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Critical Care of Traumatic Spinal Cord Injury

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Abstract

Approximately 11 000 people suffer traumatic spinal cord injury (TSCI) in the United States, each year. TSCI incidences vary from 13.1 to 52.2 per million people and the mortality rates ranged from 3.1 to 17.5 per million people. This review examines the critical care of TSCI. The discussion will focus on primary and secondary mechanisms of injury, spine stabilization and immobilization, surgery, intensive care management, airway and respiratory management, cardiovascular complication management, venous thromboembolism, nutrition and glucose control, infection management, pressure ulcers and early rehabilitation, pharmacologic cord protection, and evolving treatment options including the use of pluripotent stem cells and hypothermia.

Keywords

spinal cord injury, critical care, treatment, SCI

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Introduction

The long challenging goal in acute spinal cord injury (SCI) treatment has been retention or recovery of motor and sensory function, and appropriately so. Pursuit of this goal, however, has, perhaps inadvertently, overshadowed immediate management of other medical conditions uniquely associated with spinal insult and hindered achievable advances for this patient population. These include life-threatening conditions that are encountered in the ICU such as respiratory failure and pneumonia, sepsis, thromboemboli, and neurogenic ischemic injury to the cord and distal organ systems. As such, intensivists had to rely on evidence from case reports or those developed from broader categories of injury in intensive care units (ICUs) and emergency departments to treat the spine patients in their care.

Renewed energy and resources, we think, should be directed toward management of these acute secondary consequences of cord damage, and the improvements which this could provide to spine injury patients' quality of life. This could offer the best possible platform for restoration of spinal neural pathways themselves.

Background

Spinal cord injury is defined as the occurrence of an acute traumatic lesion of neural elements in the spinal canal (spinal cord and cauda equina), resulting in temporary or permanent neurological deficit.[1] Each year, approximately 11 000 people suffer traumatic spinal cord injury (TSCI) in the United States.[2] Estimates of TSCI incidence vary widely, from 13.1 to 52.2 per million[1,3,4] people, and the mortality rates range from 3.1 to 17.5 per million people.[5,6] It has been estimated that 227 080 to 300 938 patients lived with a SCI in the United States, in 2007.[7] The cost to society is huge. Expenses including the additional 11 000 new patients with SCI each year[8] amount to $9.7 billion (US dollars).[9]

The main TSCI causes in developed countries were traffic accidents (from 35% to 53.8%) and falls (from 22.6% to 37%), according to a recent systemic review of outcomes.[6] Of the TSCI cases, cervical spine injury represented 41.6% to 75%, thoracic spine was 16% to 36%, and lumbar spine 9%

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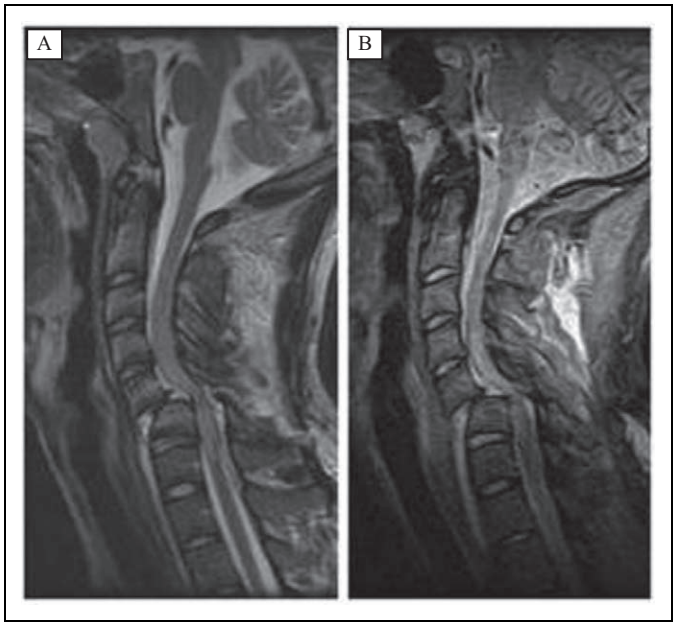

Figure 1. Magnetic resonance images (MRIs) of a patient with a cervical fracture subluxation as seen on a T2-weighted sagittal image (A), and STIR sagittal image (B).

