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Does High Dose Methylprednisolone Sodium Succinate Really Improve Neurological Status in Patient With Acute Cervical Cord Injury?

A Prospective Study About Neurological Recovery and Early Complications

Yasuo Ito, MD,* Yoshihisa Sugimoto, MD,* Masao Tomioka, MD,† Nobuo Kai, MD,* and Masato Tanaka, MD‡

Study Design. Consecutive cohort study.

Objective. To reconsider effects of the Second National Acute Spinal Cord Injury Study.

Summary of Background Data. High dose methylprednisolone sodium succinate (MPSS) for the patients with acute spinal cord injury has been considered standard treatment in the several countries. However, many authors have criticized the effect of MPSS because of lack of evidence about neurologic improvement and the high incidence of complications.

Methods. During 2-year, all patients with cervical cord injury were treated with MPSS within 8 hours of their injuries based on the Second National Acute Spinal Cord Injury Study protocol (MPSS group). During the next 2-year, all patients were treated without MPSS (non-MPSS group). There were 38 patients in the MPSS group and 41 in the non-MPSS. Early spinal decompression and stabilization was performed as soon after injury in both the groups.

Results. According to The American Spinal Injury Association (ASIA) motor score, there was an average improvement by 3 months postinjury of 12.4 points in the MPSS group and 13.8 points in the non-MPSS group. In patients with complete motor loss, average ASIA motor score improved 9.0 points in the MPSS group and 12.6 points in the non-MPSS group. For patients with incomplete motor loss, average ASIA motor score improvement was 14.1 and 15.5 points in the MPSS and non-MPSS groups, respectively.

In the MPSS group, 19 patients developed pneumonia, 13 developed urinary tract infections, and 5 developed wound infections. Incidence of pneumonia was significantly increased with the use of MPSS medication.

Conclusion. We found no evidence supporting the opinion that high-dose MPSS administration facilitates neurologic improvement in patients with spinal cord injury. We believe MPSS should be used under limited circumstances because of the high incidence of pulmonary complication.

Key words: National Acute Spinal Cord Injury Study, Methylprednisolone, neurologic recovery, acute cervical cord injury, pneumonia, infection. **Spine 2009;34: 2121–2124**

Methylprednisolone sodium succinate (MPSS) is one of the earlier pharmacologic agents used in the treatment of both experimental and human spinal cord injury based on its anti-inflammatory actions and its effectiveness in treating cerebral edema. Despite extensive experience, the role of MPSS in the treatment of traumatic spinal cord injury remains controversial.

Based on the Second National Acute Spinal Cord Injury Study (NASCIS-2), high dose MPSS for the patients with acute spinal cord injury has been considered standard treatment in the several countries.[1–6] However, many authors have criticized the NASCIS-2 and NASCIS-3 because of lack of evidence about neurologic improvement and the high incidence of complications.[7–10]

In this consecutive cohort study, we prospectively treated patients with cervical cord injury using 2 protocols (the NASCIS-2 protocol using MPSS and a protocol that did not use MPSS). Patients' neurologic recovery, and complications such as pneumonia, urinary tract infection, and gastrointestinal hemorrhage were evaluated.

■ Materials and Methods

In this prospective study, we treated patients with cervical cord injury using 2 protocols (Table 1). During the 2-year period from August 2003 to July 2005, all patients with cervical cord injury were treated with MPSS within 8 hours of their injuries based on the NASCIS-2 protocol (MPSS group). During the next 2-year period from August 2005 to July 2007, all patients with cervical cord injury were treated without using MPSS (non-MPSS group). There was no selection bias in this consecutive cohort study. Patients receiving treatment greater than 8 hours after injury or who had no palsy were excluded from this study. Early spinal decompression and stabilization was performed as soon as possible after injury in both groups.

There were 38 patients in the MPSS group: 30 men and 8 women with an average age at injury of 55 years. According to

From the *Department of Orthopaedic Surgery, Kobe Red Cross Hospital, Kobe, Japan; †Department of Orthopaedic Surgery, Hyogo Emergency Medical Center, Kobe, Japan; and ‡Department of Orthopaedic Surgery, Okayama University Gracuate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Japan.
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Address correspondence and reprint requests to Yasuo Ito, MD, 1–3-1 Wakinohamakaigandori Chuo-ku, Kobe, Japan; E-mail: y-ito@kobe.jrc.or.jp

Table 1. Clinical Characteristics of Study Subject

Total	MPSS n = 38	Non-MPSS n = 41
Gender (men/women)	30/8	33/8
Average age at injury (yrs)	55	60
ASIA impairment score*		
A	10	11
B	4	11
C	11	12
D	13	7
High energy trauma	28	28
Operation	29	28
Cord injury without fracture	24	20
Pulmonary injury	8	11

*ASIA indicates the American Spinal Injury Association.

