Treatment of Acute Spinal Cord Injuries: A Survey Among Iberolatinoamerican Spine Surgeons – Part 1: Use of High-Dose Corticosteroids

Tratamento das lesões agudas da medula espinal: Uma pesquisa entre cirurgiões de coluna iberoamericanos – Parte 1: uso de corticosteroides em altas doses

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Abstract

Objective The aim of the present study was to evaluate the current practice of using of methylprednisolone sodium succinate (MPSS) in acute spinal cord Injuries (ASCIs) among spine surgeons from Iberolatinoamerican countries.

Methods A descriptive cross-sectional study design as a survey was conducted. A questionnaire composed of 2 sections, one on demographic data regarding the surgeons and MPSS administration, was sent by email to members of the Sociedad Ibero Latinoamericana de Columna (SILACO, in the Spanish acronym) and associated societies.

Results A total of 182 surgeons participated in the study: 65.4% (119) orthopedic surgeons and 24.6% (63) neurosurgeons. Sixty-nine (37.9%) used MPSS in the initial management of ASCIs. There were no significant differences between countries ($p = 0.451$), specialty ($p = 0.352$), or surgeon seniority ($p = 0.652$) for the use of corticosteroids in the initial management of ASCIs. Forty-five (65.2%) respondents reported using an initial high-dose bolus (30 mg/Kg) followed by a perfusion (5.4 mg/kg/h). Forty-six (66.7%) surgeons who used MPSS only prescribed it if the patients presented within 8 hours of the ASCI. Most of the surgeons (50.7% [35]) administered

Keywords
- corticosteroids
- spinal cord injuries
- surveys and questionnaires

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high-dose corticosteroids because of the conviction that it has clinal benefits and improves neurological recovery.

Conclusion Results from the present survey show that MPSS use in ASCI is not widespread within spine surgeons and that the controversy regarding its use remains unresolved. This is probably due to the low level of evidence of the available data, to variations over the years, to inconsistencies in acute care protocols, and to health service pathways.

Resumo

Objetivo O objetivo do presente estudo foi avaliar a prática atual de uso do succinato sódico de metilprednisolona (MPSS, na sigla em inglês) nas lesões agudas da medula espinal (LAMEs) entre cirurgiões de coluna de países ibero-americanos.

Métodos Um estudo transversal descritivo foi realizado. O questionário continha duas seções, uma sobre os dados demográficos dos cirurgiões e acerca da administração de MPSS, e foi enviado por correio eletrônico aos membros da Sociedad Ibero Latinoamericana de Columna (SILACO, na sigla em espanhol) e sociedades associadas.

Resultados No total, 182 cirurgiões participaram do estudo: 65,4% (119) eram cirurgiões ortopédicos e 24,6% (63), neurocirurgiões. Sessenta e nove (37,9%) usaram MPSS no tratamento inicial da LAME. Não houve diferenças significativas entre países ($p = 0{,}451$), especialidades ($p = 0{,}352$) ou senioridade do cirurgião ($p = 0{,}652$) em relação ao uso de corticosteroides no tratamento inicial da LAME. Destes, 45 (65,2%) relataram a administração de um bolus de alta dose (30 mg/Kg) seguido por perfusão (5,4 mg/Kg/h). Quarenta e seis (66,7%) dos cirurgiões que usam MPSS apenas o prescrevem a pacientes tratados nas primeiras 8 horas após a LAME. A maioria dos cirurgiões (50,7% [35]) administra corticosteroides em alta dose devido à convicção de seus benefícios clínicos e melhora da recuperação neurológica.

Conclusão Os resultados do presente questionário mostram que o uso de MPSS na LAME não está disseminado entre os cirurgiões de coluna e que a controvérsia sobre sua administração ainda não foi resolvida. É provável que isto se deva ao baixo nível de evidência dos dados existentes, a variações ao longo dos anos, a inconsistências nos protocolos terapêuticos agudo e a diferentes sistemas de saúde.

