Health Services Research

Current Practice of Methylprednisolone Administration for Acute Spinal Cord Injury in Germany

A National Survey

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Study Design. Written mail-out survey.

Objective. To determine current practice in high-dose methylprednisolone succinate (MPSS) administration for treatment of acute spinal cord injury (SCI) in Germany.

Summary of Background Data. Reanalysis of the National Acute Spinal Cord Injury Studies (NASCIS) resulted in criticism of the use of high-dose MPSS for treatment of acute SCI. Subsequently, SCI treatment guidelines were revised leading to a reduction in MPSS use across North America. The impact of these revisions on SCI treatment in Germany is not known.

Methods. A questionnaire was sent to all trauma, orthopedic and neurosurgical departments of German university centers, affiliated teaching hospitals, and specialized SCI care centers. Survey included 6 questions about the administration of MPSS after acute SCI.

Results. Three hundred seventy-two respondents completed the survey (response rate: 51% overall, 76% university hospitals, 85% specialized SCI care centers). Overall, 55% of departments that treat SCI prescribe MPSS. Among them, 73% are "frequent" users administering MPSS to more than 50% of their patients. Ten percent prescribe according to NASCIS I, 43% NASCIS II, 33% NASCIS III, and 13% "generic protocols." As justification for MPSS treatment, "effectiveness" ranked before "common practice" and "medicolegal reasons." "Specialized" SCI care centers differ in that (1) MPSS is administered less frequently, (2) NASCIS I doses are not used, and (3) during the past several years, practice patterns are more likely to have shifted away from the treatment of SCI with MPSS.

Conclusion. About one-half of the institutions continue to prescribe MPSS in the setting of acute SCI. A need for further education in almost one-fourth of German departments treating acute SCI is demonstrated through responses indicating use of the outdated NASCIS I protocol, a "legal need" or "unchanged MPSS application during the last years." "Specialized" SCI centers are more likely to change their practice in accordance with evolving literature.

Key words: methylprednisolone, NASCIS, spinal cord injury, standard of care.

Level of Evidence: 3

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In Germany, every year about 2000 people with a mean age of 35 years experience a spinal cord injury (SCI).1,2 Improved field resuscitation and transportation, intensive care medicine, and surgical and rehabilitative care have all contributed to a highly improved rate of survival.3 Whereas in 1989 25% of patients died shortly after SCI from its direct consequences,4 the current mortality rate rests at 6%.1 To date, only methylprednisolone succinate (MPSS) succinate, tirilazad mesylate, naloxone, and GM-1 ganglioside have been tested in large phase III randomized controlled trials using neurological function5 as primary endpoint. In the 1990s, corticosteroids provided an intuitive therapeutic concept because they reduced the secondary spinal cord damage in experimental SCI models.6 The randomized, placebo-controlled National Acute Spinal Cord Injury Study (NASCIS) II7 purportedly demonstrated a "neuroprotective" effect of MPSS and thus led to the transient establishment of the NASCIS protocol as a "standard" therapy for patients with spinal cord injury.8 However, doubts were spawned by a critical reappraisal of the NASCIS trials that identified limitations in its study design and statistical value9 as well as evidence of detrimental adverse effects in the NASCIS III trial.9–16 In Germany, international critical re-evaluation was incorporated in the relevant financial activities outside the submitted work: board membership, consultancy, grants.

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TABLE 1. Panel of the Questionnaire Content

<table>
<thead>
<tr>
<th>Question</th>
<th>Possible Answers</th>
</tr>
</thead>
<tbody>
<tr>
<td>In what percentage of acute spinal cord injured patients do you implement a high dose methylprednisolone treatment after National Acute Spinal Cord Injury Studies (NASCIS) scheme?</td>
<td>&gt; 50%</td>
</tr>
<tr>
<td>Treatment regimen</td>
<td>NASCIS I</td>
</tr>
<tr>
<td>Medical specialty</td>
<td>Trauma surgery</td>
</tr>
<tr>
<td>Number of patients with acute spinal cord injury treated per year</td>
<td>n &lt; 10</td>
</tr>
<tr>
<td>Administration</td>
<td>Believe in effectiveness</td>
</tr>
<tr>
<td>Has the application changed in the past 5-10 years with you?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Modified from the study of Hurlbert et al.20,21 NASCIS indicates National Acute Spinal Cord Injury Studies.

