Original Article

EFFECTIVENESS OF METHYLPREDNISOLONE IN ACUTE SPINAL CORD INJURY – A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS

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ABSTRACT

Steroid therapy has been tested as a neuronal protector in spinal cord injury. Multicenter studies evaluating the efficacy of methylprednisolone (MP) in posttraumatic neurological recovery have shown promising results (NASCIS). However, several critical studies related to NASCIS results have been published.

OBJECTIVE. To review the literature concerning the use of methylprednisolone compared with placebo.

METHODS. This analysis added the mean improvement obtained by groups of patients using MP and placebo (PL) to their mean scores at baseline, before treatment, resulting in the final neurological outcome for both groups.

RESULTS. The motor score in the MP group was only 2.5 points higher than in the PL group after a one-year follow-up. In neurologically intact individuals, the motor score is 70 points. Improvement in sensory scores was also discrete (1.1 and 1.7 points for pinprick and light touch sensation, respectively). A high rate of complications was observed in a group of patients aged about 60 years who used MP.

CONCLUSION. Differences in the clinical magnitude of the benefits obtained (not confirmed by other studies) with the use of MP and PL are not significant against the potential complications when using this medication.

KEY WORDS: Spinal cord injuries. Methylprednisolone. Methylprednisolone hemisuccinate.

INTRODUCTION

Spinal trauma (ST) is the major cause of spinal cord injury damage in young adults. The resulting neurological damage is caused by primary mechanical lesion and, secondarily, by a series of subsequent cell-cell and biochemical interactions that perpetuate and amplify the initial lesion. Pharmacological treatment usually aims at reducing secondary injuries, being considered as a neuronal protector in trauma.

Steroid therapy has been tested as a neuronal protector in trauma. In 1984, a study conducted in seven U.S. states was published comparing two distinct methylprednisolone (MP) regimens in the acute phase of trauma: 100-mg bolus followed by daily 100 mg for 10 days compared with

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1,000-mg bolus followed by daily 1,000 mg for 10 days.[1] The results after 12 months of study were published in 1985.[2] None of the therapy regimens showed differences in neurological protection (NASCIS I). New experimental studies suggested that the dosage in neuroprotective steroid therapy should be higher than that used until that moment.[2] Therefore, studies using high-dose MP were then designed.[3,4]

Preliminary results described high-dose MP as efficient in the treatment of trauma in the United States; however, the publishing strategy for MP studies was viewed with some skepticism by part of the scientific community. The results were ***largely*** spread even before their initial publication, associated with advertising MP use in several trauma centers in the United States.[5]

Several critical studies regarding MP use have then been published by various Specialty Societies from different countries.[6,7,8,9,10,11]

Objectives

The objective of this study is to review randomized controlled trials comparing the effectiveness of methylprednisolone with placebo in the acute phase of spinal cord injury. The authors aimed to answer the following clinical question: does the use of methylprednisolone bring benefits and/or risks to patients with spinal cord injury after spinal fracture?

Methods

In order to guide our search for evidence within scientific information databases, the clinical question was structured according to the acronym *PICO* (P- Patients; I- Intervention; C- Comparison; O- Outcome). In addition to organizing the literature search, these components defined the inclusion criteria related to populations, interventions and outcomes to be considered.

Types of participants: Patients that suffered spinal trauma with spinal cord injury. Studies examining spinal trauma without spinal cord injury were excluded, as well as those analyzing victims of whiplash injury without neurological damage.

Types of intervention: Comparison between the use of methylprednisolone (regardless of dose) and placebo in the acute phase of ST with spinal cord injury.

Types of outcomes studied: a) Neurological status (motor and sensory functions) after spinal cord injury; b) Complications of MP therapy.

Conflict of interest: None declared.

Study designs included: In an attempt to retrieve studies with greater strength to answer the clinical question, only randomized controlled trials were included in the literature search.

Databases searched: MEDLINE, LILACS and EMBASE.

Reference review: All articles were reviewed by two independent reviewers.

Search strategy

A) MEDLINE database: A systematic review was conducted using PubMed web-based search engine (www.pubmed.com), with the question structured by "PICO" according to the descriptors below, applying the sensitive and specificity filters of PubMed Clinical Queries tool and MeSH Browser. Two distinct searches were performed for the effect of MP on SCI-associated neurological damage and complications of MP use (therapy) compared to placebo. The following descriptors were used:

1) Effect of MP on SCI-associated neurological damage

Search tool: Clinical Queries: ("Methylprednisolone") AND ("Spinal Cord Injuries") AND (Randomized controlled trial [Publication Type] OR (randomized [Title/Abstract] AND controlled [Title/Abstract] AND trial [Title/Abstract])) – 38.

