

Management of spinal cord injury: Issues of debate

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Abstract: Spinal cord injury is (SCI) a catastrophic event and one of the most common causes of severe disability and death following trauma. Successful outcome from a traumatic spinal cord injury (SCI) depends heavily upon the quality of the acute care rendered to the affected individual. In recent years, there have been significant advances in the acute management of SCI. Although life expectancy has improved greatly in patients with SCI, there is still further room for improvement. Almost every aspect of the management of SCI is controversial, due in part to a lack of good-quality evidence. The current management strategies in the areas of prehospital care and transport, emergency room management, surgical considerations and pharmacotherapy are discussed.

Keywords: trauma, spinal cord injury, intensive care

INTRODUCTION

The incidence of traumatic SCI is significant. The consequences of a spinal cord injury are often devastating, and any possibility of mitigating neurologic loss is attractive. Mechanical injury to the spinal cord initiates a cascade of secondary events that include ischemia, inflammation and calcium-mediated cell injury.

As SCI is a relatively uncommon condition and has specific medical complications, most healthcare professionals are unlikely to develop expertise in managing these patients. Physicians who conduct the initial triage and resuscitation of patients with acute spinal cord injury should consult their specialist colleagues who will be continuing the care of these patients regarding their preferences for management in view of the wide range of debatable issues. Specialized SCI centers are required so as to provide medical care during the acute phase and offer lifelong follow-up, support and advice for patients, care givers and other health professionals.

In spinal cord injuries surgery should be performed for biomechanical reasons, i.e., to correct deformity and/or to stabilize an unstable injury. Surgery for unstable injuries allows early mobilization and earlier discharge. Patients with no neurological deficit can be discharged about 6 days after surgery, whereas they require several weeks of immobility if managed conservatively. For patients with a neurological deficit, there is no conclusive

evidence to show that this deficit is improved by surgery. However, animal studies show that early decompression improves neurological outcome and suggest a window of opportunity in the first 4-6 hours. In the clinical setting, this is often not practical; therefore, surgery is performed at the earliest safe opportunity. Regarding the case for conservative management in SCI, it is agreed to that, surgery should be performed on those individuals with spinal column damage but without SCI in order to facilitate early discharge. Though only 10-15% of patients with SCI require surgery, reiteration of the lack of compelling evidence that surgical intervention results in superior neurological outcome is to be established. The biomechanical instability of the spinal column can be equally well maintained by conservative measures, such as 4-6 weeks' bedrest followed by 4-6 weeks' mobilization in a brace.

Surgery may cause hypoxia, hypotension and hypothermia, which could lead to further neurological damage. Surgery also entails additional risks such as infection and bleeding.

There is evidence to show that the majority of patients with clinically incomplete SCI managed conservatively will make a significant recovery, with 47-80% regaining the ability to walk, depending on the level and density of the lesion¹. There is no such evidence for long-term outcome after surgical management.

Medical therapy: Acute spinal cord injury

The hope that administration of a pharmacological agent delivered shortly after acute spinal cord injury (ASCI) might improve neurological function and/or assist neurological recovery has long been held. A variety of

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promising substances have been tested in animal models of ASCI, but few have had potential application to human spinal cord injury (SCI) patients. Four pharmacological substances have met rigorous criteria in laboratory testing and initial human investigations: two corticosteroids (methylprednisolone and tirlazad mesylate), naloxone, and GM-1 ganglioside. All four pharmacological agents have been evaluated in controlled, randomized, blinded clinical trials of human patients with ASCIs. Two of these substances, tirlazad and naloxone, have been studied less extensively and as yet have unclear efficacy in the management of acute human SCI. The purpose of this medical evidence based review is to define the usefulness of administration of methylprednisolone with or without GM-1 ganglioside in the contemporary management of ASCI patients.

THE ROLE OF STEROIDS

Some patients with acute SCI are treated with high-dose steroids in the hope that this will result in better neurological outcome. This practice was recommended by National Acute Spinal Cord Injury Studies (NASCIS) 2 and 3 and a Cochrane review performed by the lead investigator of these trials, clinical efficacy is based only on the results of a small subgroup of patients in NASCIS 2, who received methylprednisolone within 8 hours of injury. Concerns regarding the quality of these data have been raised.

The Corticosteroid Randomization after Significant Head Injury (CRASH) trial showed that high-dose methylprednisolone in the context of acute trauma resulted in a significant increase in mortality. Dr Short concluded that there was insufficient evidence to support the use of high-dose steroids in acute traumatic SCI and, indeed, that there was evidence that it may do harm.