updated multidisciplinary surgical (S3/consensus finding group) Polytrauma Guideline in 2011,17 where the administration of MPSS was no longer considered as the “standard” treatment. The second valid guideline derives from the German Society of Neurologists, which in 2008 indicated that MPSS treatment (NASCIS III) may be applied.18 The recent update of this guideline states however that MPSS is no longer recommended due to a higher risk of side effects.19 No information is available as to whether the treatment of patients with acute has changed accordingly.

In this study, we survey the current status of SCI treating departments with regard to the use of high-dose MPSS in therapy after acute SCI in Germany (“treatment reality”). Our aim was to analyze (1) how the German medical community responded to the evolution and demise of a treatment “standard,” (2) whether a “treatment consensus” currently exists, and (3) how current German practice compares with that in North America.

MATERIALS AND METHODS

A modified, standardized questionnaire was sent to the clinical directors of Trauma, Orthopedic, and Neurological Surgery departments in Germany in January 2011. University departments were selected according to the website of the German Association of University Hospitals (VUD, http://www.uniklinika.de/) and the respective teaching hospitals according to the universities. Furthermore specialized hospitals were included indicated by the website of the German Society of Paraplegia (DMGP, www.dmgp.at).

The survey was directed to the department directors, responsible for the type of treatment, to detail the use of high-dose MPSS after traumatic SCI representative for their department. It was ensured that multiple answers per department from different physicians were excluded and the institutional practice was stated. To allow for comparability the survey was modeled after prior similar reports.20,21 Items 1, 2, 4, and 6 consisted of single-choice answers; items number 3 and 5 allowed for multiple answers (Table 1).

Survey requests were directed toward 3 target groups. In order of increasing specialization, the first group consisted of trauma, orthopedic, and neurological surgeons practicing within university-affiliated teaching hospitals located off campus. The second group comprised similar surgeons practicing in university hospitals. Lastly, questionnaires were sent to directors in “specialized” SCI treatment centers (third group) indicated by the DMGP forming a “core group” in this study. As an “extended core group” classical university hospitals (second group) were added to this group. If a teaching hospital was among the DMGP hospitals, responses were allocated to the DMGP group.

Besides stratification according to degree of SCI specializa-
tion, we also grouped answers of SCI treating departments according to the frequency of SCI care that ranged from “sporadic” (<10 patients/yr) to “frequent” (>40 patients/yr). A reply envelope was sent with each questionnaire to expedite the response procedure. A reminder and second copy of the questionnaire were sent to all nonresponders after a lapse of 4 weeks. The threshold for freedom from bias was assumed to be a 70% response rate according to Fillion.22

Descriptive statistics were used for the survey analysis. Results were given in absolute and relative percentages. The data were assembled in such a way that single- and multispecifications were considered. To exclude irrelevant answers, only answers from SCI-treating practitioners were considered (Figure 1). A differential analysis with regard to several medical specializations (trauma, orthopedic, neurological surgeons, and others) was conducted. For comparison of proportions, the Fisher exact test was applied with a significance level of $P < 0.05$. Statistical testing was performed using PASW Statistics 18 (SPSS Inc, Chicago, IL).
In total, 372 of 730 departments (112 “extended core group” and 618 teaching hospitals) responded to the questionnaire, signifying a 51% overall response rate (Figures 1 and 2). Within the “extended core group” of university hospitals and DMGP departments, 78% (n = 87) responded to the questionnaire. Questionnaires were returned by 44% (n = 162) of the orthopedic/trauma departments, 25% (n = 91) of the neurosurgical departments, 19% (n = 70) of departments with multiple medical specialities, and 1% (n = 3) of departments with other specialties. Another 12% (n = 46) did not specify their medical subspecialization. Overall, 25% (n = 94) of the responders did not treat spinal cord injured patients; this group was not considered for further analysis.
Of the departments treating patients with spinal cord injuries, 47% (n = 131) defined themselves as orthopedic/trauma surgeons, 32% (n = 88) as neurosurgeons, 0.4% (n = 1) as other specialists, and 21% (n = 57) reported a combination of specialties (Figure 3).