to 17.6%.[6] Incomplete injury was reported more often than complete injury. The rate of tetraplegia injury ranged from 50.8% to 54.1% in the United States; and in Australia the rate of tetraplegia injury was 57.7%.[10-12]

Pathophysiology

It has been well recognized that 2 entwined phases of injury occurred after TSCI.[13-15] Primary injury occurs due to cord hyperflexion, hyperextension, axial loading (compression or stretching), and/or rotation of the spinal canal with resultant laceration, contusion, and compression or concussion of the spinal cord[13-15] (Figure 1). Secondary injury begins immediately after trauma and lasts for several days to weeks as an interdependent cascade of systemic and cellular events initiated by the primary injury. It includes (1) vascular change including ischemia caused by direct vascular injury, hypotension related to neurogenic shock, loss of autoregulation, vasospasm, and vasospasm-induced thrombosis; (2) inflammatory response with endothelial damage, the release of inflammatory mediators, changes in vascular permeability, development of edema, immigration of peripheral inflammatory cells, and activation of microglia; (3) chemical change or ionic derangements, including increased intracellular calcium, increased extracellular potassium, and increased sodium permeability; (4) cellular dysfunction including neurotransmitter accumulation, free radical production, eicosanoid production and lipid peroxidation, endogenous opioid release, and programmed cell death or apoptosis; (5) anatomic and functional change including widespread edema.[13-17] The degree of SCI is dependent on the extent of mechanical damage inflicted by the primary event and also on those processes occurring during the secondary phase of injury. An improved understanding of the pathophysiology of acute SCI has led to novel pharmacologic strategies to attenuate the effects of the secondary injury.[18]

Spine Stabilization and Immobilization

Principles of spine stabilization are well established and have changed little in recent years. Clinical stability is defined as the ability of the spine under physiologic loads to prevent initial or additional neurologic damage, intractable pain, or gross deformity.[19] Stability is critical in decisions regarding critical care management and can be assessed using clinical, anatomic, and radiographic characteristics. Spinal instability is quite common in the setting of SCI and can be further confirmed in patients by the presence of mechanical pain, posterior ligamentous disruption, and subluxation or deformity on radiographs.[20,21] The goal of immobilization is to prevent or limit secondary neurologic injury in the presence of an unstable spine. Common measures to accomplish this include suspending the head between 2 sandbags, placement of a rigid cervical collar, transportation on a rigid spine board, spinal traction with tongs, halo-vest orthosis, and log rolling of the patient.[22,23] Because spinal injury can occur at several noncontiguous levels, immobilization of the entire spine is recommended until injury is ruled out with appropriate physical examination and imaging.[24] Complications included pain, pressure sores, overt spinal instability requiring surgical fixation, difficult intubation, aspiration, increased intracranial pressure, and respiratory failure.[22,25,26]

Spine immobilization is not without its reservations, however. Recent research on penetrating trauma found immobilization prior to hospitalization was associated with higher mortality[27] Detrimental effects of delayed transport due to time spent securing the spine outweighed its benefits, according to these findings. Rigid cervical collars also have been shown to lead to elevated intracranial pressure through obstruction of internal jugular venous outflow.[28]

To date, level 1 trauma centers have been shown to have better outcomes in acute SCI than lower level trauma centers or nondesignated hospitals.[29] Therefore, if the patient is hemodynamically stable, it is advocated that emergency medical services in urban areas consider bypassing the nearest hospital to take patients with SCI to level 1 trauma centers directly. Such level 1 centers are required to have in-house neurosurgical consultation and can therefore more rapidly assess patients and intervene.[30,31]

Surgery

Potential complications such as bowel and bladder dysfunction, paresis, and paralysis may be alleviated by prompt diagnosis, surgical decompression and stabilization, and intensive care management.[32] Together with careful clinical and radiography evaluation, the benefits of removing spinal cord compression have been shown for decades, especially for patients whose clinical condition worsens acutely.[33-36] Surgical decompression is recommended when there is failure to progress

consistently after an initial period of improvement, persistent compression of neural tissue demonstrated radiographically, or gross spinal cord instability.[33,36] Aside from securing immediate postoperative stability, decompression should be considered when there is a progressive or incomplete neurological deficit with radiographic evidence of a space occupying lesion within the canal.[19]

