

# Current Use of Methylprednisolone for Acute Spinal Cord Injury by Spine Surgeons of Thailand

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## ABSTRACT

**Objective:** To determine current decision making in methylprednisolone succinate (MPS) administration for acute spinal cord injury (ASCI) treatment in Thailand.

**Methods:** A questionnaire was sent to all orthopedic surgeons who attended the annual meeting of the Spine Society of Thailand 2016. The questionnaire had 3 parts of questions including demographic data, opinions in MPS use in general ASCI patients and patients who meet the exclusion criteria in NASCIS III study.

**Results:** Fifty five respondents completed the survey (overall response rate was 27.1 %) and there was 78.18% prescribe MPS to ASCI patients. Among them, 40 % prescribe according to NASCIS II and 55.6% NASCIS III. The main reasons for MPS administration are practice standard (38.6%), effectiveness (31.8%) and liability issue (22.7%). In patients who met the exclusion criteria of NASCIS III, most respondents do not prescribe any steroids in patients who had age below 14 years old (42.2%), pregnancy (77.8%), severe underlying disease (72.7%), body weight more than 109 kg (40.9%), gunshot injury (59.1%) and previous spinal cord injury (46.5%). Interestingly, there were 93.2% prescribed MPS to patients who sustained ACSI more than 8 hours.

**Conclusion:** Because the institutional standard supported MPS use, most participants prescribed MPS in ASCI despite current clinical data from recent studies. Most participants who did not use MPS in patients had exclusion criteria of NASCIS III.

**Keywords:** Methylprednisolone, acute spinal cord injury, Thailand, survey

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## INTRODUCTION

Spinal cord injury is the one of the major injuries that affect quality of life. Previous studies reported the various processes of acute spinal cord injury (ASCI) and relevant treatment including hypothermia,<sup>1</sup> riluzole,<sup>2</sup> granulocyte colony-stimulating factor,<sup>3</sup> and methylprednisolone succinate (MPS).<sup>4,5</sup> Currently, only high-dose MPS was generally prescribed as

standard treatment of ASCI. In 2006, the Royal College of Neurosurgical Surgeons of Thailand and many professional organization published the clinical practice guideline for cervical spine injury. Unfortunately, high-dose MPS was not mentioned in this guideline.<sup>6</sup>

However, many recent studies reported that high-dose MPS did not improve neurological recovery and significantly increased complications including gastrointestinal bleeding, hyperglycemia<sup>7,8</sup> and pneumonia.<sup>9</sup> Additionally, Qain et al., reported MPS may cause acute corticosteroid myopathy that delayed the recovery.<sup>10</sup> In 2013, Walter et al., published the guidelines for ASCI that recommended against MPS administration.<sup>11</sup>

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Since the evidence of severe side effects exceeding the benefits was increasing, MPS use in ASCI decreased substantially.<sup>12</sup> Druschel et al., performed a national survey in Germany and reported that only 55% of departments prescribe MPS for ASCI.<sup>13</sup> Miekisiak et al., also performed a survey in 251 Polish spinal surgeons. The result showed that 73.1% of respondents used MPS (41.7% NASCIS II protocol and 24.1% NASCIS III protocol). 14 Hurlbert and Hamilton performed a survey in Canada and reported that 76% of spine surgeons do not prescribe MPS for ASCI.<sup>15</sup>

The purpose of the present study was to assess the current status of MPS use and to determine their rationale for using MPS in ASCI patients who met the exclusion criteria of NASCIS III study among Thai orthopedic surgeons who

attended the annual meeting of the Spine Society of Thailand 2016.

## MATERIALS AND METHODS

The questionnaire had three parts. The first part had demographic questions that pertained to gender, age, type of hospital and number of annual ASCI treated. The second part had six questions including availability of MPS, percentage of steroid prescription, personal steroid guideline, the main reason of steroid use and change of steroid protocol within past 5 years. The last part had 8 questions about rationale for using MPS in specific group of patients who met exclusion criteria of NASCIS III study. The questionnaire was shown in Table 1.