Table 3. Neurological Recovery

	MPSS	Non-MPSS
ASIA impairment score		
Total	17/38 (45%)*	26/41 (63%)*
Without fracture	12/24 (50%)*	13/20 (65%)*
ASIA motor score		
Total	12.4†	13.8†
Complete motor loss	9.0†	12.6†
Incomplete motor loss	14.1†	15.5†
Without fracture	13.7†	14.0†

*Neurological improved patient number (neurologic improvement was defined as increase in at least one clinical grade).
†Average increased point.
ASIA indicates the American Spinal Injury Association.

The American Spinal Injury Association (ASIA) impairment score, at admission there were 10 patients in grade A, 4 in grade B, 11 in grade C, and 13 in grade D. According to type of injury, 28 of 38 (74%) patients had high energy trauma such as a traffic accident or a fall from a high place. Cervical operations such as laminoplasty or fixation were performed in 29 of 38 (76%) patients. Average time for operation was 2.4 days. Cervical cord injuries without fracture were observed in 24 of 38 (63%) patients. Pulmonary injuries such as hemopneumothorax were observed in 8 of 38 (21%) patients.

There were 41 patients in the non-MPSS group: 33 men, and 8 women with an average age at injury of 60 years. According to the ASIA impairment score at admission, there were 11 patients in grade A, 11 in grade B, 12 in grade C, and 7 in grade D. According to the type of injury, 28 of 41 (68%) patients had high energy trauma. Cervical operations were performed in 28 of 41 (68%) patients. Average time for operation was 2.6 days. Cervical cord injuries without fracture were observed in 20 of 41 (49%) patients. Pulmonary injuries were observed in 11 of 41 (27%) patients.

We assessed ASIA impairment score and motor score (range: from 0 to 100) at admission and 3 months after injury. We also evaluated complications such as pneumonia, urinary tract infection, wound infection, and gastrointestinal hemorrhage. For the purpose of statistical analysis, Student t tests, Fisher exact test, and χ^2 test for independence were calculated with a value of $P < 0.05$ regarded as significant.

■ Results

Neurologic Recovery

According to the ASIA impairment score, which defines neurologic improvement as an increase in at least 1 clinical grade, neurologic improvement was observed in 17 of 38 (45%) patients in the MPSS group, and 26 of 41 (63%) patients in the non-MPSS group ($P > 0.05$) (Tables 2, 3).

According to the ASIA motor score, there was an average improvement by 3 months postinjury of 12.4 points in the MPSS group and 13.8 points in the non-MPSS group ($P > 0.05$). In patients with complete motor loss, average ASIA motor score improved 9.0 points in the MPSS group and 12.6 points in the non-MPSS group ($P > 0.05$). For patients with incomplete motor loss, average ASIA motor score improvement was 14.1 and 15.5 points in the MPSS and non-MPSS groups, respectively ($P > 0.05$).

In patients without fracture, ASIA impairment score increased in 12 of 24 (50%) patients from the MPSS group and 13 of 20 (65%) patients from the non-MPSS ($P > 0.05$) group, whereas the average ASIA motor score improved 13.7 points in the MPSS group and 14 points in the non-MPSS group ($P > 0.05$).

Complications

In the MPSS group, 19 patients developed pneumonia, 13 developed urinary tract infections, and 5 developed wound infections. In the non-MPSS group, 11 patients developed pneumonia, 13 developed urinary tract infections, and 4 developed wound infections. In general, infection (pneumonia, urinary tract infection, and wound infection) was observed in 26 of 38 (68%) patients in the MPSS group and 18 of 41 (44%) patients in the non-MPSS group ($P = 0.028$) (Table 4). Incidence of pneumonia was significantly increased with the use of MPSS

Table 2. The American Spinal Injury Association Impairment Score

MPSS Group						Non-MPSS Group					
	Grade at Follow-up						Grade at Follow-up				
	A	B	C	D	E		A	B	C	D	E
Grade at admission						Grade at admission					
A	9	1				A	9	1	1		
B		1	3			B			7	4	
C			3	8		C			3	8	1
D				8	5	D				3	4

MPSS indicates methylprednisolone sodium succinate.