Timing of decompression of the neural elements, however, is controversial. Animal data have consistently suggested increased neuronal loss from prolonged compression though the major determinant of recovery success was the force of the injury.[37,38] The relevant interventional timing in humans remains unclear and the role of surgical decompression in patients with SCI is only supported by class III (case series, retrospective reviews, and expert opinion) and limited class II (prospective cohort studies or controlled studies with well-defined comparison groups) evidence.[39] A systematic review of medical journal publications from 1966 to 2009 showed that although a number of studies indicate patients who undergo early surgical decompression can have similar outcomes when compared to patients with delayed decompression, there is evidence to suggest that early surgical intervention is safe and feasible and can improve clinical and neurological outcomes and reduce health care costs.[40] Despite the lack of definitive timing evidence, some data suggest outcomes after traumatic SCI are potentially optimized if surgical spinal cord decompression and stabilization are carried out within 8 to 24 hours from the time of injury.[40]

In our experience, the overwhelming majority of SCIs secondary to blunt trauma at our center occur concomitantly with severely destabilizing injuries to the spinal column. In all of these cases, open reduction and internal stabilization with spinal instrumentation is done urgently (within 12-24 hours from the time of injury). In those cases with an incomplete injury in the cervical spine, we may consider conducting spinal traction and reduction in the ICU prior to internal fixation. However, it is our experience that rapid transfer to the operating room is often the most effective way of quickly decompressing the cord and stabilizing the spinal column.

Beyond the technical aspects of intraoperative spinal reconstruction, there are a number of fundamental concerns that must be addressed while operating on an SCI. First, during the operation, perfusion pressure to the spinal cord must be maintained at a mean arterial pressure (MAP) greater than 85mm Hg. Thus, all patients require arterial lines. With multisystem trauma patients, blood loss may be severe and spinal shock may be present from intrinsic cord damage, putting patients at risk of hypotension during surgery. When the spinal cord is compromised via compression, stretch, or twisting, perfusion pressure must be maintained so as not to worsen the spinal cord ischemia. Second, although practiced prior to hospitalization, mobilization of all patients into scans and on and off the operating table must be done in a carefully controlled manner so as not to introduce iatrogenic SCI. We have seen patients worsen neurologically following seemingly gentle transfers into a computed tomography (CT) or magnetic resonance imaging (MRI) bed. Third, neuromonitoring is essential in all cases of SCI for 2 reasons. First, patients, who possess successful transmission of somatosensory- or motor-evoked potentials (SSEPs or MEPs) across the injury site, can be counseled that they are likely to eventually exhibit function distal to the injury even if they wake up from the surgery immediately plegic distal to the lesion. Second, certain spinal fracture reductions may put the spinal cord at risk via stretching or twisting. Therefore, monitoring helps to avoid iatrogenic injury during open reduction and fixation. Finally, it is the surgeon's imperative that any compression on the spinal cord must be relieved prior to finishing the operation. This can be done with direct visual inspection of the spinal cord or via the use of intraoperative ultrasound. In our experience, we obtain postoperative CT and MRI scans to corroborate ideal spinal implant position and spinal cord decompression, respectively, on all patients.

Pharmacologic Cord Protection

Since the published results from the landmark National Acute Spinal Cord Injury Studies (NASCIS) II trial during the early 1990s, synthetic glucocorticosteroid methylprednisolone sodium succinate (MPSS) has become widely used in the treatment of SCI, via a putative suppression of lipid peroxidation and hydrolysis, which destroys neuronal and microvascular membranes.[41,42] However, many have questioned the efficacy of MPSS because of its marginal effects, the increased risk of infection and metabolic complications, gastrointestinal bleeding, and steroid myopathy associated with the 48-hour-long infusion.[31,43-45] The results of recent animal studies remain controversial.[43,46-48] A recent systematic review of MP that included 62 studies showed beneficial effects of MP administration were obtained in 34% of the studies, no effects in 58%, and mixed results in 8%, thus demonstrating the barriers to the translation of animal study findings on the effectiveness of MP in the treatment of acute SCI to humans.[46]