Search tool: MeSH Browser: "Methylprednisolone" [Mesh] AND "Spinal Cord Injuries" [Mesh] AND ("Randomized controlled trial" [Publication Type] OR "Randomized controlled trial as Topic [Mesh]) – 43.

2) Complications of MP therapy

Search tools: Clinical Queries and MeSH Browser: "Methylprednisolone"[Mesh] AND "complications"[Subheading] OR "adverse effects"[Subheading] AND "Randomized Controlled Trial[ptyp] AND "Spinal Cord Injuries"[Mesh] AND "Randomized Controlled Trial[ptyp] – 11.

B) LILACS database:

Search: "methylprednisolone" or "methylprednisolone hemisuccinate" or "methylprednisolone succinate" [Subject descriptor] and "spinal cord injuries" or "spinal cord trauma" [Subject descriptor] – 9.

C) EMBASE database:

Search: 1) "methylprednisolone" and "Spinal cord injuries" and "controlled clinical trial" (limits: human/lim and 1974-2008) – 19. 2) "methylprednisolone" and "Spinal cord injuries" and randomized controlled trial/lim AND [humans]/lim AND [embase]/lim AND [1974-2008] – 4.

Among all authors, 11 were neurosurgeons. We consulted with the authors on whether any other scientific works, not uncovered by our web-based search, should be incorporated into the results of the present review, but no additional studies were suggested.

Critical appraisal and selection of studies

The studies were classified according to the Jadad score, from one to five. The Jadad score[12] assigns one point to each positive answer if the article describes the method of randomization and blinding to treatment and evaluates and describes withdrawals and dropouts in the study sample. Furthermore, an additional point is assigned if the method of randomization is appropriate, the method of blinding is appropriate, and withdrawals and dropouts are less than or equal to 20% of the initial sample. The total score may range from 0 to 5. Scores greater than or

equal to three reveal a study with adequate methodological quality.

Studies scoring Jadad 3 or greater were included for critical appraisal according the checklist below.

The checklist analyzed methodological quality and internal validity performed by the authors considering: the study design, whose objective is a randomized controlled trial; the level of evidence for inclusion was established as 1b according to the Oxford table (http://www.projetodiretrizes.org.br/projeto_diretrizes/texto_introdutorio.pdf); inclusion criteria for selection (patients with spinal cord injury that were randomized within 12 hours of injury); exclusion criteria were nerve root or cauda equina injury, gunshot wound, pregnancy, life-threatening morbidity, drug-addicted persons, individuals using corticoids for any reason, aged less than 13 years, using 100 mg of methylprednisolone or 1 mg of naloxone, and those cases in which follow-up was considered difficult; description of the method of randomization and presence of blinded allocation; blinding of raters; therapy protocol consisting of an intervention group using methylprednisolone at any dose and/or administration regimen and a control group using placebo; participants were blinded to which drug was being administered; the outcomes considered included neurological function (as the main outcome), assessed between six weeks and one year after injury; neurological function was assessed concerning components of motor function, pain appreciation (pinprick), and superficial sensation (light touch); instruments to measure the outcome of interest (final standardized motor score and the sensory score related to pinprick-evoked pain and light touch); period of patient follow-up and description of losses; presence or not of migration between groups; sample size calculation and estimated differences between groups; significance level was set at $p<0.05$; presence of intention-to-treat analysis and a summary of the benefits and risks.

Statistical analysis: The difference between motor and sensory scores obtained from the sample at admission (baseline) and at the end of the follow-up (posttreatment) was assessed, the mean score being expressed as the proportion of the approximate normal score for whole numbers, using the chi-square test.

Results

The three search strategies uncovered 72 scientific works. These studies were evaluated according to PICO inclusion and exclusion criteria and to study design.

