Review Article

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Evaluation of Surgical Intervention in Acute Spinal Cord Injured Patients – A Review

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Abstract : Spinal Cord Injury is a devastating form of Neurotrauma known to mankind since antiquity. It strikes mostly the young, and leads to lifelong disability. The pathology, besides the mechanical disruption of neural tissue, involves complex biological events which are gradually unfolding and being recognised clinically and in the laboratory. Surgical stabilisation is important for early rehabilitation. The role of methyleprednisolone in acute spinal cord injury is still not convincing.

Keywords: methyleprednisolone, spinal cord injury

Introduction

Acute spinal cord injury is an important cause of mortality and morbidity. The prognosis for the patient remains grim with staggering financial and social costs[1,2,3]. Secondary changes start soon after primary injury (within hours) which further aggrevates the delicate functioning balance of neural tissue by causing secondary damage. Animal experiments have given convincing evidence that duration of neurological compression after SCI is extremely important, longer period of compression being associated with poor prognosis.

The main causes of acute SCI include motor vehicle collisions, sports and recreational activities, work-related accidents, falls, and violence[51,68], Despite modest clinical benefits with methylprednisolone (MP), the prognosis for a patient with a severe SCI remains grim[1,4,5].

The Biology of Acute SCI

The biology of acute SCI involves both primary and secondary injury mechanisms.[3,6,7,8,9]

Most traumatic cord injuries occur as a result of rapid cord compression because of a fracture-dislocation or burst fracture[10]. Acute spinal cord distraction, acceleration-deceleration with shearing, and transection from penetrating injuries are additional mechanisms of trauma.[11, 12] There is strong evidence[1,3,13] that the primary initial injury initiates a series of events that include the following:

1) ischaemia, impaired autoregulation, neurogenic shock, hemorrhage, microcirculatory disruption, vasospasm, and thrombosis[1, 3, 8].
2) ionic derangements, including increased intracellular calcium and sodium, and increased extra cellular potassium[1,6,7].
3) accumulation of neurotransmitters, including serotonin, catecholamines, and extra cellular glutamate, which contribute to cellular injury;
4) arachidonic acid release, free radical and eicosanoid production, and lipid peroxidation[1];
5) endogenous opioids;
6) edema;
7) inflammation;
8) loss of adenosine triphosphate-dependent cellular processes; and
9) apoptosis[1,14,15.] The development of these secondary injury events, which lead to tissue destruction during the first few hours after injury, is of relevance to the surgical and non-surgical treatment of SCI.

NASCIS II study has reported a modest beneficial effect of high-dose MP if given within 8 hours of injury in patients with complete and incomplete spinal cord injuries[4,5,16] which emphasizes the importance of the timing of intervention. Moreover, the NASCIS III study provided suggestive evidence that treatment within 3 hours may be better than treatment initiated 3-8 hours after trauma[5,17].

METHYL PREDNISOLONE SODIUM SUCCINATE-MPSS

It prevents post traumatic lipid peroxidation, prevents destruction of neuronal and microvascular membranes and improves neurological function.

Patients initiated on treatment within 3 hours of injury need 24 hours administration and patients initiated

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between 3 and 8 hours need 48 hours administration. Dosage is in bolus and maintenance[4,5,16,17].

Bolus: 30-mg/Kg-body weight to be given in 30 ml of water over 15 minutes.

