA. 18,19

Clinical Studies of Electro-acupuncture for Spinal Cord Injuries

For many years, EA and DN have been used alone and in conjunction with surgical decompression and corticosteroid therapy for animals with spinal cord injury from intervertebral disk disease. 3,20-22 In one clinical study, 50 dogs with intervertebral disk disease and varying degrees of neurological deficits greater than 48 hours duration were randomly divided into two groups.²³ One group received a combination of EA and DN combined with decreasing doses of prednisone and tramadol for pain control as needed. The other group received only prednisone and tramadol. Acupoints used in this study included SI-3, BL-62, BL-20, BL-23, BL-25, BL-60, ST-36, KID-3, GV-1, Bai-hui, LI-4 and GB-30.²³ These acupoints were electrically stimulated with 3 Hz alternated with 100 Hz for 3 seconds each. Total stimulation time was 20 minutes. The combination of EA and conventional medical therapy significantly increased the success rate of treatment (88.5%) for dogs with all grades of dysfunction when compared to the success rate of treatment for dogs receiving only the conventional medical therapy (58.3%). Time to recover ambulation in dogs receiving EA integrated with conventional medical treatments was also significantly shorter than in dogs receiving conventional medical treatment alone.

In another clinical study, 40 dogs with confirmed thoracolumbar intervertebral disk disease and severe neurological deficits (Grades 4 or 5 out of 5), dogs were treated with either prednisone alone, prednisone and decompressive surgery alone, prednisone

and EA/DN (electro-acupuncture plus dry needle acupuncture) or prednisone, decompressive surgery and EA/DN.²⁴ The acupoints treated varied slightly with the location of the spinal cord lesion. The EA was performed connecting BL-18 to BL-23 and ST-36 to GB -34 on each side. 24 Alternating current EA with frequencies of 2 to 15 Hz were used for 20 minutes. The voltage was increased until muscle twitching was observed. Dry needle acupuncture was performed at BL-40, KID-3 and GB-30. The EA/DN treatment was performed once per week for 1 to 6 months. Treatment was discontinued when dogs improved from Grade 4 or 5 to Grade 1 or 2 neurological deficits. At six months after the initiation of the experiment, the dogs receiving prednisone and EA/DN alone had the best clinical recovery of all the groups.²⁴

In a retrospective study of the outcome of 80 paraplegic dogs with intact deep pain and intervertebral disk herniation, 37 dogs were treated with prednisone alone and 43 dogs were treated with prednisone plus EA. Acupoints GV-7 and GV-2 were treated with EA at 0.5-2.5 millivolts and mixed frequencies of 2 and 15 Hz for 30 minutes. Acupoints on the Bladder Channel near the lesion and bilaterally at GB-30, GB-34 and ST-36 were treated with DN for 30 minutes. The combination of EA/DN with prednisone was more effective than prednisone treatment alone to recover ambulation, relieve back pain and decrease relapses.

The successful use of DN and EA for spinal cord injury recovery has also been documented in human clinical case reports. ²⁶⁻²⁷ When DN and EA were used to treat humans with acute spinal cord injury, the long-term neurological recovery including motor, sensory and bowel/bladder functions was improved. Patients that received EA at CV-3 and BL-32 with 30-50 milliampere, 20 Hertz pulses for 15 minutes for 4-5 treatments per week regained their bladder control within a significantly shorter period than did the non-treatment group. ²⁸ Electro-acupuncture has been reported to be useful to manage chronic pain associated with spinal cord inuries. ²⁹ No adverse side effects of EA and DN were seen in these studies. ^{26,27}

As shown in this review, there is growing scientific support from controlled basic science studies that EA and DN have neuroprotective effects, shorten the recovery times and improve outcomes in animals with experimental spinal cord injuries. 9-19 Clinical research has further shown that EA and DN combined with conventional treatments is significantly more effective to treat spinal cord injury from intervertebral disk herniation and other causes, than conventional treatments alone. 23-29 At least in rats EA of GV acupoints above and below the lesion were more effective than Hua-tuo-jia-ji acupoints at the same level. 11 Current acupuncture treatment recommendations for animals with spinal cord injuries have been based on the clinical experiences of different individuals.^{3,4,20-25} Further studies are needed to determine the most effective

acupoints, acupuncture techniques and duration and frequency of acupuncture treatments to develop the optimum standards of care for acupuncture treatment of spinal cord injuries in animals.

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