1) Effect of MP on SCI-associated neurological damage
Evidence retrieved from PubMed – 1st quality analysis of published articles – Selection by study design

The literature review via PubMed (PICO) returned 41 articles: 10 review studies,[5,6,8,10,13,15,16,17,18,20] 13 commentaries and discussion,[7,9,11,19,21,23,24,25,26,27,28,29,30] two experimental animal studies,[29,30] three studies on the use of GM-1 ganglioside,[33,34,35] one article analyzing the role of surgery in neurological recovery,[17] one article performing a parallel evaluation of the effect of MP on liver enzymes,[38] and one secondary analysis.[39] All of these studies were excluded. Ten articles were described as randomized clinical trials and were selected for analysis.[1,2,3,4,40,41,42,43,44, 45]

These 10 randomized clinical trials were set apart for reanalysis:

Evidence retrieved from PubMed – 2nd quality analysis of articles – Critical appraisal of selected evidence

Articles excluded by PICO:

The articles by Bracken et al. published in 1984[1] and in 1985[2] were described as the National Acute Spinal Cord Injury Studies (NASCIS I) at their first publication and after a one-year follow-up. These two articles did not compare MP with placebo.

The articles by Petitjean et al.[43] and Pointillart et al.[41] can be considered superposable, since they describe the same topics in English and French. These studies did not include a placebo control group, comparing the MP group only to a group without treatment. Similarly, the studies known as NASCIS III[42] did not use placebo as an intervention control group and, therefore, were not analyzed.

The article by Epstein et al.[45] compared the effect of methylprednisolone, heparin and cimetidine on gastrointestinal bleeding in patients with spinal cord injuries. This study did no perform an appropriate randomization of subgroups and, therefore, was excluded (Jadad score <3).

Studies included with a Jadad score greater than three:

Only two articles compared methylprednisolone with placebo in the outcome *neurological improvement* six weeks and six months after injury (NASCIS II[3]) and one year after injury (NASCIS II[4]). NASCIS II[3] was described by means of two publications: one article describing the results after six weeks and six months and another article describing the results after one year.[4] Of the initial sample of 487 patients, 97% of the participants were assessed one year after injury, and 87% of the sample received the predetermined pharmacological therapy.

NASCIS II generated randomization lists by computer and described the method of randomization, blinded allocation to treatment, analysis, and withdrawals and dropouts. There were 20% of losses, that is, the withdrawal/dropout threshold for final analysis. The study was classified as Jadad score 5, being then analyzed. Sample size was not calculated prior to the study. There was no migration between treatment groups. There was no temporary evaluation of possible unacceptable injuries in either treatment group. Intention-to-treat was not analyzed, although the injured-patient group as a whole was compared to the placebo group (with no differences between treatments) and a subgroup analysis of patients treated within eight hours of injury was performed.

2) Studies on complications of MP therapy
Evidence retrieved – 1st quality analysis of articles – Selection according to type of publication

The articles by Bracken 1984,[1] 1991,[30] and 1993[26]

did not use a placebo control group[1] or were classified as a discussion; these articles were, therefore, excluded. The articles by Petitjean et al.,[43] Bracken 1997,[44] Pointillart et al.,[40] and Bracken 1998[42] were not controlled against placebo, being, therefore, excluded. The study by Epstein et al.[45] was not actually randomized, being, therefore, excluded.

Evidence retrieved – 2nd quality analysis of published articles

Of the 11 trials initially selected, two were randomized clinical trials and were set apart for reanalysis. Only the study by Matsumoto et al.[40] had not been analyzed in the selection of works related to MP effect on bone marrow damage. Both NASCIS II[3,4] and the study by Matsumoto et al.[40] were analyzed for complications. The quality analysis of both NASCIS II was described above.

The study by Matsumoto et al.[40] was randomized, did not calculate sample size and did not show an intention-to-treat analysis. There was no migration between treatment groups and no withdrawals. The article was classified as Jadad score 5.

Evidence retrieved from LILACS – 1st quality analysis of published articles – Selection by study design

LILACS database search returned nine articles: six review studies,[46,47,48,49,50,51] one experimental animal study,[55] one case series analysis,[53] and one case report.[54] LILACS database search did not uncover any randomized study.

Evidence retrieved from EMBASE – 1st quality analysis of published articles – Selection by study design

EMBASE database search returned 16 articles, in addition to those obtained from MEDLINE database: the study by Cengiz[55] analyzed the effect of timing of surgery on trauma, 13 articles were review studies,[56,57,58,61,60,61,62,63,64,65,66,67,68] the study by Pettersson[69] analyzed whiplash injury, and the article by Trembly[70] was classified as a conference paper.