Maintenance: 5.4 mg./Kg/hour for 23 to 48 hours. Total dose of methylprednisolone is to be mixed in 100 ml of water and given at the rate of 5 ml per hour. There is no apparent beneficial effect if given after 8 hours, and the practice of prescribing the drug in dosages like 500 mg twice a day or eight hourly has nothing to commend it. In other conditions when MP is to be administered it has to be in doses of 30mg/Kg body weight given by IV infusion over a period of 30 minutes, which can be repeated 6 or 8 hourly if required.Use of MP for the treatment of acute SCI since NASCIS II was published in 1992 has been considered a standard of care in the US, although the Food and Drug administration has not granted an "Indication of use" to this drug for treating SCI.The period used to relate a complication to MP is six weeks. Immunosuppression lasting 12 to 14 days has been reported. Although the National Acute Spinal Cord Injury Studies (NASCIS II and NASCIS III)[4,5,16] have shown modest improvements in recovery of patients with SCI with high dose steroids, this therapy has only a modest functional impact in these patients. NASCIS II has to found 5.1% improvement in motor score in 45.9% of patients. It is generally believed that the rate of complications is not high enough to withhold the use of MP in SCI[18]. MP is safe and reviews have not provided any support to the notion that high dose MP increases risk for mortality or major morbidity. Complication of therapy with MP include non-healing or delayed healing of wound, wound infection, GI bleeding, wound complications, pulmonary complications(pneumonia), avascular necrosis of femoral head, decubitus ulcer, urine infection, deep vein thrombosis, pulmonary embolism, hyperglycaemia and sudden death.

MANAGEMENT OF SCI

The management of acute spinal cord injury has traditionally concentrated on preventative measures as well as, for the better part of the previous century, conservative care. Pharmacologic interventions, in particular intravenous methylprednisolone therapy, have shown modest improvements in clinical trials and are still undergoing evaluation. More recent interest has focused on the role of surgical reduction and decompression, particularly "early" surgery. A review of the current evidence available in the literature suggests that there is no standard of care regarding the role and timing of surgical decompression. But there is sufficient data to support overall treatment standards or guidelines for this topic. Class III evidence suggests the need for urgent decompression in incomplete spinal cord injury with neurologically deteriorating patient. It has now been observed that early surgery (less than 24 hours) does not increase the complication rate.

The Role and Timing of Decompression in Acute Spinal Cord Injury

It is feared that early surgery increases the rate of complications. Many patients with SCI are critically ill because of cardiorespiratory compromise. Many surgeons have argued against early intervention in these patients. Modern surgical techniques have advanced considerably over the past two decades and surgery has become safe and efficacious and has shown no difference in complication rates between early operative and non-operative groups [29,30]. It has also been shown that those patients operated within 24 hours had a lower rate of complications than those undergoing surgery later[31].

Exclusive policy of non-surgical treatment can lead to high complication rate. It is now proved that in the best of hands neurological worsening can occur in 10% of patients with incomplete injury to spinal cord with non-operative treatment[13].

The clinical uncertainty in the role and timing of surgery is reflected by the wide variations in the practice pattern. A recent retrospective, multicentre study of SCI management in 585 patients in North America undertaken by Charles Tator and his colleagues[32]; in this study, 23.5% of patients underwent surgery within 24 hours whereas more than 40% were managed by delayed surgery after more than 5 days. In a series of comparison of operative versus conservative management it was observed that operative management was associated with overall lower mortality rate of 6.1% as against 15.2% in conservatively treated group. Despite higher rate of thromboembolic complications in surgical group. NASCIS II database has shown that (class II evidence) patients undergoing surgery in less than 25 hours had improved outcomes as compared to non-operative patients. The results of surgery, however, were similar between less than 25 hours and delayed more than 200 hours. According to Chen et al[33] surgical patients improved within 2 days, showed faster recovery of neurological function, better long-term neurological outcome, shorter hospital stay, fewer complications and better rehabilitation. Early decompression may enhance neurological recovery in selected patients. (Class III

evidence). Aebi et al[34] reviewed retrospectively 100 patients for timing of reduction of dislocation (manual or surgical) performed within the first 6 hours in 25% of cases and within 24 hours in 57% of cases. They observed that overall 31% recovered, and 57% of recovered patients were those reduced within 6 hours. But it is difficult to determine a time window for effective application of decompression. Secondary injury caused by ischemia, free radial mediated lipid peroxidation and calcium-mediated cytotoxicity suggest early intervention within hours after injury. To obtain a neuroprotective effect for surgical decompression there is Class II and III evidence that either early (less than 25 hours) or delayed (more than 200 hours) surgical intervention is safe and equally effective[7,9,35,36].