**TABLE 1.** Show demographic data of participant.

Question	Choice	Number(%)
Sex	Male	64 (100%)
Age	<45 yrs	39 (66.1%)
	>45 yrs	20 (33.9%)
Type of hospital	Community / General Hospital	12 (18.5%)
	Regional Hospital	26 (40.0%)
	University Hospital	19 (29.2%)
	Private Hospital	8 (12.3%)
Number of annual ASCI treat	<10	28 (62.2%)
	10-20	13 (28.9%)
	>20	4 (8.9%)
Do your hospital has steroid for ASCI?	MPS	46 (90.2%)
	No MPS but have other steroid	5 (9.8%)
	No steroid at all	0 (0.0%)
How many percentage of ASCI patients that you prescribe steroid?	Less than 50%	20 (36.4%)
	More than 50%	23 (41.8%)
	Never use steroid	10 (18.2%)
	No ASCI patient	2 (3.6%)
If you prescribe steroid for ASCI, which protocol do you use?	NASCISII	18 (40.0%)
	NASCISIII	25 (55.6%)
	MPS every ASCI case, other protocol	0 (0.0%)
	Other steroid	2 (4.4%)
Main reason for drug use	Effectiveness	14 (31.8%)
	Medicolegal liability	10 (22.7%)
	Institutional standard	17 (38.6%)
	Combined	3 (6.8%)
	Not change	37 (82.2%)
Do you change your steroid protocol during past 5 years?	Change	8 (17.8%)

The questionnaire was distributed to orthopaedic surgeons who attended annual meeting of Spine Society of Thailand 2016. Inclusion criteria was Thai board-certified orthopaedic surgeons. The answer of the participants who did not prescribe any steroid to all patients were excluded from second and third part analysis. Descriptive statistics analysis was used for this survey. For comparison of proportions, the Fisher exact test was applied with a significance level of  $p < 0.05$ . Statistical testing was performed using SPSS18 (SPSS Inc, Chicago, IL).

## RESULTS

Responses were received from 55 surgeons from 203 participants (27.1% response rate). All respondents were male and average age was  $43.36 \pm 8.80$  years (range 28-63 years). Forty seven percent worked in tertiary care hospitals and 20 % worked in university hospitals. Ninety percent had MPS in hospital. Ten participants (18.2%) declared that they did not prescribe any steroid to all ASCI patients. The preferred steroid protocols were 40.0% NASCIS II, 55.6% NASCIS III and 4.4% use other steroid (dexamethasone). However, most participants (62.2%) treated ASCI patients cases per year. The main reason for MPS prescription was 31.8% effectiveness in enhancing chance of recovery, 22.7% medicolegal liability and 38.6% institutional standard of treatment. The main reasons for MPS in surgeon who had ASCI less than 10 cases per years were institutional standard (4/17, 41.2%), medicolegal liability (6/17, 35.3%) and effectiveness (4/17, 23.5%). The main reasons for MPS in surgeon who had ASCI more than 10 cases per years were institutional standard

(11/27, 40.7%), effectiveness (11/27, 40.7%) and medicolegal liability (5/27, 18.5%). However, there was no statistical significance between two groups ( $p=0.353$ ). Eighty two percent did not change their personal steroid protocol. The demographic data showed in Table 1.

In term of steroid protocol in NASCIS III excluded patients, most of the participants did not prescribe any steroid including 42.2% in less than 14 years old, 77.8% in pregnancy, 72.7% severe underlying disease, 40.9% in body weight more than 109 kg, 59.1% in gunshot injury, and 46.5% in previous spinal cord injury. However, participants' protocol divided into 2 groups in illegal immigrants. Thirty four percent prescribed MPS according to NASCIS III protocol, but 31.8% did not prescribe any steroid. Interestingly, 81.8% use MPS according to NASCIS III in patients who sustained ASCI more than 8 hours. The data showed in Table 2.

## DISCUSSION

High-dose MPS was generally prescribed as standard treatment of ASCI, but many recent studies showed that MPS had not only non-significant neurological recovery, but also increased serious complications. There were many surveys in different countries which reported that the rate of MPS prescription in ASCI decreased and MPS was used in 2 different protocols including NASCIS II and NASCIS III studies.<sup>12-15</sup> Additionally, there was a special ASCI group which met the exclusion criteria in NASCIS III. The steroid use in that group depended on physician judgement because of lack of evidence to support. The aim of the present study was to determine MPS prescription in Thailand.