Of the 372 respondents, 75% (n = 278) reported treating patients with acute blunt SCI. Among those, 53% (n = 146) reported a mean of fewer than 10 patients treated per year ("sporadic" SCI care unit); 42% (n = 115) treated between 10 to 40 injuries per year and only 5% (n = 15) more than 40 per year ("frequent" SCI care unit) (Figure 4). Notably, a significant correlation (P < 0.05) was evident between the level of institutional SCI specialization and the number of patients treated. In the "extended core group" 79% (n = 60) of treating departments are "medium to frequent" SCI units, whereas only 35% (n = 70) of departments in teaching hospitals treat more than 10 patients with SCI per year (P < 0.05). Similarly, only 11% of hospitals treating fewer than 10 patients/yr ("sporadic" SCI units) belonged to the "extended core group." Interestingly, the majority (53%) of institutions treating SCI are located in "sporadic" SCI units, whereas only 5% are located in "frequent" SCI units (Figure 4).

Fifty-five percent (n = 154) of German hospitals that treat SCI still prescribe MPSS (Figure 1). Of those, 74% (n = 113) apply MPSS in more than 50% of patients with SCI and 27% (n = 41) in under 50%. Forty-five percent (n = 124) do not prescribe MPSS at all (Figures 5, 6). A trend toward reduced MPSS administration exists in comparing “sporadic” (<10 patients), “middle” (10–40 patients), and “frequent” (>40 patients) SCI units. This does not reach statistical significance.
"generic protocol" (modified steroid administration not matching any particular NASCIS study) is prescribed by 13% (n = 21) of treating departments (Figure 7). A “generic protocol” (modified steroid administration not matching any particular NASCIS study) is prescribed by 13% (n = 21) of treating departments (Figure 7). More than two-thirds of “specialized” SCI institutions dose patients with SCI according to NASCIS II guidelines, whereas fewer than half of patients with SCI receive this protocol in university and teaching hospitals (Figure 7). Conversely NASCIS III guidelines are used proportionately more frequently in non-DMGP institutions. Administration of MPSS according to NASCIS I doses was claimed only in university and teaching hospitals, noticeably absent in “specialized” DMGP hospitals. Similar trends were evident when comparing “sporadic” to “frequent” SCI centers where the highest percentage of departments prescribing NASCIS I were observed in the “sporadic” group (Figure 7).

Approximately one-third (36%, n = 55) of the respondents who prescribe MPSS for SCI cite effectiveness (in promoting neurological recovery) as their main reason. Almost an equal proportion (29%, n = 45) do so because it is the usual practice at their institution or by their colleagues. Only 11% (n = 17) prescribe MPSS in fear of litigation. Twenty-

**Figure 3.** Representation of medical specialties of departments treating SCI patients in Germany. Almost two-thirds of the responders were orthopedic/trauma departments, whereas only one-third designated themselves as neurosurgical departments. According to the German Federal Chamber of Physicians the ratio presented reflects the recent distribution of medical specialists in Germany, with three-quarters fewer neurosurgeons than orthopedic/trauma surgeons. Subdivision according to the DMGP, university and teaching hospitals illustrates a higher proportion of trauma/orthopedic departments in DMGP hospitals. DMGP indicates German Society of Paraplegia; SCI, spinal cord injury.

**Figure 4.** Treating departments in “sporadic, medium, and frequent” SCI care units. Fifty-three percent (n = 146) of the treating institutions reported treating a mean of fewer than 10 patients per year (“sporadic” SCI care unit) that points to a fragmentalized acute SCI care in Germany. DMGP indicates German Society of Paraplegia; SCI, spinal cord injury.