Tables 2-3 summarize the clinical studies (prospective and retrospective) that have examined the role of decompression in the treatment of SCI. The clinical uncertainty in the role and timing of surgical intervention in acute SCI is reflected by the wide variations in practice patterns.

Experimental Studies of Decompression in Acute SCI in Animal Models

There is compelling evidence from laboratory studies in animal models that persistent compression of the spinal cord is a potentially reversible form of secondary injury. The severity of SCI in animal models is related to the force of compression, duration of compression, displacement, impulse, and kinetic energy[8,14,40,41]. Numerous experimental studies of decompression after SCI have been performed in various animal models. These studies have a wide range of species, including models in primates, dogs, cats, and rodents, and have consistently shown that neurologic recovery is enhanced by early decompression.

A number of authors have advocated early operative internvention in patients with acute SCI. For example, Aebi et al[34] Wiberg and Hauge[15] Hadley et al[42] and Wolf et al[43] recommended early reduction (4-10 hours) and operative fixation of spinal fractures associated with SCI. Some evidence is presented in these studies, which suggests that early decompression may enhance neurologic recovery in selected patients with SCI. Thus, the benefits of surgical intervention need to be weighed against the spontaneous recovery that may occur in nonoperatively managed patients with acute SCI[13, 20].

Both anterior and posterior cervical fusion procedures are successful in achieving spinal stability for most patients with subaxial cervical spinal injuries. Indications

Table 1. Surgical Decompression in Acute SCI: Retrospective Case Series (Class III)

Authors, Year (reference)	No. of Patients (level)	Timing of Intervention	Conclusions
Maynard et al 1979[11]	123 (cervical): 51 early 10 late	Early <4 wk	Surgery within 4 wk not associated with improved neurologic recovery
Benzel and	99 (cervical) Larson 1986[35]	17-52 days	Surgery improves neurologic function in incomplete SCI; no relationship between time to decomp and neuro recovery
Weinshel et al 1990[39]	90 (cervical)	6hr-60 days (ave 13	Decompression improves Days neurologic recovery in motor Complete cervical SCI
Tator et at 1999[32]	585 (all levels)	23.5% of cases underwent surgery in less than 24 hours	65% of patients in North America with SCI undergo surgery; no consensus as to timing of intervention.

Table 2. Retrospective (Class III) clinical Studies of Closed Reduction on Neurologic Recovery After Acute Cervical SCI

Authors, Year (reference)	No. of Patients	Treatment	Outcome
Burke and Berryman 1971[49]	76	Closed reduction under anesthesia 50%	Early reduction improved neurologic neurologic outcome in incomplete SCI
Sonntag 1980[12]	15	Closed reduction in 11; open in 4	Transient root palsy in one; root recovery in two cases
Aebi et al 1986[34]	100 cervical	Retrospective non-randomised	25%<6 hours 57%<24 hours 31%recovery.
Lee et al 1994[45]	210	Rapid traction up to 150 Ibs	Rapid realignment improves neurologic outcome

for surgical treatment offered in the literature include failure to achieve anatomic injury reduction (irreducible injury), persistent instability with failure to maintain reduction, ligamentous injury with facet instability, spinal kyphotic deformity more than 15 degrees, vertebral body fracture compression of 40% or more, vertebral subluxation of 20% or more, and irreducible spinal cord compression. Anterior fusion without plate fixation is associated with an increased likelihood of graft

displacement and the development of late kyphosis, particularly in patients with distractive flexion injuries. Similarly, late displacement with kyphotic angulation is more common in patients treated for facet dislocation injuries with posterior fusion and wiring compared with those treated with posterior fusion and lateral mass plate or rod or interlaminar clamp fixation.

The Effect of Reduction of Dislocation on the Neurological Recovery in Acute SCI

The clinical benefits of early reduction of fracture dislocations of the spine by closed techniques or open surgery are difficult to assess in the absence of Class I data (Table 5)[12,34,44,45]. Reports of significant neurologic improvement in some cervical cases decompressed early by traction are encouraging but do not provide convincing, clinical evidence to support standards or overall guidelines[46]. Moreover, a number of studies have not found any neurologic benefit by reduction[25,47] with the possible exception of patients with bilateral facet dislocation[48].

