

Guidelines for the Management of Patients With Spinal Cord Injury: The Use of Methyprednisolone Sodium Succinate

M. Fehlings, J. Wilson, B. Aarabi, P. Anderson, P. Arnold, D. Brodke, A. Burns, R. Chen, K. Chiba, J. Dettori, J. Furlan, L. Holly L, S. Howley, T. Jeji, S. Kalsi-Ryan, M. Kotter, S. Kurpad, K. Kwon, R. Marino, A. Martin, E. Massicotte, G. Merli, J. Middleton, H. Nakashima, N. Nagoshi, K. Palmieri, M. Shamji, A. Singh, A Skelly, L. Tetreault, A. Yee, J. Harrop



Introduction

Given its potent anti-inflmmatory actions, methylprednisolone sodium succinate (MPSS) has a long history of use across a wide spectrum of disease. The objective of this study is to develop guidelines that outline the appropriate use of MPSS in patients with traumatic spinal cord injury.

Methods

A systematic review of the literature was conducted to address the following key questions: (1) what is the efficacy, effectiveness and safety of MPSS compared with no pharmacologic treatment?; and (2) what is the evidence that MPSS has differential efficacy or safety in subpopulations?

Inclusion and Exclusion Criteria Component Adults with traumatic acute spinal cord injury (cor Pediatric patients < 13 years of Pregnancy Penetrating injuries to spinal cord Cord compression due to tumor, hematoma, degenerative disease (e.g. without neurological deficit following trauma Intervention mogrator Placebo Standard care without pharmacologic intervention Efficacy/effectiveness Change in motor scores Change in sensation (light touch, pinprick) Non-clinical out afety Complications, adverse events KQ 1, 2, 3: Comparative studies (RCTs and F/U rate of at least 50% $n \ge 10$ per group Observational comparative studies must control for F/U rate of at <50% n < 10 per group No control for injury severity severity of spinal cord injury as evaluated by mote status at baseline and/or complete or incomplete is KQ 3: Subgroup analyses from comparative studie Studies published or translated into English in pee Duplicate publications of the which do not report on diffe Single reports from multice White papers hed in late

A multidisciplinary guideline development group used this information, in combination with their clinical expertise, to develop recommendations for the use of MPSS. The benefits and harms, financial impact, acceptability, feasibility and patient preferences of each recommendation were carefully considered.



Results

Three randomized controlled trials (four publications) and one prospective cohort study evaluated the efficacy and safety of MPSS, while three additional studies (two randomized controlled trials and one prospective cohort study) provided further evidence on its safety.



1) There were no differences in motor scores at any time point in patients treated with MPSS compared to those not receiving steroids. Pinprick sensation was significantly improved at six months in one randomized controlled trial but not in two other trials at 12 months. Similar results were seen for light touch.





2) When MPSS was administered within 8 hours of injury, pooled results at 6- and 12-months indicate modest improvements (3.88, 95% CI: 0.50, 7.27, p=0.02) in mean motor scores in the MPSS group compared with the control group.

Motor Scores in Patients Treated with MPSS within 8 hours of Injury

	MPSS			Control				Mean Difference	Mean Difference		
Study	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
RCT											
Bracken 1990-3	15.99	13.06	65	11.21	13.03	68	49.2%	4.78 [0.34, 9.22]			
Otani 1994	14.2	15	70	10.3	15.4	47	30.5%	3.90 [-1.73, 9.53]			
Pointillart 2000 Subtotal (95% CI)	18	27.4	27 162	23.7	24.6	23 138	4.7% 84.4%	-5.70 [-20.12, 8.72] 3.88 [0.50, 7.27]	-		
Heterogeneity: Tau ²	= 0.00; 0	$hi^2 = 1$.85, df	= 2 (P -	= 0.40);	$I^2 = 05$	6		-		
Test for overall effect	t: Z = 2.2	5 (P =	0.02)								
Prospective cohort											
Evaniew 2015 Subtotal (95% CI)	13.7	15.6	44 44	14.1	21.6	44 44	15.6% 15.6%	-0.40 [-8.27, 7.47] -0.40 [-8.27, 7.47]			
Heterogeneity: Not a	pplicable										
Test for overall effect	t: Z = 0.1	0 (P =	0.92)								
Total (95% CI)			206			182	100.0%	3.21 [0.10, 6.33]	-		
Heterogeneity: Tau ²	= 0.00; 0	$hi^2 = 2$.81, df	= 3 (P =	= 0.42);	$1^2 = 05$	6		has to be a		
Test for overall effect	t: Z = 2.0	2 (P =	0.04)						-10 -5 0 5 1		
	Gerensee	Chil -	0.06	45 - 1.6	0 - 0 2	21 12 -	OF		ravors control Favors MPSS		

3) There was no statistical difference between treatment groups in the risk of death, wound infection, GI hemorrhage, sepsis, urinary tract infection pneumonia or decubiti.