Results

1) Effect of MP on SCI-associated neurological damage

A) Results for motor function

Motor function was assessed according to an expanded score, ranging from 0 to 70 points (ranging between no muscle contraction and all normal responses, tested in 14 muscle groups). The results for motor function were described as the magnitude of change in neurological status after injury due to treatment, instead of being described as the patient's pre and posttreatment absolute scores. A cutoff point for clinical benefit was not defined. In this study, the mean motor score for the whole study sample at admission (baseline) was compared to the final score of patients treated with methylprednisolone and placebo. The results were initially described for the whole sample and, subsequently, for the subgroup treated within eight hours of injury.

Taking into consideration the whole sample of patients using methylprednisolone, regardless of the duration of MP administration, there was no difference in motor recovery between the MP group and the placebo group. In addition, sensory changes did not reach the significance level set for this study. Similarly, patients treated after eight hours of injury did not show differences in neurological outcomes after treatment.

Analysis of motor improvement after six weeks:

Table 1 summarizes the improvement in motor function in NASCIS II. The subgroup treated within eight hours of injury accounted for 37.9% of the total study sample (185/487).

Patients receiving methylprednisolone (MP) had an initial motor score of 23.7 points, whereas those receiving placebo (PL) had a score of 24 points. After six weeks, the MP group improved 10.6 and the PL group 7.2 points. When final motor scores were compared (initial score plus improvement), MP score corresponded to 34.3 and PL score to 31.2 points of the total 70 points, with a difference of 3.1 points (4.4% of the total 70 points for patients without neurological deficit).

Analysis of motor improvement after six months:

Patients receiving methylprednisolone (MP) had an initial motor score of 23.7 points, whereas those receiving placebo (PL) had a score of 24 points. After six months, the MP group improved 16 and the PL group 11.2 points. When final motor scores were compared (initial score plus improvement), MP score corresponded to 39.7 and PL score to 35.2 points of the total 70 points, with a difference of 4.5 points.

Analysis of motor improvement after one year:

The evaluation of the whole sample of randomized patients, regardless of the start date of treatment, did not show any differences between MP and placebo after one year in either of the three neurological functions (motor function, pinprick response, and touch sensation).

Of the total patients in the initial group receiving MP and PL, 37.5% were analyzed in the subgroup that received medication within eight hours of injury (183/487). Motor function improved 17 points in the MP group and 12 points in the PL group (difference of 5 points in improvement). The difference in the final neurological status of the MP group in comparison with the PL group was of 2.5 points (38.3-35.5), 3.57% of the total 70 points.

B) Results for sensory function

In the six-week analysis, the mean score for pinprick response at baseline was 53 points (60.9% of the total points) in the MP group and 54.4 points (62.5%) in the PL group, with a difference of 1.4 points (1.6%). The MP group improved 8.9 points (group treated within 8 hours of injury) and the PL group improved 4 points, with a difference of 5.9 points. The final score was 61.9 points in the MP group and 58.4 points in the PL group, with

Table 1. Motor scores at baseline, improvement obtained and final score six weeks, six months and one year after injury in the methylprednisolone (MP) and placebo (PL) groups

Period of follow-up		MP	PL	Difference	ℵ2
	Motor score at baseline*	23.7 (33.8%)	24 (34%)	0.3 (0.4%)	
Six weeks	Improvement obtained**	10.6 (15.14%)	7.2 (10.28%)	3.4 (4.8%)	
	Final score***	34.3 (49%)	31.2 (44.5%)	3.1 (4.4%)	p=0.78
	Motor score at baseline*	23.7 (33.8%)	24 (34%)	0.3 (0.4%)	
Six months	Improvement obtained**	16 (22.8%)	11.2 (16%)	3.4 (4.8%)	
	Final score***	39.7 (56.71%)	35.2 (50.28%)	4.5 (6.4%)	p=0.67
	Motor score at baseline*	21.1 (30.1%)	23.8 (34%)	2.7% (0.4%)	
One year	Improvement obtained**	17.2 (24.57%)	12 (17.14%)	5.2 (7.4%)	
	Final score***	38.3 (54.71%)	35.8 (51.14%)	2.5 (3.57%)	p=0.52

*Obtained from the mean motor score for the whole study sample at admission (baseline). **Improvement of the subgroup treated within eight hours of injury. ***Final score of the subgroup treated within eight hours of injury. In parentheses: percentage of the normal total of 70 points (0 to 70). ℵ2 = Chi-square test.