Table 4. Complications

	MPSS	Non-MPSS
Infection*		
Total	26/38 (68%)†	18/41 (44%)†
Pneumonia		
Total	19/38 (50%)†	11/41 (27%)†
Complete motor loss	11/14 (79%)†	8/22 (36%)†
Cord injury without fracture	7/24 (29%)	3/20 (15%)
Aged patient‡	9/14 (64%)	6/14 (43%)
Gastrointenstinal hemorrhage		
Total	6/38 (16%)	2/41 (5%)

*Infection included pneumonia, urinary tract infection and wound infection.
†The difference was significant ($P < 0.05$).
‡Aged patient means 65 year old or more.

medication. Among patients who had complete motor loss, we diagnosed pneumonia in 11 of 14 (79%) patients in the MPSS group and 8 of 22 (36%) patients in the non-MPSS group ($P = 0.019$). Among patients who had cervical cord injury without fracture, we diagnosed pneumonia in 7 of 24 (29%) patients in the MPSS group and 3 of 20 (15%) patients in the non-MPSS group ($P > 0.05$). Among patients aged 65 years or older, 9 out of 14 (64%) and 6 out of 14 (43%) developed pneumonia in the MPSS and non-MPSS groups, respectively ($P > 0.05$).

In the MPSS group, 6 of 38 (16%) patients had gastrointestinal hemorrhage, whereas in non-MPSS group, 2 of 41 (5%) patients had gastrointestinal hemorrhage ($P > 0.05$).

■ Discussion

Although a large research effort is devoted to inhibiting the secondary injury mechanism of SCI, the only widely used, nonoperative intervention is the early initiation of the high-dose methylprednisolone protocol.[1,5,6,11] This consists of a 30 mg/kg MPSS bolus given over 15 minutes followed by a 5.4 mg/kg/h infusion for a total of 24 hours, if treatment is initiated within 3 hours, or for 48 hours, if initiated within 3 to 8 hours of injury. These recommendations are based on the results of the NASCIS-2 and -3 studies.[1,11]

High-dose MPSS remains a controversial treatment. Many authors have had doubt about the NASCIS-2 and NASCIS-3 studies.[7–10] Gerndt *et al* reported steroid therapy was associated with a 2.6 fold increase in the incidence of pneumonia and increases in ventilated and intensive care days.[7] Pointillart *et al* noted there was no statistical difference in neurologic improvement in their prospective study between their MPSS and non-MPSS groups, and almost half of their MPSS-treated patients that were analyzed for complications had hyperglycemia.[8] Matsumoto *et al* reported that patients that were treated with MPSS had a higher incidence of pulmonary and gastrointestinal complications than those that were not.[9] They concluded that aged patients with cervical spinal injury were more likely to have pulmonary side effects after high-dose therapy with MPSS and thus deserve special care.[9] Tsutsumi *et al* reported that in patients with incomplete paralysis at admission, the ASIA motor scores in the MPSS group improved more significantly than those in the non-MPSS group at 6 weeks and 6 months post injury.[12] However, among patients with complete paralysis at admission, patients in the MPSS group did not show significantly greater change in motor score than those in the non-MPSS group.[12]

In our prospective study, MPSS medication did not improve neurologic status in patients with complete or incomplete motor loss. Infection (pneumonia, urinary tract infection, and wound infection) was observed in 26 of 38 (68%) patients in the MPSS group and 18 of 41 (44%) patients in the non-MPSS group. In particular, the incidence of pneumonia was significantly increased with MPSS medication. We found no evidence supporting the opinion that high-dose MPSS administration facilitates neurologic improvement in patients with spinal cord injury. We believe MPSS should be used under limited circumstances because of the high incidence of pulmonary complication.

■ Key Points

- We found no evidence supporting the opinion that high-dose MPSS administration facilitates neurologic improvement in patients with spinal cord injury.
- Incidence of pneumonia was significantly increased with the use of MPSS medication.
- According to ASIA motor score, there was an average improvement by 3 months postinjury of 12.4 points in the MPSS group and 13.8 points in the non-MPSS group.
- In patients with complete motor loss, average ASIA motor score improved 9.0 points in the MPSS group and 12.6 points in the non-MPSS group.
- For patients with incomplete motor loss, average ASIA motor score improvement was 14.1 and 15.5 points in the MPSS and non-MPSS groups, respectively.

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