In summary, the available medical evidence does not support a significant clinical benefit from the administration of methylprednisolone in the treatment of patients after ASCI for either 24 or 48 hours duration. Three North American, multicenter randomized clinical trials have been completed and several other studies have been accomplished addressing this issue^{2,3,4}. The neurological recovery benefit of methylprednisolone when administered within 8 hours of ASCI has been suggested but not convincingly proven. The administration of methylprednisolone for 24 hours has been associated with a significant increase in severe medical complications. This is even more striking for

methylprednisolone administered for 48 hours. In light of the failure of clinical trials to convincingly demonstrate a significant clinic benefit of administration of methylprednisolone, in conjunction with the increased risks of medical complications associated with its use, methylprednisolone in the treatment of acute human SCI is recommended as an option that should only be undertaken with the knowledge that the evidence suggesting harmful side effects is more consistent than the suggestion of clinical benefit^{5,6,7,8}.

ROLE OF GM-1 GANGLIOSIDE

GM-1 ganglioside has been evaluated in both animal and human studies of ASCI⁹. The available medical evidence does not support a significant clinical benefit from the administration of GM-1 ganglioside in the treatment of patients after ASCI. Two North The neurological recovery benefit of GM-1 ganglioside when administered for 56 days after the administration of methylprednisolone within 8 hours of ASCI has been suggested but not convincingly proven. At present, GM-1 ganglioside (a 300-mg loading dose and then 100 mg/d for 56 d), when initiated after the administration of methylprednisolone given within 8 hours of injury (NASCIS II protocol), is recommended as an option in the treatment of adult patients with ASCI.

These therapies – steroids and GM-1 ganglioside hence seem to be not a standard treatment nor a guideline for treatment but, rather a treatment option, for which there is very weak level II and III evidence as per the available literature¹⁰.

SCI: Repair by transplantation of olfactory ensheathing cells:

Loss of function after SCI is due almost entirely to damage to long-fibre pathways travelling between the brain and the spinal cord. When nerve fibers are cut they try to regenerate, but they require a glial pathway along which to grow. Transplantation of olfactory ensheathing cells (OECs) provides the fibers with such a pathway. These glial cells make up the pathway along which the olfactory nerve fibbers travel through the skull floor and into the olfactory bulbs. When transplanted autologously 2 months after complete unilateral lesions of the upper cervical corticospinal tract in adult rats, these cells encourage the growth of the cut nerve fibres, suppress excessive neuromatous branching and act as a bridge between the cut ends of the tract. In the same way that OECs allow olfactory nerve fibres to enter the

olfactory bulb, these cells, when transplanted, allow the regenerating nerve fibres to re-enter the spinal cord and to continue along the corticospinal tract. This results in restoration of climbing and respiratory function in the animals.

This method also has the potential to treat damage to spinal roots, auditory and optic nerves, and forms of stroke where loss of function is due principally to nerve fibre damage. Human trials in this area of study being done will show results the near future¹¹.

Autonomic dysreflexia

Autonomic dysreflexia (AD) occurs in people with a SCI at or above T6 and results in hypertension, bradycardia and varied symptoms such as profuse sweating and headache. It can be triggered by stimuli to the viscera (eg urinary system, uterus), skeletal muscle (eg spasms) and skin (eg pressure ulcers) and by other miscellaneous stimuli, including bone fractures and surgery. With such a variety of causes, it may present to any health professional.

The exact mechanism of AD is unclear, but it is likely to involve multiple factors, including changes in the spinal reflex arc, lack of supraspinal control and increased responsiveness of organs to catecholamines after SCI. The observation that this response is not seen in people with SCI below T6 may be related to the large sympathetic outflow at T5/6. AD is an important condition. Missing it can be devastating, as it can result in arrhythmias, myocardial failure, seizures, visual deficits, cerebral infarcts and hemorrhages and, potentially, death. The hypertension related to AD may contribute to the high rates of cardiovascular and cerebrovascular deaths seen in people with SCI.

The crucial component in treatment of AD is its recognition by patients and health professionals. Once recognized, a cause should be sought and rectified. This is most commonly related to the urinary tract, eg a blocked catheter. Drugs can be used if required, such as lidocaine to block the afferent signal, spinal anaesthetics, particularly during labour or surgery, or antihypertensive agents such as sublingual nifedipine or glyceryl trinitrate (GTN). Patients should be aware of the potential for medication to cause marked hypotension.

Most physicians are probably aware of AD, but some cases may be missed. As AD is a potentially fatal condition that can present to any specialty, it is important

that patients and all health professionals, including nurses, therapists and complementary medical practitioners, are aware of it. Thorough clinical assessment on a daily basis will help in identifying this complication and institution of optimal measures to counter the effects will aid in a positive outcome¹¹.