Table 2. Improvement in pain appreciation (pinprick) and superficial sensation (light touch) scores between groups six months after injury

PINPRICK				
Groups	**Methylprednisolone (MP)**	**Placebo (PL)**	**Difference**	**ℵ2**
Score at baseline*	53 (60%)	54.4 (62.5%)	1.4	
Improvement at the final assessment (points)**	12.9	5.9	7	
Final score (Initial score + improvement)***	65.9 (75.7%)	60.3 (69%)	5.6 (6.4%)	p= 0.59
TOUCH				
Groups	**Methylprednisolone (MP)**	**Placebo (PL)**	**Difference**	**ℵ2**
Score at baseline*	54.3 (62%)	55.7 (64%)	1.4	
Improvement at the final assessment (points)**	9.8	4.6	5.2	
Final score (Initial score + improvement)***	64.1 (73%)	60.3 (69%)	3.8 (4.3%)	p=0.71

*Obtained from the mean sensory score for the whole study sample at admission (baseline). **Improvement of the subgroup treated within eight hours of injury. ***Final score of the sample treated within eight hours of study. In parentheses: percentage of the normal total of 87 points (29 to 87) for the final difference between treatment groups. □2 = Chi-square test.

Table 3. Improvement in pain appreciation (pinprick) and superficial sensation (light touch) scores between groups one year after injury

PINPRICK				
Groups	**Methylprednisolone (MP)**	**Placebo (PL)**	**Difference**	**χ^2**
Score at baseline*	51.3 (58%)	52.6	1.3	
Improvement at the final assessment (points)**	10.8	8.4	2.4	
Final score (Initial score + improvement)***	62.1 (71%)	61	1.1 (1.2%)	p= 0.84
TOUCH				
Groups	**Methylprednisolone (MP)**	**Placebo (PL)**	**Difference**	**χ^2**
Score at baseline*	53.3 (61%)	55 (60%)	1.7	
Improvement at the final assessment (points)**	9.4	6.0	3.4	
Final score (Initial score + improvement)***	62.7 (72%)	61 (70%)	1.7 (1.9%)	p=0.90

*Obtained from the mean sensory score for the whole study sample at admission (baseline). **Improvement of the subgroup treated within eight hours of injury. ***Improvement obtained in the sample treated within eight hours of study. In parentheses: percentage of the normal total of 87 points for the final difference between treatment groups. χ^2 = Chi-square test.

a final difference of 3.5 points (4% of the total points) (chi-square test; p=0.80). Regarding touch sensation after six weeks, the MP group scored 54.3 points (62.4%) and the PL group scored 55.7 points (64%) at baseline, with a difference of 1.4 points. The MP group improved 7.1 points and the PL group improved 4 points, with a difference of 3.1 points. The final score was 61.4 points (70%) in the MP group and 59.7 points (68%) in the PL group, with a difference of 1.7 points (1.9%).

Tables 2 and 3 describe the improvement in sensory scores after six months and one year, respectively, and follow the same design of the above-mentioned table for motor improvement, showing initial (baseline) scores and improvement at the end of each study period. The difference in final sensory scores for pain appreciation (pinprick) between groups was 3.5, 5.6 and 1.1 points after six weeks, six months and one year, respectively. Regarding superficial sensation (light touch), the difference for the same study periods was 1.7, 3.8 and 1.7 points, respectively.

2) Results- Studies on complications of MP therapy:

NASCIS II: NASCIS II reported no statistically significant differences between complications in the MP and PL groups, but data were not available for reanalysis.

Study by Matsumoto et al.: MP and PL groups were composed of 23 patients each. The percentage of complications between the MP and PL groups was 56.5 vs. 34.8 (95%CI 0.498-0.064), with no significant difference. When complications were analyzed according to type, the occurrence of pulmonary and gastrointestinal complications was higher in the MP group than in the PL group. There was a trend toward bronchopneumonia (BCP) in the group of patients older than 60 years. There were eight BCP cases in the MP group and one case in the PL group. Probability of BCP in the MP group was 52.2 vs. 4.3% in the PL group. Absolute BCP risk in the MP group was 34.7 vs. 4.3% in the PL group. Increased absolute BCP risk due to use of MP was 47.9% (0.25-0.69), and the necessary number for the occurrence of BCP was two patients. It is worth mentioning that, in that study, the patients' mean age was about 60 years.