**Figure 5.** (A) MPSS usage in "sporadic and frequent" SCI care units. MPSS applying departments show a tendency to use MPSS more specifically (<50% of the patients) in “frequent” SCI care units (>40 patients/yr) than in “sporadic” SCI care units (<10 patients/yr). Thus, as a trend, MPSS usage is reduced in “frequent” SCI care units but this does not reach statistical significance. (B) MPSS usage in DMGP, university and teaching hospitals. Specialized DMGP departments show a tendency to use MPSS more specifically than in university or teaching hospitals. DMGP indicates German Society of Paraplegia; SCI, spinal cord injury; MPSS, methylprednisolone succinate.

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one percent of respondents indicated a combination of these reasons while 5% (n = 7) abstained from this issue (Figure 8). Only one-quarter (n = 40) of institutions that administer MPSS have modified their routine in the past decade, whereas three-quarters (n = 114) have not altered their prescribing technique (P < 0.05). Institutions currently not prescribing steroids for SCI were more likely to have converted from MPSS-use to nonuse (60%, n = 75) than they were to have maintained a nonprescribing status (34%, n = 42). Departments in “specialized” SCI units converted more frequently to being non-MPSS users (56%) than did departments in university (29%) or teaching hospitals (23%).

In summary, although “specialized” SCI units house fewer treating physicians they care for more patients with acute SCI and administer MPSS less frequently compared with university and teaching hospitals. However, the majority of departments treating SCI in Germany still use MPSS primarily because they think it is effective in treating the neurological injury. An almost equally large group does so because it is their routine. Specialized DMGP hospitals are more likely to have stopped prescribing steroids within the past 10 years, as are the physicians who work in them.

DISCUSSION

With a structured, formerly published, modified questionnaire20,21 the present nationwide survey investigated the practice and role of MPSS in the acute treatment of SCI in Germany. The survey was sent to all medical institutions involved in treatment of acute SCIs including all associated medical disciplines, such as trauma surgery, orthopedic, and neurosurgical departments.

The overall response rate was 51%. As the included hospitals are not securely involved in the treatment of patients with...
SCI, the target population may be overestimated and thus the response rate is underestimated. However, the response rate from university hospitals (76%) and specialized SCI care units (85%) where the majority of patients with SCI receive their care reached or exceeded the 70% benchmark. This argues against bias due to inadequate sample size. In addition, the geographical distribution of responding institutions fairly covered the whole of Germany without excluding any particular area/state (Figure 2). Our observed response rate also corresponds to similar studies where 66% to 75% of questionnaires were returned. Almost two-thirds of our responders were surgeons representing orthopedic/trauma departments; only one-third declared themselves as surgeons representing neurosurgical departments. This proportion matches the ratio of medical specialists in Germany, where the number of neurological surgeons is three-quarters lower than the number of orthopedic/trauma surgeons.

In Germany, the majority of departments that treat acute SCI (52%) are units that see fewer than 10 injured patients per year. By contrast, only 5% are “specialized” SCI units that are more likely to treat 40 or more patients per year. This suggests that acute SCI care is currently fragmented throughout the country, perhaps in an undesirable way considering evidence that supports early treatment of these patients in “specialized” SCI centers. Such specialization has been linked to a reduction in (1) hospitalization time; (2) overall mortality, and (3) the number and severity of complications.

Other studies estimated that in the early to mid-2000s MPSS was prescribed for acute SCI by 75% to 95% of trauma centers, dropping to 68% and 32% by 2009. Working with a different retrospective study design focusing on treated patients rather than perceptions of treating departments, a recent single-center Swiss investigation reports a similar dynamic drop from 96% to 23% in MPSS treatment of SCI during a 10-year period. These authors report that SCI, the target population may be overestimated and thus the response rate is underestimated. However, the response rate from university hospitals (76%) and specialized SCI care units (85%) where the majority of patients with SCI receive their care reached or exceeded the 70% benchmark. This argues against bias due to inadequate sample size. In addition, the geographical distribution of responding institutions fairly covered the whole of Germany without excluding any particular area/state (Figure 2). Our observed response rate also corresponds to similar studies where 66% to 75% of questionnaires were returned. Almost two-thirds of our responders were surgeons representing orthopedic/trauma departments; only one-third declared themselves as surgeons representing neurosurgical departments. This proportion matches the ratio of medical specialists in Germany, where the number of neurological surgeons is three-quarters lower than the number of orthopedic/trauma surgeons. This is an interesting contrast compared with the study of Hurlbert and Moulton which reports a higher proportion of neurological surgeons treating acute SCI in Canada than orthopedic/trauma surgeons.