**TABLE 2.** Show data of specific group.

Group	NASCIS II	NASCIS III	No steroid	Other steroid
Age less than 14 years	10 (22.2%)	15 (33.3%)	19 (42.2%)	1 (2.2%)
Pregnancy	5 (11.1%)	5 (11.1%)	35 (77.8%)	0 (0.0%)
Illegal immigrants	10 (22.7%)	15 (34.1%)	14 (31.8%)	5 (11.4%)
Serious comorbidities	5 (11.4%)	4 (9.1%)	32 (72.7%)	3 (6.8%)
patients weighing more than 109 kgs	13 (29.5%)	12 (27.3%)	18 (40.9%)	1 (2.3%)
Gunshot wound	6 (13.6%)	10 (22.7%)	26 (59.1%)	2 (4.5%)
Previous spinal injury	8 (18.6%)	14 (32.6%)	20 (46.5%)	1 (2.3%)
Injury more than 8 hours	0 (0.0%)	5 (11.4%)	31(81.8%)	3 (6.8%)

**TABLE 3.** Show comparing data from previous publication with present study.

	<b>Eck et al (2006)<sup>16</sup></b>	<b>Druschel et al (2013)<sup>13</sup></b>	<b>Miekisiak et al (2014)<sup>14</sup></b>	<b>Present study (2016)</b>
Country	USA	Germany	Poland	Thailand
Participants	Surgeon members of the NASS (Orthopedic surgeons and neurosurgeons)	Directors of all trauma, orthopedic and neurosurgical departments of German university centers, affiliated hospitals, and SCI care centers	Orthopedic surgeons and neurosurgeons	Orthopaedic surgeon
Number of respondents (Response rate)	305 (23%)	372 (51%)	110 (43.8%)	51 (%)
% MPS use	93.4 %*	55%	73.50%	78.18%
Protocol				
NASCIS I	N/A	10%	0%	0%
NASCIS II	N/A	43%	41.7%	40%
NASCIS III	N/A	33%	24.1%	55.6%
Rationale				
Medicolegal	36.07%	11%	36.70%	22.7%
Institutional standard	20.98%	29%	30.40%	38.6%
Effectiveness	21.31%	36%	32.90%	31.8%
Combined	7.21%	21%	0%	6.8%

\*Steroid use not only indicate MPS

The present study showed that 78.2% of participants prescribed MPS to ASCI patients (40% NASCIS II and 55.6 % NASCIS III). The main reasons were 31.8% effectiveness, 38.6% institutional standard of care and 22.7% medicolegal issue. Most participants did not prescribe MPS to NASCIS III excluded patients except illegal immigrants. The NASCIS III protocol was preferred to use in this excluded group, from NASCIS III study, but NASCIS II protocol was preferred in severe comorbidity and body weight more than 109 kg patients.

The previous study reported rate of MPS use in ASCI ranged 55-73.5%.<sup>13-14</sup> Druschel et al., performed a national survey in Germany and reported that only 55% of departments prescribe MPS for ASCI.<sup>13</sup> Miekisiak et al., also performed a survey in 251 Polish spinal surgeons. The result showed that 73.1% of respondents used MPS (41.7% NASCIS II protocol and 24.1% NASCIS III protocol).<sup>14</sup> Eck et al., reported a survey result from USA that 93.4% of participants use steroid in ASCI, but did not clarify the rate of MPS use.<sup>16</sup>

Overall, the NASCIS II protocol was prescribed about 40% while the rate of NASCIS III protocol was only 24.1-33%. The main reasons for MPS use were preventing medicolegal liability (11.00 - 36.70%), adopted as institutional standard (20.98 - 30.40%) and believing in effectiveness (21.31-36.00%).<sup>13,14,16</sup> The comparison data is shown in Table 3.

The present study showed that Thai orthopaedic surgeons use MPS in ASCI about 78.18% which was higher than previous studies. Additionally, NASCIS III was the most popular protocol while other surveys were NASCIS II. The most common reasons for MPS varied from study to study. The present study's most common reason was institutional, Eck et al., and Miekisiak et al., studies were medicolegal issue. Druschel et al., study was effectiveness.

The limitation of this study were small size of sample, low response rate, and limited participants that did not include neurosurgeon, emergency medicine specialist, surgeon or general practitioners who were involved in emergency

service. However, the results of the present study showed the current opinion of Thai orthopaedic surgeons about MPS use in ASCI that different from the previous study. Moreover, these results may guide the professional organization to publish the updated guideline that is related to current practice in Thailand.

## CONCLUSION

The present study showed that most of Thai orthopaedic surgeons still prescribed MPS in ASCI despite opposing data from recent studies because institutional guideline remained supporting MPS use. However, most participants did not prescribe MPS in patient groups who met the exclusion criteria of NASCIS III study.

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## Potential conflicts of interest

None.