Palavras-chave
- corticosteroides
- inquéritos e questionários
- traumatismos da medula espinal

Introduction

The ideal management of acute spinal cord injuries (ASCIs) has been a matter of long-lasting debate and investigation.[1–3] The recommendations for the use of high-dose corticosteroids, particularly methylprednisolone sodium succinate (MPSS) in the management of patients with ASCI has changed over the years and, despite all the efforts, the optimal pharmacological treatment is still controversial.[4,5] Several studies, including the National Acute Spinal Cord Injury Studies (NASCIS), have investigated the safety and effectiveness of high-dose corticosteroids. While in 2002 the clinical practice guidelines from the Congress of Neurological Surgeons (CNS) and from the American Association of Neurological Surgeons (AANS) recommended the administration of MPSS for either 24 or 48 hours despite the lack of solid evidence, in 2013 the same group recommended against this practice due to concerns of increased adverse events.[6,7] In 2017, a multidisciplinary guideline development group conducted a systematic review of the literature and issued a clinical practice guideline recommending the administration of high-dose MPSS for 24 hours (and not 48 hours), only when started within the first 8 hours after injury, although they advised that the quality of evidence was moderate, and the strength of the recommendation was weak.[4]

Despite the latter recommendation, low level of evidence in most studies, variations over the years, inconsistencies in acute care protocols, and health service pathways resulted in clinical practice variation and disagreement regarding the best practice. The aim of the present study was to evaluate the current practice of MPSS administration in ASCI patients among spinal surgeons from Iberolatinoamerican countries.

Methods

A descriptive cross-sectional study designed as a survey was conducted. The survey had two intents: to understand the current practice of MPSS use and the timing for surgery in

spinal cord injury (whose results are part of a separate study).

A link to a questionnaire was sent by email, requesting the participation of members of the Sociedad Ibero Latinoamericana de Columna (SILACO, in the Spanish acronym) and associated societies. Most questions had multiple response choices and an answer to all questions was mandatory. The questionnaire had Portuguese and Spanish versions and was composed of two sections: surgeon demographic data and data on MPSS administration. The questions regarding the administration of MPSS are detailed in the results section. A reminder to answer the questionnaire was sent twice and the answers were obtained between May 6th and June 30th, 2020.

IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. The groups were compared using the Student *t*-test and the Mann-Whitney test (quantitative variables) or with the Fisher test and the Pearson chi-squared test (qualitative variables). Statistical significance was set at $p < 0.05$.

Results

Demographic Data

A total of 182 surgeons participated in the study; 65.4% (119) were orthopedic surgeons and 34.6% (63) were neurosurgeons. More than 75% of the participants were from Portugal, Brazil, or Spain; countries with < 30 participations were grouped as Central and South America ($n < 30$) and 17 reported from Ecuador (9.3%), 12 from Paraguay (6.6%), 5 from Bolivia (2.7%), 3 from Chile (1.6%), 2 from the Dominican Republic (1.1%), 2 from Argentina (1.1%), 1 from Mexico (0.6%), and 1 from Uruguay (0.6%). Most (56.6%) surgeons had > 10 years of spine surgery practice. A total of 109 (59.9%) respondents worked in an institution with a spinal unit. In case of need for surgical treatment, 162 respondents treated the patient in their institutions, while 20 referred the patient to another institution (►**Table 1**).

Table 1 Characteristics of the Participants

Characteristics (total)	$n = 182$
Specialty	
Orthopedic	119 (65.4%)
Neurosurgery	63 (24.6%)
Country	
Portugal	54 (29.7%)
Brazil	53 (29.1%)
Spain	32 (17.6%)
Central and South America ($n < 30$)	43 (23.6%)
Practice in spine surgery	
< 5 years	43 (23.6%)
5–10 years	36 (19.8%)
> 10 years	103 (56.6%)
Spinal Unit	
Yes	109 (59.9%)
No	73 (40.1%)

Questions

1) Do you routinely administer corticosteroid therapy to patients with ASCI?

In response to this question, 69 (37.9%) surgeons stated that they used corticosteroids in the initial management of ASCI. There was no significant difference between countries ($p = 0.451$), specialty ($p = 0.352$), surgeon seniority ($p = 0.652$), or type of institution (with or without dedicated spinal unit) ($p = 0.404$) for the prescription of corticosteroids in the initial management of ASCI (►**Table 2**).