LIFE EXPECTANCY IN SCI

Life expectancy after SCI has improved greatly in recent decades. This increase is due mainly to improvements in initial and first-year survival, with less improvement in long-term survival. For patients living more than 18 months, predicted life expectancy is 70% of that of the background population in people with complete tetraplegia and 84% in those with complete paraplegia¹².

Five years after SCI, the mortality rates from septicemia, pneumonia, pulmonary embolus and heart disease are, respectively over 40, 13, eight and three times those of the background population¹³. Urinary problems, which previously were the leading cause of death in people with SCI, are now declining, but there is still a nine fold excess mortality. Worryingly, the incidence of suicide is twice as common in people with SCI compared with the general population and is increasing. All the major causes of death after longstanding SCI are, to some extent, preventable.

We should be aiming for life expectancy in people with SCI to approach that of the general population. This requires long-term review of individuals with ongoing therapy, medical and nursing support. Professionals should be trained to be aware of potential physical and psychological problems in order that these may be treated early. Economic factors also need to be addressed, as people with low incomes are nearly five times more likely to die than their better-off peers with SCI¹⁴.

ISSUE OF RENAL FAILURE AND BLADDER MANAGEMENT

Renal failure used to be the leading cause of death (22.4%) in those individuals with SCI who survived the first 12 months. In half of these deaths, amyloidosis was involved. This was attributed to chronic septic pressure ulcers with underlying osteomyelitis. Recently, deaths due to renal failure have more than halved (9.3%)⁵. This reduction is likely to be due to a combination of factors: improved early management in specialized SCI centers in order to avoid formation of pressure ulcers and amyloidosis. Increased use of antibiotics and better

catheters improved long-term bladder management, usually provided in the same SCI centre regular renal surveillance¹⁵.

Various methods of bladder management are used in different centres. All aim to minimize infections and high bladder pressures. Surveillance methods vary, but all aim to detect and treat problems early, before the development of renal failure. Optimal surveillance methods and frequency have yet to be established. With improved patient education, easy access to a SCI centre and appropriate surveillance, it may be possible to reduce renal failure further.

PRESSURE ULCERS

Pressure ulcers are considered by some as a side effect of healthcare or specific conditions, but they are rarely inevitable. Most pressure ulcers are due to a deterioration in the individual's condition or to a situation change such as the use of an inappropriate mattress. Patients and their care providers may not be aware that they are at increased risk in these circumstances. A pressure ulcer may be inevitable or excusable in the following circumstances: a patient who is terminally ill and is distressed by preventive measures unavoidable events during initial medical stabilization sudden deterioration within the community before help is called a severely emaciated or obese patient the patient's beliefs and behaviours, precluding implementation of a prevention programme¹¹.

When a pressure ulcer is detected, the cause should be sought and rectified and provision made for prevention of ulcers in the future. Care providers should identify patients at risk, and preventive guidelines, including patient education, should be followed and audited.

Pressure ulcers generally are preventable. There are occasions when they are excusable because of overriding priorities. The development of a pressure ulcer may justify a legal claim of 'failure of care' if deemed avoidable. All SCI centres should already have preventive measures instituted and should audit these regularly in order to minimize pressure ulcer formation.

CONCLUSION

Individuals with SCI have specific medical needs, both acute and long-term. Although life expectancy has improved greatly in patients with SCI, there is still further room for improvement. Almost every aspect of the

management of SCI is controversial¹⁶, due in part to a lack of good-quality evidence. Further research is ongoing and, together with increased awareness and education of patients, carers and professionals, will enable us to improve life expectancy still further.

Gene Therapy: We are at the dawn of a new age in spinal cord injury therapies. Techniques are now available to modify genetic responses of the spinal cord, to promote repair and regrowth of the spinal cord. Scientists can now introduce any gene to the spinal cord and control the expression of the genes. Powerful tools are available to manipulate and create genetically modified cells for transplantation to the spinal cord. Cell transplants have been shown to promote survival and growth of cells in the cord. Recent experience with implanting neural stem cells into the spinal cord suggests that we will be able to do cell replacement and gene therapy at the same time.

It is clear that the ultimate outcome for an individual suffering a SCI is largely determined by the quality of the acute treatment provided. Careful management at the injury scene, efficient transport to the hospital, and skilled, experienced personnel with appropriate knowledge of surgical and pharmacological treatment give the injured person the best chance to make a meaningful neurological and functional recovery, while limiting the acute medical complications.

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