## REFERENCES

1. Dididze M, Green BA, Dietrich WD, Vanni S, Wang MY, Levi AD. Systemic hypothermia in acute cervical spinal cord injury: a case-controlled study. *Spinal Cord* 2013;51(5):395-400.
2. Fehlings MG, Wilson JR, Frankowski RF, Toups EG, Aarabi B, Harrop JS, et al. Riluzole for the treatment of acute traumatic spinal cord injury: rationale for and design of the NACTN Phase I clinical trial. *J Neurosurg Spine* 2012;17(1 Suppl):151-6.
3. Kamiya K, Koda M, Furuya T, Kato K, Takahashi H, Sakuma T, et al. Neuroprotective therapy with granulocyte colony-stimulating factor in acute spinal cord injury: a comparison with high-dose methylprednisolone as a historical control. *Eur Spine J* 2015;24(5):963-7.
4. Bracken MB, Shepard MJ, Holford TR, Leo-Summers L, Aldrich EF, Fazl M, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. *JAMA* 1997;277(20):1597-604.
5. Bracken MB, Shepard MJ, Collins WF Jr, Holford TR, Baskin DS, Eisenberg HM, Flamm E, Leo-Summers L, Maroon JC, Marshall LF, et al. Methylprednisolone or naloxone treatment after acute spinal cord injury: 1-year follow-up data. Results of the second National Acute Spinal Cord Injury Study. *J Neurosurg* 1992;76(1):23-31.
6. Clinical Practice Guidelines for Cervical Spine Injury 2006 [updated Dec 13, 2012; May 12, 2016]. Available from: [http://www.neuro.or.th/index.php?option=com\\_content&view=article&id=72:-clinical-practice-guidelines-for-cervical-spine-injury&catid=60:2012-09-16-03-51-18&Itemid=68](http://www.neuro.or.th/index.php?option=com_content&view=article&id=72:-clinical-practice-guidelines-for-cervical-spine-injury&catid=60:2012-09-16-03-51-18&Itemid=68).
7. Chikuda H, Yasunaga H, Takeshita K, Horiguchi H, Kawaguchi H, Ohe K, et al. Mortality and morbidity after high-dose methylprednisolone treatment in patients with acute cervical spinal cord injury: a propensity-matched analysis using a nationwide administrative database. *Emerg Med J* 2014;31(3):201-6.
8. Aomar Millan M, Cortinas Saenz M, Delgado Tapia J, Geronimo Pardo M, Calatayud Perez V, Peyro Garcia R. [Assessment of neurologic function and complications in a retrospective cohort of patients with acute spinal cord injury due to trauma treated with large-dose methylprednisolone]. *Rev Esp Anestesiol Reanim* 2011;58(10):583-8.
9. Suberviola B, Gonzalez-Castro A, Llorca J, Ortiz-Melon F, Minambres E. Early complications of high-dose methylprednisolone in acute spinal cord injury patients. *Injury* 2008;39(7):748-52.
10. Qian T, Guo X, Levi AD, Vanni S, Shebert RT, Sipski ML. High-dose methylprednisolone may cause myopathy in acute spinal cord injury patients. *Spinal Cord* 2005;43(4):199-203.
11. Walters BC, Hadley MN, Hurlbert RJ, Aarabi B, Dhall SS, Gelb DE, et al. Guidelines for the management of acute cervical spine and spinal cord injuries: 2013 update. *Neurosurgery* 2013;60 (Suppl 1):82-91.
12. Felleiter P, Muller N, Schumann F, Felix O, Lierz P. Changes in the use of the methylprednisolone protocol for traumatic spinal cord injury in Switzerland. *Spine (Phila Pa 1976)* 2012;37(11):953-6.
13. Druschel C, Schaser KD, Schwab JM. Current practice of methylprednisolone administration for acute spinal cord injury in Germany: a national survey. *Spine (Phila Pa 1976)* 2013;38(11):E669-77.
14. Miekisiak G, Kloc W, Janusz W, Kaczmarczyk J, Latka D, Zarzycki D. Current use of methylprednisolone for acute spinal cord injury in Poland: survey study. *Eur J Orthop Surg Traumatol* 2014;24 (Suppl 1):S269-73.
15. Hurlbert RJ, Hamilton MG. Methylprednisolone for acute spinal cord injury: 5-year practice reversal. *Can J Neurol Sci* 2008;35(1):41-5.
16. Eck JC, Nachtigall D, Humphreys SC, Hodges SD. Questionnaire survey of spine surgeons on the use of methylprednisolone for acute spinal cord injury. *Spine* 2006;31(9):E250-3.