In Spinal Cord Compromised Patient - “Why I use Steroids”
By Michael Gerling, MD
(No Relevant Disclosures)

Methylprednisolone Sodium Succinate (MPSS) - Why I Use it?

Spinal Cord Injury (SCI) - Multi-Stage Cascade of injury:

1) Primary Lesion- Injury with direct damage to Axonal pathways and other supporting structures

2) Secondary Lesion- Inflammatory phase with massive influx of peripheral inflammatory cells (macrophages, T-cells) and activation of resident microglia. This results in further ischemia, edema, hemorrhage and cytotoxicity, leading to the formation of glial scar tissue surrounding a central cavitation on the site of the initial trauma in the spinal cord. The latter is known to act as an important physical and chemical barrier for endogenous regeneration of ascending and descending nerve tracts.

3) After SCI- The Functional outcome is impacted by the inflammatory phase…. Hence, MPSS!

Recommended Dosing:

If administered within 3 hours of injury...

- Bolus 30mg/kg over 15 minutes,
- Maintenance infusion of 5.4 mg/kg per hour infused for 23 hours.

If administered between 3 and 8 hours after injury…

- Continue maintenance up to 48 hours
Meta-analysis

Cochrane

**Bracken MB**. Steroids for acute spinal cord injury. *Cochrane Database Syst Rev.* 2012 Jan 18;1


- Eight trials / 7 using MPSS
  - MPSS improves neurologic outcome up to one year
  - Post-injury North American trial results were replicated in a Japanese trial but not in the one from France.
- Meta-analysis of RCT trials:
  - significant recovery in motor function after methylprednisolone therapy, when administration commenced within eight hours of injury.
  - if methylprednisolone therapy is given for an additional 24 hours (a total of 48 hours), additional improvement in motor neurologic function and functional status are observed. This is particularly observed if treatment cannot be started until between three to eight hours after injury.
  - The risk of bias was low in the largest methylprednisolone trials.
  - Overall, there was no evidence of significantly increased complications or mortality from the 23 or 48 hour therapy.


- Recommendations were based on one Cochrane systematic review, six Level I clinical studies and seven Level II clinical studies that addressed changes in neurological function and complications following methylprednisolone therapy
- 23 hours, is only a treatment option for which there is weak clinical evidence (Level I to II-1)
- There is insufficient evidence to support extending methylprednisolone infusion beyond 23 hours if chosen as a treatment option.
Trials

National Acute Spinal Cord Injury Study (NASCIS)

NASCIS I
- Prospective Trial of MPSS
- No Control group
- Low MPSS dosing


NASCIS II
- Investigators evaluated several standard neurological parameters but not functional activity


NASCIS III
- Both neurological and functional recovery were assessed in NASCIS III, a trial that followed an almost identical protocol to NASCIS


- Modeling Functional Outcomes: The Functional Independence Measure (FIM) uses functional improvement in the NASCIS/American Spinal Cord Injury Association motor scores that were documented in NASCIS III 1 year after SCI. The models are also applied to the extent of motor recovery demonstrated in NASCIS II.
- Motor function and FIM is strongly nonlinear and dependent on initial level of injury and degree of injury severity. Thus, estimates are provided overall and for patients with complete and incomplete neurological loss at time of injury.
- Overall improvements attributed to MPSS: 18.6% of patients would improve six or more FIM points and 9% nine or more points, respectively.
  - Complete SCI: the mean motor improvement of 3.6 predicted that 63.9% of the patients would improve three or more FIM points and 12.1% six or more points to a maximum of eight points.
  - Incomplete SCI: a 7.3 mean improvement in motor function predicted that 27.4% would gain six or more FIM points and that 21% would gain nine or more points to a maximum of 15 points.
- “Analysis of the current best evidence from SCI and other randomized surgical trials in which high-dose MP has been administered provides no grounds for concern about commonly studied adverse effects.”


- Retrospective Review 70 patients
  - with incomplete paralysis at admission, the ASIA motor scores in the MPSS group were improved more significantly than those in the non-MPSS group at 6 weeks and 6 months after injury.
  - with complete paralysis at admission, the patients in the MPSS group did not show significantly change in motor score
  - The MPSS group had 10 patients with early complications, while the non-MPSS group had 14. The differences between the 2 groups showed no statistical significance.


- Non-randomized, Prospective Trial
  - 38 patients
  - No difference in ASIA improvements
  - Complications MPSS group significantly higher: 19 patients developed pneumonia, 13 developed urinary tract infections, and 5 developed wound infections.

- 32 SCI patients at Level 1 Trauma Center
- 14 w MPSS
- Pneumonia rates statistically similar but longer hosp and higher cost after MPSS

Surveys and Popular Opinion


- German Practice; 372 Practicing Orthopedic and Neurosurgeons
- 55% of departments that treat SCI prescribe MPSS.
- 73% are "frequent" users


- South Carolina Administrative Database; 1,227 randomly selected patients with SCI
- 48.7% Use of High dose Steroids
- trauma centers and emergency departments were more likely to use MPSS
SCI Patient Opinion Survey


- 77 out of 384 SCI patients
- Given summary of literature on MPSS use in SCI
- Literature summarized and reviewed by 28 SCI expert multispecialty panel
- 59.4% felt that the small neurological benefits with MPSS were ‘very important’ (p<0.0001).
- Patients had ‘little concern’ for potential side-effects of MPSS (p = 0.001)
- Only 1.4% felt that MPSS should not be given to SCI patients regardless of degree of injury (p<0.0001)

CONCLUSIONS:

MPSS therapy is the only pharmacologic therapy shown to have efficacy in a phase three randomized trial when administered within eight hours of injury.

There is an urgent need for more randomized trials of pharmacologic therapy for acute spinal cord injury.