			MPSS			Control				
Outcome	Author (Near)	Events	Total	(%)	Events	Total	(%)	Effect Estimate (%)	Weight (%)	RD (%) (95% CI
Death	Bracken 1990-2	7	162	(4.32)	12	171	(7.02)		28%	-2.70[-7.64,2.25
	Otani 1994	1	81	(1.23)	3	70	(4.29)		24%	-3.05[-8.37,2.27
	Matsumoto	0	23	(0)	0	23	608		11%	0.00[-8.08,8.08
	Evaniew 2015	0	44	(0)	0	44	100		37%	0.00[-4.33,4.33
	Pooled: Overall Effect P	8-0.261;1	310 Heteroge	(2.58) eneity: IA	15	308	(4.87)	-		-1.51 [-4.13, 1.12
Wound Infection	Bracken 1991-2		166	(2.05)	6	167	(3.99)		10%	3.46(-1.45.8.37
would intection	Pointillart 2000	0	35	101	0	30	101		21%	-0.221-6.08.5.63
	Matsumoto	0	23	101	0	23	100		1106	0.00[-8.08.8.08
	Evaniew 2015	0	44	101	0	44	600		38%	0.00[-4.33.4.33
	Pooledt	ii.	258	(4.26)	6	264	(2.27)			0.98[-1.70.3.66
	Overall Effect: P -	0.472	-leteroge	meity: PS	2=0%					
Gl Hemorrhage	Bracken 1990-2	7	156	(4.49)	5	167	(2.99)		54%	1.49 [-2.66 , 5.64
	Pointillart 2000	2	35	(5.71)	0	30	EDB		- 31%	5.33[-4.08,14.75
	Matsumoto	4	23	(17.39)	0	23	100		- 15%	16.67 [0.04, 33.29
	Pooled:	13	214	(6.07)	5	220	(2.27)			4.51 [-1.92, 10.94
	Overall Effect: P	0.169;1	leteroge	meity: IA	2 = 39.9%					
Sepsis	Bracken 1990-2	9	156	(5.77)	11	167	(6.59)		47%	-0.82 (-6.07 , 4.43
	Pointillart 2000	-4	35	(11.43)	1	30	(3.33)		- 9%	8.10[-4.25_20.44
	Matsumoto	1	23	(4.35)	0	23	ED0		- 10%	4.17 [-7.08, 15.41
	Evaniew 2015	1	44	(2.27)	1	-44	(2.27)		34%	0.00[-6.23.6.23
	Pooled: Overall Effect: P +	15 0.6% H	258 eteroger	(5.81) wity: M2	13	264	(4.92)	-		0.74[-2.88, 4.35
DE	Bracken 1995-2	6	156	(1.65)	2	162	(1.2)		81%	2.651-0.79. 6.09
	Pointillart 2000	11	35	(31.43)		30	(30) -		- 25	1.43[-21.05.23.91
	Evaniew 2015	2	44	14.551	0	44	101		1876	4.441 -2.92.11.80
	Broject	19	216	(8.09)		241	14.563			
	Overall Effect: P	0.052;1	teteroge	melty: PA	2=0%		(424)	-		234[-0.15,6.03
Urinary Infection	Bracken 1990-2	71	156	(45.51)	27	167	(45.11)		39%	-0.59[-11.47,10.28
	Pointillart 2000	8	35	(22.86)	4	30	(13.33)		+ 13%	9.521 -8.96.28.00
	Matsumoto	1	23	(4.35)	1	23	(4.35)		33%	0.00[-11.79,11.79
	Evaniew 2015	11	44	(25)	9	44	(20.45)		- 15%	4.55[-12.94,22.03
	Pooled:	91	258	(35.27)	9 1	264	(34.47)			1.731 -5.04, 8.49
	Overall Effect P -	0.617;1	leteroge	meity: IA	2 = 0%					
Pneumonia	Bracken 1990-2	44	156	(28.21)	41	167	(24.55)		67%	3.65 [-5.96. 13.27
	Evaniew 2015	7	44	(15.91)	4	44	(9.09)		- 33%	6.82 [-6.93 . 20.56
	Pooled:	51	200	(25.5)	45	211	(21.33)			4.69[-3.19, 12:57
	Overall Effect P	0.243;1	leteroge	meity: IA	2 = 0%					
Decubitis	Bracken 1990-2	29	156	(18.59)	32	167	(19.16)		43%	-0.57 [-9.11 , 7.97
	Matsumoto	0	23	(0)	1	23	(4.35)		30%	-4.17[-15.41, 7.08
	Evanieur 2015		44	(13.64)		44	14 5 53		27%	9.091 -3.77 20.95
	Beelest		222	(16.75)		224	114.040		- 1/10	
	Overall Effect: P -	0.782;1	4eteroge	meity: M	2 = 26.6%	- 14	[14.30)			0.991 -6.01, 7.98
One or More Complications	Wilson 2012	78	213	(11.40	82	178	(46.07) -		1025	-12.59[-22.10, -3.09
one or more complications	Pooledt	78	233	(33.48)	82	178	(46.07)		TOPH	-13/01-3310 - 500
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Evidence Based Recommendations and Guidelines

Our recommendations were: (1) "We suggest not offering a 24-hour infusion of high dose MPSS to adult patients who present after 8 hours of acute SCI"; (2) "We suggest that a 24 hour infusion of high dose MPSS be offered to adult patients within 8 hours of acute SCI as a treatment option"; and (3) "We suggest not offering a 48-hour infusion of high dose MPSS for adult patients with acute SCI."

Conclusions

These guidelines should be implemented into clinical practice to improve outcomes and reduce morbidity in patients with SCI by encouraging clinicians to make evidence-informed decisions.