As in the animal studies, debate still exists in clinical practice.[49-51] It cannot be said at this point that MP has no beneficial effect in the treatment of acute SCI, but it seems clear that if any benefit exists, it is probably small and has not been demonstrated by the NASCIS studies.[50] Moreover, high steroid levels may produce acute corticosteroid myopathy.[50] A 2006 questionnaire showed, despite these caveats, the use of the NASCIS protocol remains high in the United States.[44] Meantime, a 2008 questionnaire of 42 spinal surgeons and 22 residents across Canada, 5 years after the publication of practice recommendations, found 76% of spinal surgeons there did not prescribe MP for SCI, in sharp contrast to the 76% who prescribed it 5 years earlier. Of the 24% who did use steroids, the NASCIS II dosing regimen was most commonly followed. One third of physicians continue to administer MP because of fear of litigation.[49]

Given the uncertainty of the literature and the practice survey results, the continued use of MP for SCI should be considered not only for its possible benefits but also for its safety profile with careful consideration of the associated adverse effects to the SCI patient in the ICU.

Intensive Care Management

Critical care management plays a vital role in the acute treatment of patients with traumatic spinal cord damage. Injuries to the cervical and upper thoracic spine are red flags for potential respiratory and cardiovascular compromise and are the obvious and key concerns for physicians in hyperacute and intensive care settings. Aside from this, ICU management of spinal injuries, including that in dedicated neurologic units, recently has directed attention to other central nervous system (CNS) deficits localized to specific regions of cord damage. Isolated and multiple organ failures often arise from spine injury and can be assessed by the Multiple Organ Dysfunction Score (MODS) and the Sequential Organ Failure Assessment (SOFA) scales. Associated injuries at remote sites from the initial site of injury in the spine occur not infrequently. Patients with SCI are at a higher risk of systemic inflammation, which may precipitate organ damage.[52] Remote complications of insult to specific regions of the cord manifest themselves in other important ways that may be clinically occult. For instance, infections without an obvious source may stem from spine-injury-related abdominal dysfunction such as bowel ischemia, cholecystitis, or pacreatitis. Bladder and bowel management have important neurologic implications for patients with spine injuries. Symptomatic autonomic dysreflexia, with characteristic elevated blood pressure, headache, and sweating, typically is linked to SCI above the level of T-5 or T-6. But it is also associated with reflex voiding and manual removal of stool among SCI patients.[53,54]

Airway and Respiratory Management

Ventilatory insufficiency and impaired airway secretion clearance are common complications of SCI and can lead to respiratory failure, which is the leading cause of death in both the acute and chronic stages. The ramifications of breathing assistance are compelling. Among patients with similar SCI, a requirement for mechanical ventilation decreases survival to 33% from 84%.[55] After SCI, weak or paralyzed abdominal muscles preclude an effective cough, leading to impaired airway secretion clearance. Techniques of manually assisted coughing by abdominal compression following a maximum insufflation capacity (MIC) maneuver and mechanical insufflation-exsufflation (MI-E) for facilitating airway secretion clearance have been shown to be more effective and safe in clearing secretions than standard suctioning, which effectively clears only the right main stem bronchus.[56] This is significant because atelectasis or pneumonia are most common in SCI in the left lower lobe, which may be due to the tendency to retain secretions combined with the increased difficulty of clearing secretions from the left lung.[57] Functional recovery of airway-protective behaviors including augmented breaths, the cough reflex, and expiration reflexes, has been reviewed recently. Evidence for functional recovery is restricted to alterations in motor strategy and changes in the frequency of occurrence of these behaviors in humans.[58] Numerous methods have been used to improve pulmonary function, including resistive inspiratory muscle training and electrical stimulation methods, but the effect remains unclear without the support of a meta-analysis of clinical trials.[59]