2) What is the dose that you prescribe?

A total of 45 of the 69 surgeons who used corticosteroids (65.2%) reported using a high-dose steroid bolus (30 mg/Kg) followed by a perfusion (5.4 mg/Kg/h); 13 (18.9%) used a high-dose bolus (30 mg/Kg) only, and 11 (15.9%) administered a low-dose steroid bolus (125 mg) followed by a perfusion (5.4 mg/Kg/h). There were no significant differences between countries ($p = 0.086$), specialty ($p = 0.368$), surgeon seniority ($p = 0.226$), or type of institution (with or without a dedicated spinal unit) ($p = 0.135$) for the corticosteroids dose administration.

3) In case of perfusion, how long do you keep it?

Of the 56 surgeons who reported using perfusion, 30 (53.61%) maintained the perfusion for 24 hours, and 26 (46.4%) maintained the perfusion for 48 hours or longer. There was a significant difference in the perfusion duration between countries ($p < 0.01$), despite the low frequencies for each group. There were no differences in specialty ($p = 0.088$), surgeon seniority ($p = 0.712$), or type of institution (with or without a dedicated spinal unit) ($p = 0.129$) for the perfusion duration (►**Table 3**).

4) Corticosteroids initiation in relation to time after injury.

Out of those who used corticosteroids, 46 (66.7%) respondents only prescribed them to patients within 8 hours of ASCI, while 23 (33,3%) administered corticosteroids to patients with acute SCI even after 8 hours after injury. Eleven respondents started that they administered the perfusion within 12 hours, 5 within 24 hours, and 7 started the perfusion until 48 hours after the injury.

There were no significant differences between countries ($p = 0.159$), specialty ($p = 0.715$), surgeon seniority ($p = 0.606$), or type of institution (with or without a dedicated spinal unit) ($p = 0.861$) for the corticosteroid initiation in relation to time after injury.

5) In patients with spinal shock, do you also institute corticosteroids?

Out of the 69 surgeons who routinely prescribed corticosteroids, 57 (82.6%) still prescribed them in cases of spinal shock, and 12 (17.4%) surgeons did not use corticosteroids in these cases. There were no significant differences between

Table 2 Demographic characteristics and corticosteroids administration

	n	Corticosteroids		Proportion (%)	*p-value*
		Yes	No		
Specialty					0.352
Orthopedic	119	48	71	40.3	
Neurosurgery	63	21	42	33.3	
Country					0.451
Portugal	54	19	35	35.2	
Brazil	53	20	33	37.7	
Spain	32	16	16	50	
Central and South America ($n < 30$)	43	14	29	32.6	
Practice in spine surgery					0.652
$<$ 10 years	79	31	48	39.2	
$>$ 10 years	103	38	65	36.9	
Spinal unit					0.404
Yes	109	44	65	40.4	
No	73	25	48	34.2	

Table 3 Demographic characteristics and perfusion duration

	24-hour perfusion	$\geq$ 48-hour perfusion	Proportion of respondents who perform 24-hour perfusion (%)	*p-value*
Specialty				0.088
Orthopedic	18	21	46.2	
Neurosurgery	12	5	70.6	
Country				$<$ 0.01
Portugal	10	1	90.9	
Brazil	8	4	66.7	
Spain	7	9	38.9	
Central and South America ($n < 30$)	5	12	29.4	
Practice in spine surgery				0.712
$<$ 10 years	13	10	56.5	
$>$ 10 years	17	16	51.5	
Spinal Unit				0.129
Yes	23	15	60.5	
No	7	11	38.9	

countries ($p = 0.210$), specialty ($p = 0.906$), surgeon seniority ($p = 0.075$), or type of institution (with or without a dedicated spinal unit) ($p = 0.908$) for corticosteroid administration in case of spinal shock.

6) What is the reason for you to institute corticosteroids? A total of 35 surgeons (50.7%) reported administering high-dose corticosteroids due to their conviction regarding its clinal benefits and improved recovery: 16 (23.2%) for legal concerns and 18 (26.1%) to follow an institutional protocol.