Despite the potential appeal of aggressive, closed reduction of locked cervical facets, one multicenter, cross-sectional study in 585 cases documented an 8.1% rate of neurologic deterioration with attempts at closed reduction[32]. This data is sobering and emphasize the difficulty in interpreting accounts of the beneficial effects of rapid closed reduction by traction in the absence of Class I data.

Aebi et al[34] undertook a retrospective review of 100 patients with cervical spine injuries and attempted to find an association between neurologic recovery and the timing of fracture reduction by closed or open techniques. A manual or surgical reduction was performed within the first 6 hours after the accident in only 25% of the cases, and within the first 24 hours in 57%. Overall, 31% of the 100 patients recovered, and 75% of the recoveries were in patients reduced within the first 6 hours (Table 5). Bilateral facet dislocation should be urgently reduced surgically of manually[34].

Acute Central Cervical Spinal Cord Injuries

Central spinal cord injuries are among the most common, well-recognized spinal cord injury patterns in acute trauma patients. Originally described by Schneider et al[50] in 1954, this pattern of neurologically incomplete spinal cord injury is characterized by disproportionately more motor impairment of the upper than of the lower extremities, bladder dysfunction and varying degrees of sensory loss below the level of the lesion[50]. It has been associated with hyperextension injuries of the cervical spine. The natural history of acute central cervical spinal cord injuries indicates gradual recovery of neurological function for most patients, albeit usually incomplete and related to the severity of the original injury and the age of the patient[50,51,52,53,54]. The role of surgery and its timing for patients with acute central spinal cord injuries are the subjects of considerable debate[51,55,56,57]. The optimal management of patients who have sustained acute central cervical spinal cord injuries is the subject of this review.

In 1951, Schneider[50] described two patients with acute neurologically incomplete cervical spinal cord injuries for whom he suggested that early operation was indicated. Both patients had anterior spinal cord compression from acute traumatic cervical disc herniations. Both patients made incomplete but significant neurological recoveries after delayed surgical decompression via laminectomy, dentate ligament sectioning and transdural discectomy.

Schneider later reported experience in the management of 20 patients with acute central cervical cord injuries[51]. Of the 20 patients, 17 were managed medically: 2 patients died without improvement, 14 patients improved but had profound residual deficits, and 1 patient regained normal function. Three patients were treated with surgical decompression. The patient with early decompression improved dramatically. They reported that central cord edema, venous congestion, and ischemia were components of the pathophysiology of this unique injury.

In 1971, Bosch et al[58] described observations made during their management of 42 patients with subacute central cervical spinal cord injuries treated at a rehabilitation hospital. The authors concluded that at least some return of neurological function in the immediate post-injury period could be expected in about 75% of cases, with 6% of patients regaining function in hands. In their long term follow-up, only 59% of these patients with central cervical spinal cord injuries retained functional skills with conventional medical management.

Contemporary reviews confirm earlier reports that most patients with incomplete cervical spinal cord injuries meeting the clinical neurological criteria of acute central spinal cord injury will show neurological improvement over a period of time[50,51,52,54,58]. Some patients with these injuries will die, and many will remain profoundly impaired at late follow-up. These patients in general are older, have spinal cord injuries without bony vertebral injury, and have medical problems, or they are younger but have fracture-dislocation injuries

as a cause of their neurological deficits. A large portion of patients will regain walking skills over time but will not have useful hands[58].

The conclusion of Schneider et al[51] was that central cord edema, venous congestion, and ischemia were important components of the pathophysiology of these injuries. When combined with the hypothesis of Turnbull et al[59] that vascular compression and distortion attributable to antero posterior flattening of the cord plays a major role, there is a case for decompression of the injured cord. Ischemia of the cord, caused by either the primary injury or secondary events, might be improved with augmentation of spinal cord perfusion.