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European specialized SCI care units are already adhering to the newer guidelines. However, our results indicate that withdrawal of MPSS as standard of care has not been fully implemented in Germany “nonresolved role of MPSS”

Instead, our findings suggest that at least a quarter of all departments that treat SCI in Germany need further education about the risks and benefits of MPSS administration. Specifically these are the institutions that prescribe MPSS according to the outdated NASCIS I protocol and those that indicate “worries about being sued” or “because everyone else does.” The group of SCI departments that report having made no change in their MPSS application routine in the last 5 to 10 years (24%) represents another cohort that might benefit from exposure to updated literature. Finally, the 36% of steroid prescribers who cite “benefit” as the reason they give MPSS certainly have less firm ground to stand on in view of recently updated guidelines in Germany\(^{17,18}\) and around the world.\(^{29-31}\)

The “washout” time of MPSS as a standard of care seems to be prolonged in Germany, especially in “sporadic” SCI care units. The effect of guidelines in changing physician behavior can be limited.\(^{32}\) Furthermore, although guidelines require acknowledgement and adherence by treating physicians so that they are actually followed, they should not affect clinicians’ autonomy.\(^{33}\) The literature reveals that it takes several years until new scientific evidence is adopted in current practice, even when there is obvious impact in patients’ morbidity and mortality.\(^{34}\) Thus, it cannot be predicted when the mentioned new guidelines (S3 multidisciplinary surgical polytrauma guideline and guideline from the German Society of Neurologists) will be fully implemented in current treatment strategies. In this context, this study could be seen as a starting point to follow-up on response rate with a repetition of the survey. The related Canadian analysis that served as a study model uses a similar approach\(^{30}\) and thus shares the same limitations. The investigated study population “SCI treating unit chairmen” is not identical to the one investigated by the Hurlbert group “individual surgeons” and limits a direct comparability of the results. Nevertheless, it reports that only 24% of physicians treating SCI applied MPSS in 2006 compared with 76% in 2001, representing a reduction of more than 50%. In Germany only 25% of responding departments admit to changing their practice pattern in the past 10 years.

We acknowledge there are limitations to our research. Due to the design of our study, we cannot exclude false-positive answers with regard to MPSS use, which might be higher in “sporadic” SCI units. Nevertheless, even false-positive answers underscore the need to change perception about the role of MPSS in SCI. This analysis might spur further discussion and prospective analysis in respective, SCI-treating medical societies. Furthermore, we focused on the most reliable and representative/authoritative sources, the head of department. Here, we cannot and do not intend to detect diverging treatment perceptions of the chairmen and fellows in their respective SCI treating units.

In this study, we cannot fully distinguish between noninformed MPSS use and informed autonomy of the SCI physician. Nonetheless, reasons provided by treating departments point to a high rate of a noninformed MPSS use. Despite the fact that current guidelines have largely abandoned MPSS in the treatment of acute SCI, our nationwide survey suggests that its continued, heterogeneous application is as a result of persisting insecurity within the majority of physicians treating this condition.

**CONCLUSION**

In conclusion, this study demonstrates a “fragmented” SCI care with a remarkable flux of SCI patients referred to non-specialized centers. This, and the continued frequent administration of MPSS in acute SCI may result in an increase in overall mortality as well as number and severity of complications. Together, this leads to a need for further communication/education concerning the treatment guidelines in spinal cord injured patients.

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**Key Points**

- The majority of German SCI treating departments see less than 10 injured patients per year, suggesting that acute SCI care is currently fragmented throughout the country.
- Unexpectedly, the majority of German SCI treating departments persistently applies MPSS, mostly based on the belief of its “effectiveness” to ameliorate neurological injury.
- This survey indicates that withdrawal of MPSS as standard of care has not been fully implemented and that further education about the risks and benefits of MPSS administration is necessary.

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**References**