Discussion

Acute spinal cord injury is a devastating condition and, despite extensive research, very little can be offered to

patients other than timely surgical decompression and stabilization. Corticosteroids have been used due to their potent anti-inflammatory properties and to their potential role in the inhibition of the inflammatory cascades that contribute to secondary spinal cord damage after ASCI.[8]

Over the last 30 years, research has investigated the effectiveness of corticosteroid use in ASCI. In the decade of 1990, with the publication of the second NASCIS trial, MPSS appeared as the first therapeutic drug to aid in the management of ASCI,[9] and its use over the forthcoming years was widespread. However, the use of MPSS has gradually become a matter of concern as its clinical effectiveness was debatable and due to concerns regarding adverse side effects.[10] This led to changes in recommendations from some of the most relevant medical societies that first recommended its use and later advised against it.

In 2017, a systematic review of the literature was conducted, and a multidisciplinary Guideline Development Group used it, in combination with their expertise, to publish a practice recommendation for MPSS in ASCI. This group agreed suggesting the 24-hour perfusion of high-dose MPSS for adult patients within 8 hours of ASCI, with a moderate quality of evidence and a weak strength of recommendation. This recommendation was supported by the major finding that, although there were no overall differences in the motor scores in patients treated with MPSS compared with those not receiving corticosteroids, in the subgroup of patients in whom MPSS was administered within 8 hours of injury, there was an overall improvement in mean motor scores at 6 and 12 months (effect size: 3 randomized controlled trials: 3.88; $p = 0.02$; 3 randomized controlled trials + 1 prospective cohort = 3.21; $p = 0.04$) with no statistical difference in risk of complications for a 24-hour perfusion.[6]

Over the past years, several surveys have been conducted to analyze MPSS use and associated practices.[11] The number of surgeons that routinely used MPSS in the United Kingdom decreased from 68% in 2004 to 19% in 2012, and a Swiss study reported a decrease from 96% in 2001/2003 to 23% in 2008/2010.[12,13] These changes were probably justified by the NASCIS III study and the subsequent changes in clinical guidelines.[14]

A 2015 survey including 970 AOSpine Latin America members from 20 countries found that 56.1% of the participants routinely used MPSS, with an association with country, specialty, length of clinical practice, and number of ASCIS treated yearly, but only half of the clinicians reporting the use of MPSS did so for believing in its clinical benefit.[15]

Thus, it would be expected that after the publication of the 2017 guidelines, there would be an increase in MPSS administration for ASCI within 8 hours of injury. This was not verified in the present study, as the number of surgeons using MPSS was 37.9%, as already verified in a Latin American survey from 2015.[15] The authors also found that even though 37.9% of the surgeons admitted administering MPSS, no more than 35% of them did so according to the guidelines – a high-dose corticosteroid bolus (30 mg/Kg) + perfusion (5.4 mg/Kg/h) within 8 hours after the injury.

A worldwide corticosteroid prescription survey performed in 2018 with 2,659 participants reported that corticosteroids were used by 52.9% surgeons with the administration of MPSS inversely influenced by the number of ASCI patients treated per year.[11] Although the proportion of MPSS administration was similar in the present study, MPSS prescription was not affect by the surgeon seniority, country, or specialty.

Inconsistencies regarding the prescription were a constant in the present study, and it was not possible to identify any factor influencing them (country, specialty, surgeon seniority, or type of institution [with or without a dedicated spinal unit]). To better uniformize the treatment of these patients, more research and more information is needed, as well as the definition of protocols, to standardize corticosteroid prescription.

To the best of our knowledge, this is the first Iberolatinoamerican study performed after the 2017 guidelines regarding MPSS administration. Nevertheless, the present study has some limitations, starting with the relatively small number of participants from some countries and the fact that it is performed post-hoc, so the information bias is inherent.

Conclusion

The results from the present survey show that MPSS use in ASCI is not widespread within spine surgeons of Iberolatinoamerican countries and that the controversy regarding its use remains unanswered. This is probably due to the low level of evidence of the available data, to variations over the years, and to inconsistencies in acute care protocols.

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Conflict of Interests
The authors declare have no conflict of interests to declare.

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