Role Of Late (> 4 Weeks) Decompression On Neurological Recovery.

In 1980, Brodkey et al[56] reviewed the management of the acute central cervical spinal cord injury syndrome. They provided operative treatment to seven patients with traumatic central cervical spinal cord injuries within 18 to 45 days after acute injury who had profound residual neurological deficits with conservative medical treatment. Myelography revealed significant defects in all of these patients. Four patients underwent anterior cervical discectomy with fusion (ACDF), one was treated with multilevel laminectomy, one had multilevel ACDF, and one received multilevel laminectomy and then delayed (4 yr) multilevel ACDF. All patients had an accelerated neurological recovery after the surgical procedure. Late surgery, thus, play an important role in the pathophysiology of central cord syndrome with improvements in surgery is carried out even several years after injury.

DISCUSSION ON MP

Since findings of the NASCIS II were published more than a decade ago[17], use of MP for the treatment of acute SCI has been considered a standard of care in the United States (and some other countries)[4,5,7,10,16,17,62] despite the fact that the Food and Drug Administration has not granted an "indication of use" to this drug for treating SCI[18]. In a number of recent reports and letters authors have questioned the safety and efficacy of MP in the treatment of acute SCI [27,64,65].

Methylprednisolone and related glucocorticoid agents have a host of physiological actions, but many believe that, with respect to acute neurotrauma, they are most valuable as anti-inflammatory agents[66,67,68,69,70,71]. This property of glucocorticoids has long been recognized by neurosurgeons. Steroids were widely used for treating injury to the spinal cord prior to publication of the NASCIS II findings[72,73]. There is also an extensive body of literature in which authors have reported on the successful use of steroids for minimizing postsurgical pain following lumbar discectomy[69,70,71] although positive effects have not been shown in all such studies. Patients who awaken after spine surgery with evident deterioration of central nervous system function are also often treated with high-dose of steroids[70, 74].

Controversy

Controversy surrounds use of the drug MP as a neuro-protective agent after SCI. On the one hand, there is evidence derived from animal spinal cord lesion studies demonstrating MP-associated benefit with respect to tissue preservation or regeneration[6,35,75]. In contrast, the NASCIS II and III trials have been criticized extensively for issues related to study design, data management and the manner in which data were published.[76,77] Moreover, NASCIS III suffered from an error in randomization that led to a large difference between groups in the numbers of patients with intact motor function. Some of these criticisms have been addressed[78,79], yet debate continues over the known risks in comparison with benefits of this treatment regimen after human SCI.

Complications

The 6-week time period over which complications were tallied was chosen to be consistent with other studies. This follow-up duration is identical to that reported in the NASCIS II and III trials[80]. Gerndt el al[72] have stated that MP-related complications "would be most apparent within the first few weeks of administration." In a prospective trial, Matsumoto, et al[82] followed patients with steroid-related complications for 2 months after administration of MP. Based on detailed analysis of blood samples, Galandiuk et al[83] reported evidence of immunosuppression for 12 to 14 days following steroid therapy in patients with acute SCI. Longer periods of follow-up might falsely implicate steroid use as a contributor to complications that more likely risks associated with prolonged immobility and repeated catheterization[84].

In light of these weaknesses, the aim is simply to provoke spinal surgeons into considering the fact that prophylactic delivery of MP during surgery should be avoided[84] in individuals with recent SCI who have already received MP at the time of their initial hospitalization.

CONCLUSIONS

Methyl Prednisolone

Methyl Prednisolone in acute spinal cord injury is not aimed at preventing secondary spinal cord damage. It is safe to be administered in prescribed dosage without increasing morbidity or mortality.

Role of Surgery

1. When there is an indication surgery should be performed as overall mortality in conservative group is 15.2% as against 6.1% in operative group.
2. There is no statistically significant difference between early and late surgery.
3. Dislocation should be reduced early.
4. There is a place for surgical decompression and stabilization in acute central cervical spine cord injury.
5. Late surgery has played an important role in improving the neurological function in most patients.

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