Regarding gastrointestinal bleeding (GIB), there were four cases in the MP group and none in the PL group (odds of 17.4 and 0%, respectively). Increased absolute GIB risk due to use of MP was 17.4% (95%CI 0.01-0.32), and the necessary number for the occurrence of damage was six patients.

Discussion

Critical appraisal

Studies using a placebo control group:

Although there is substantial literature on MP use, the number of randomized studies comparing MP with placebo in neurological protection is restricted to two studies (NASCIS II[3] and Matsumoto et al.[40]). NASCIS II was described in two publications six months and one year after injury.[3,4].

The studies by Pointillart et al.[41] and Petitjean et al.[43] were written in English and French, respectively, and have the same results, describing the same study in two different languages and being, therefore, considered as one single study. The study by Pointillart et al.[41] did not use a placebo control group and was, therefore, excluded.

Report of results in NASCIS II:

NASCIS II[3] described the results as the amount of change from baseline neurological examination, instead of measuring neurological status at baseline and at the final assessment. In baseline (pretreatment) groups, there were less neurologically intact patients in the MP group than in the PL group (5 vs. 8.8%). This(ese) study(ies) did not show differences between MP and PL groups. A neurological function improvement was observed only when the subgroup of patients treated within eight hours of injury was analyzed, which accounts only for 38% of the total sample. This effect represented a difference of 3.1 points in neurological improvement between MP and PL groups concerning motor function after six weeks, 4.5 points after six months, and 2.5 points after one year. In neurologically intact individuals, the motor score is 70 points.

No improvement was observed in patients treated with MP after eight hours of injury and in patients with complete motor injury (plegic patients) with sensory preservation (Frankell B) at any moment. The difference revealed to be too small to express a real clinically significant benefit. We attempted to describe the odds ratio for improvement in functional classification, but the original data were not available and the 95% confidence interval (CI) was too wide (-2.9 to 25.5). Studies with wide 95%CI have been classified as level of evidence II.

Subgroup analysis:

Findings based on subgroup analyses should not describe results, but rather formulate hypotheses. NASCIS did not provide the results as absolute data, hindering recalculation of risk increase or decrease and of the necessary number of treatment patients to show benefits or risks.

Definition of the amount of clinically significant improvement:

There is no such a definition in NASCIS II of a cutoff point, which prevented us from defining whether there was presence or absence of clinical improvement. The analysis of results from subgroups without previous sample size calculation yields the possibility of producing results caused by random effects.

The results were obtained from a sample less than 40% of the original study sample.

Both NASCIS II were not associated with a functional independence scale that could reveal an improvement in the patient's functional status. This limitation was corrected in NASCIS III. The functional independence measure (FIM) was used; however, a placebo control group was not used. The real benefit of the increase of 2.5 points in the final motor score one year after injury seems to be clinically insignificant.

Displaying the results as changes from baseline neurological status, before performing an analysis of treatment-induced neurological status in heterogeneous samples, may have contributed to the results.

Analysis model used in the present review:

The method chosen to quantify a possible difference between groups included adding the patient's improvement score to the mean score for groups at baseline, resulting in the final neurological outcome for both groups. Similar to motor scores, improvement in sensory scores was discrete.

Real clinical benefits of MP therapy:

The main discussion about these results refers to the real clinical significance of the difference in the improvement obtained with the use of MP. The results from NASCIS II were not reproduced, and the original data have never been made available for reanalysis.

The study by Matsumoto et al.[40] aimed to investigate complications resulting from MP therapy by means of a randomized, double-blind study comparing complications of MP use with placebo, in patients treated within 8 hours of injury. Mean age was high (60.6 years [18-84]). Inclusion criteria were the same as those used in NASCIS II. The study included only patients treated without surgery for SCI in the cervical spine, with predominantly centro-medullary neurological damage. The use of medication increased the risk of pulmonary and gastrointestinal complications in that study sample.

Conclusion

Due to the modest differences found in the treatments, the results do not suggest clinical benefits.

The use of MP is associated with an increased risk of pulmonary complications and gastrointestinal bleeding in patients aged about 60 years.

Summary of evidence

The differences between motor and sensory final scores of patients in the MP and PL groups were not significant and were minimal in relation to the maximum normal score possible, thus failing to suggest clinical benefits. In addition, the use of MP may be associated with an increased risk of pulmonary complications and gastrointestinal bleeding.

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