Standard invasive management options to improve breathing included intubation, tracheostomy, and electrophrenic respiration.[60] Diaphragm pacing, tested in tetraplegic patients in a recent 10-year study, presents the exciting prospects of reduced dependence on positive airway pressure, retention of olfaction and taste, reduced diaphragm atrophy, and possible neuroplasticity effects with the development of alternate phrenic neuronal pathways.[55] Tracheostomy offers many advantages for critical patients who require prolonged mechanical ventilation, although the invasive procedure might cause severe airway stenosis and other complications. Advantages to this approach include improvements in artificial ventilator support through a drop-dead space, facilitated bronchial clearance, decreased complications of prolonged orotracheal intubation, reduced aspiration risk, lower incidence of ventilator-associated pneumonia, facilitated weaning from mechanical ventilation, supported phonation and swallowing, and reduced length of sedation to prevent related complications.[61] Despite such potential benefits, there is still an open debate about tracheostomy timing. Although evidence does not show early tracheostomy helps avoid risks of ventilator-associated pneumonia or reduce mortality, this technique still has been suggested in traumatic patients with SCI likely to require prolonged mechanical ventilation. Early placement (days 1–7 from intubation) offers advantages for shortening mechanical ventilation, reducing the ICU stay, and lowering rates of severe orotracheal intubation complications, such as tracheal granulomas and concentric tracheal stenosis.[62] As with other aspects of SCI treatment, guidance for acute respiratory care of these patients is limited to sparse clinical study findings. Guidelines for respiratory management of SCI published by the Consortium for Spinal Cord Medicine in 2005 rely on consensus findings of the drafters because scientific evidence to support many of its recommendations for management of acute SCI did not exist.[63,64]

Management of Cardiovascular Complications

Cardiovascular complications in the acute stage following TSCI require prompt medical attention to avoid neurological compromise, morbidity, and death. Hypotension (both supine and orthostatic), autonomic dysreflexia, cardiac arrhythmias (including persistent bradycardia), and neurogenic shock are attributed to the loss of supraspinal control of the sympathetic nervous system that commonly occurs in patients with severe spinal cord lesions at the level of T-6 or higher.[24,31,65] Hypotension and shock are particularly deleterious to the injured spinal cord, contributing to cord hypoperfusion and perpetuating secondary injury.[66] Hypotension may be avoided by (1) the use of abdominal binders, lower-limb compression, and oral vasopressors such as midodrine as options to maintain adequate cord perfusion during transportation; (2) monitoring the cardiac

and hemodynamic parameters in the acute phase of SCI; (3) maintaining a minimum MAP of 85 mm Hg during the hyperacute phase (1 week after SCI); (4) timely detection and appropriate treatment of neurogenic shock and cardiac arrhythmias; and (5) immediate and adequate treatment of episodes of acute autonomic dysreflexia.[31,65]

Efficacy of blood pressure augmentation for spine injury remains an open question. Specific clinical trial findings for MAP elevation in SCI are lacking, and what evidence does exist for boosting perfusion to the damaged cord is frequently derived from case reports. The perceived greater benefit of vasopressor support for complete spine injury compared with partial cord damage, for example, is based on nonrandomized studies.[67] When blood pressure elevation is pursued, volume expansion is typically the first-line approach. The next step, vasopressor therapy, is a double-edged pharmacologic sword in these patients. Vasoactive agents with mixed α- and β-receptor effects, such as dopamine and norepinephrine, normally are applied before α-selective agonists like phenylephrine,[67,68] as concurrent bradycardia so often is associated with spine injury, especially when the higher cervical cord is involved. But as one recent report noted, vasopressors are by no means a benign treatment option in neurologic injury. Pressors increase cerebral blood flow and can produce elevated intracerebral pressure (ICP) and cerebral edema. For patients with concurrent brain injury, this is of special concern as cerebral autoregulation may already be deranged.[69] Furthermore, dopamine may have a deleterious effect on hepatosplanchnic oxygenation.[70,71] And midrodine's reported increase in urinary retention also warrants caution.[69]

Because failure to correct hypotension is ethically untenable and class I evidence for pressor therapy in spine injury therefore is unobtainable in human subjects, the American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Disorders of the Spine and Peripheral Nerves recommended pressors only as an option for spinal cord trauma.[72] We concur with the recommendation assuming that appropriate clinical consideration of significant potential side effects is given in these patients.

Venous Thromboemolism

Deep venous thrombosis (DVT) and pulmonary embolism (PE) are high-risk complications after traumatic SCI due to loss of mobility and, potentially, altered fibrinolytic activity, abnormal platelet function, and impaired circadian variations of hemostatic and fibrinolytic parameters.[24,31,65,66] In the absence of contraindications, prophylaxis of venous thromboembolism should begin no later than 72 hours after the onset of SCI and continuing up to 3 months afterward, depending on the severity and level of injury. Such prophylaxis includes mechanical methods like sequential pneumatic compression devices (SCDs) and gradient elastic stockings (GES), and anticoagulants.[31,65,73] Low-molecular-weight heparin (LMWH) is the first choice for anticoagulant prophylaxis in patients with acute SCI.[31,65] Compared with unfractionated heparin, at 5000 U 3 times daily, it has similar rates of DVT incidence, but lower rates of PE and bleeding.[73]

For patients with SCI having contraindications to LMWH, prophylactic inferior vena cava filters (VCF) are an option. However, there are warning signs in the literature for this approach. An earlier generation of such devices, the Greenfield filter, was associated with greater complications in cervical spine injury patients, including movement inside the blood vessel.[74] Newer designs overcome some of these issues by allowing easier filter retrieval to avoid problems associated with longer use.[75] Temporary IVC filters placed with ultrasound guidance at the ICU bedside may offer some benefit during the high-risk acute phase of multitrauma treatment.[76] But prophylactic VCF placement in SCI may actually increase the subsequent risk of DVT substantially.[77] And a single-center study questioned the need for such filters routinely in all cases of spine injury, with the findings that the overall patients with SCI may have no greater incidence of PE or DVT when treated with nonfilter prophylaxis, although it concluded that some subgroups like those with long-bone fractures may warrant placement of the devices.[78]

Nutrition and Glucose Control

With a relative scarcity of research on nutritional supplementation in the acute spine injury setting, feeding criteria often are inferred from head trauma and burn literature. Nutritional therapies in isolated spinal trauma are unique from head trauma[79] as well as other individual and multitrauma injury types and involve a temporal progression that may dictate feeding changes over time. Patient metabolism can drop markedly in the period immediately following spine injury, with basal energy demands reduced by as much as half—the converse of what is seen in agitated head-injury patients. A lowered metabolic rate often continues into the chronic spine injury phase, in which obesity is a secondary complication.[80] Acutely after cord damage, nitrogen excretion increases, with muscle denervation and atrophy as suspected causative factors. Supplementing this nitrogen loss is uniquely difficult for SCI among injury types, and the subsequent deficit can last for 2 months.[81] When it is undertaken, feeding may be complicated when interruption of parasympathetic innervation causes reduced gastric motility or paralytic neurogenic ileus. Sphincter dysfunction, fecal incontinence, and constipation also are common complications of SCI.[82] Further, impaired gut motility and cervical spine immobilization can increase aspiration risks with enteral feeding.[83]

Amid these physiologic changes, early versus late and enteral versus parenteral routes of delivery are feeding considerations in acute spine injury. More immediate nutritional supplementation showed no significant difference from delayed feeding in terms of infection incidence, duration of ventilation, or nutritional status in this population, according to one report.[83] Another study noted no major complications when enteral feeding was carried out within a median of 2 days from injury in paraplegic and quadriplegic patients.[84]

Infectious complications are at higher risk with parenteral feeding in a general population of critically ill patients,[85] but whether that holds true with SCI is unclear. Aside from nitrogen depletion, elevated blood glucose levels are a concern with spine injury. Impaired glucose tolerance and insulin resistance are more commonly seen in SCI, perhaps explained by the loss of insulin-mediated uptake sites in skeletal muscle atrophied by cord damage. But one study found that the degree of physical activity in chronic patients with SCI, rather than spinal lesion level, independently predicted this effect.[86] Glycemic levels also may be affected by other SCI therapy. Administration of MP is associated with increased hyperglycemia incidence in patients with SCI.[45] The role of blood glucose levels in acute spinal injury in humans, however, has not been thoroughly investigated. The Society of Critical Care Medicine 2008 sepsis guidelines recommend a target blood glucose level <150 mg/dL for patients with sepsis.[87] The NICE-SUGAR trial in 2009 found improved mortality among critically ill patients with a blood glucose target level <180 mg/dL, with a tighter control range of 80 to 108 mg/dL,[88] although the topic remains controversial.[89] A specific glycemic control range for patients with SCI is yet to be determined. In the interim, we believe the higher target blood glucose level supported by the NICE-SUGAR trial is warranted for these patients until SCI-specific study findings are available.

Infection Management

Urinary tract infections (UTIs), associated with incontinence, are a common presentation of the spinal injury infectious process.[24] Hence, urine voiding management is an important, although still controversial, consideration. The risk of urological complications has been shown to be lower with sterile intermittent catheterization than chronic indwelling catheters in this patient population.[90] However, another study found the epididymo-orchitis risk increased with intermittent catheterization in SCI.[91] When acute symptomatic UTI does occur in SCI, longer antibiotic treatment (14 days) has shown improved results[92] compared with a shorter course, but antibiotic prophylaxis is not supported.[93] Part of the increased UTI risk is linked to a mechanical dysynergia that occurs after SCI, with concurrent detrusor contraction and sphincter activation leading to increased bladder pressure. This may cause vesicourethral reflux, renal damage, and septic shock. Renal disease was the major cause of mortality in paraplegics in past decades.[94] Along with antimuscarinic drug therapy, artificial nerve stimulation techniques, such as sacral neuromodulation, have been investigated as possible acute treatments for this phenomenon.[95]

Respiratory infections are perhaps an even greater concern in SCI. Pneumonia has become the leading cause of death in SCI[96,97] and occurs at a rate of 60% to 70% in complete and 20% to 30% in incomplete cervical SCI.[64] Additionally, SCI poses an increased risk of ventilator-associated pneumonia[98] and that risk increases by 1% to 3% for each additional day of intubation.[99] Respiratory complications are as important as the level of spine injury in predicting hospital length of stay and costs.[96] Together with antimicrobials, mucus and secretion clearing and reduced aspiration are management options for these infectious complications.

Pressure Ulcers and Early Rehabilitation

Pressure ulcers are a significant problem in acute inpatient rehabilitation and should be a primary concern for the physician during the acute stage. Pressure sores are graded from 1 to 4, based on the classification scheme of Enis and Sarmiento.[100] To qualify as a grade 1 pressure sore (the minimum requirement for a pressure sore to be counted), the area must at least exhibit redness that does not blanch to the touch and requires intervention. Of patients in system rehabilitation, 23.7% to 31.7% developed at least 1 pressure ulcer.[12] The sacrum continues to be the most common location for this skin breakdown, accounting for 39.0% of new ulcers, followed by the heels (13.0%), ischium (8.0%), and occiput (6.1%).

Early rehabilitation and intervention may be key factors in the prevention of many of the potential complications that occur, primarily due to immobility.[101] The multidisciplinary team needs to focus attention on pressure ulcer prevention, splinting, mobilization, nutrition, and gastrointestinal, genitourinary, and pulmonary issues, as well as planning the support essential for transition to a rehabilitation center. Recently, an effort has been made to steer ICU culture away from conventional dependence on bed rest toward early mobilization of patients, with attendant benefits for prevention of muscle loss and improvement in respiratory function.[102] How much of this thinking is applicable to the unique aspects of acute SCI remains to be seen. However, timing of rehabilitation may be important for longer-term outcome in these patients. One report, for instance, found that rehabilitation started within 2 weeks of SCI was associated with a better long-term functional independence.[103]

Evolving Therapies

A variety of molecular pathways are likely involved in the underlying pathologies of SCI, such as hypoxia, ischemia, lipid peroxidation, free radical production, neutral protease activation, prostaglandin production, and programmed cell death or apoptosis.[104] Several promising agents are under active investigation. Curcumin, which by inhibiting apoptosis and neuron loss, and quenching astrocyte activation, may be potentially beneficial for neuronal survival.[105] Prostacyclin (PGI2) is a well-known cytoprotective agent that increases tissue blood flow and inhibits leukocyte activation and reduces posttraumatic SCI by inhibiting tumor necrosis factor (TNF) production.[106,107] Activation of sensory neurons by the administration of calcitonin gene-related peptide (CGRP), which is a neuropeptide released from the sensory neurons, might ameliorate compression trauma-induced SCI, inhibiting TNF production through the enhancement of endothelial PGI2 production.[107]

Pluripotent Stem Cells

Pluripotent stem cells represent an attractive strategy for treating neurologic diseases, and early successes in animal models have generated optimism for their use to restore or maintain function in humans.[108] Stem cells are currently a source of hope in the repair of the CNS with different types of cells in the experimental protocols: embryonic stem cells, bone marrow mesenchymal stem cells, and neural stem cells.[109-112] Recent searches for neural and glial (astrocytes and oligodendrocytes) progenitor and/or stem cells in the adult human spinal cord showed some cells, once cultured, are able to differentiate into the 3 cell types (neurons, astrocytes, and oligodendrocytes) and animal stem cell transplantation showed better locomotor recovery.[113] Transplantation of oligodendrocyte precursor cells (OPCs) has shown potential benefit for SCI, recently.[114] Oligodendrocyte precursor cells have also been isolated from the adult human brain and are able to be cultured to express the oligodendrocyte phenotype.[115] Isolated OPCs from the rat subependymal zone resemble neonatal OPCs and still retain the capacity to myelinate axons.[116] Oligodendrocyte precursor cells derived from the human subventricular zone are also capable of forming myelin in a demyelination lesion of the CNS and restoring conduction across the lesion site.[117] In a nonhuman primate study, transplantation of adult-derived precursors isolated from the subventricular zone into a demyelination lesion within the spinal cord showed the presence of axon remyelination within the lesion site 3 weeks postimplantation.[118]

Therapeutic Hypothermia

Therapeutic hypothermia has been a proven neuroprotective strategy in global ischemia after cardiac arrest[119,120] and is also showing therapeutic promise in the area of TSCI,[121-134] but the success rates in humans currently are under investigation.[135,136] Cellular mechanisms of hypothermic neuroprotection have not been fully elucidated. But evidence indicates these include reduction in the initial rate of ATP depletion,[137,138] alteration of gene expression and protein synthesis,[139,140] reduction in the release of excitotoxic neurotransmitter,[141] changes to intracellular messengers,[142] inhibition of inflammatory responses,[143] and a decrease in the excitatory postsynaptic potential slope in a temperature-dependent manner.[144]

Some recent focus on cooling in SCI has origins in ischemic and isolated trauma injury types that, while tangential to generalized trauma of the spine, may nonetheless be instructive to a broader range of traumatic cord damage treatments. For example, ischemia of the distal cord and cauda equina are feared complications of the blood supply interruption inevitable during abdominal aortic aneurysm repair and other procedures that require aortic clamping. Moderate hypothermia (32.0-34.0°C) increases the tolerable ischemic interval for such procedures as much as 2.5 times, with a reduction of temperature by 5°C in an animal model , and the effect is longer with lower temperatures in humans.[145,146] Local hypothermia, such as epidural cooling, has shown some success in ischemic cord injury models.[147,148]

Hypothermia as an acute treatment for traumatic spinal insult also received popular attention with the 2007 case of a US professional football player who experienced a C3/4 fracture dislocation during a game and reportedly suffered complete motor and sensory loss below the clavicles. The athlete was cooled during hospital transport with intravenous chilled saline, and ice packs, and subsequently was reported to have recovered upper and lower extremity motor function.[149] Questions arose, however, regarding the precise severity of the initial injury and hence the degree of actual recovery.[150] Contemporary study findings on the safety and efficacy of intravascular hypothermia for acute SCI have been encouraging.[151,152] Important factors in the therapeutic potential of hypothermia include cooling technique (surface or intravascular), rate, duration, and degree of temperature depression, and importantly, rewarming and its associated complications such as infection.[151] When hypothermia is applied clinically, some protection may be endowed to other organs besides the spinal cord, such as the brain and kidneys.[146,153-155]. Timing also is vital. Hypothermia begun during transfer to the hospital may prove critical to the outcome of paralysis.[156] Systemic hypothermia can be induced more easily, rapidly, and safely without obvious impairment of physiological parameters in small animals.[124-134,153-155,157]

However, a prospective randomized trial of hypothermia for acute SCI is yet to be undertaken.[135] And despite the heightened recent interest in temperature modulation for spinal function preservation and recovery, the Joint Section on Disorders of the Spine, of the American Association of Neurological Surgeons, and the Congress of Neurological Surgeons, published a statement in November 2007, concluding there is insufficient scientific evidence to support or oppose systemic or local hypothermia for traumatic spine injury.[158,159]

Summary

Until the science of neural repair and regeneration advances, severe SCI invariably will be thought of as a chronic illness. However, the importance of vigilance in the acute, critical care phase, of treatment after cord damage is abundantly apparent in reports on the condition in recent years. Immobilization and airway and cardiovascular management are primary acute considerations. But important secondary neural injuries and systemic complications such as respiratory and UTIs are crucial outcomes for these patients and can be avoided with prompt attention in the intensive care setting.

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