COMPARATIVE ANALYSIS OF THE EFFECT OF STEROID THERAPY AND BLOOD PRESSURE MAINTENANCE ON THE MID-TERM OUTCOMES OF SPINAL CORD INJURY

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Objective. To analyze the dynamics of neurological symptoms and the structure of complications when using methylprednisolone and the method of maintaining target values of mean arterial pressure during surgical treatment of patients in the acute period of spinal cord injury (SCI).
Material and Methods. The study included 110 patients in the acute period of SCI with compression of spinal cord segments who were admitted to the clinic from January 2012 to March 2018 and underwent decompression and stabilization surgery within the first 2–3 hours after admission. In order to improve the blood supply to the damaged segments of the spinal cord and to prevent multiple organ failure, the main direction of intensive care in two groups of patients was to maintain the target blood pressure at the level of 85–90 mm Hg during the first 7–10 days. The MPD group included 43 patients who received methylprednisolone as a neuroprotector at a dose of 30 mg/kg bolus within the first hour after admission, followed by infusion at a dose of 5.4 mg/kg/h for 23 hours; and the MAP group included 67 patients who did not receive methylprednisolone. Non-invasive monitoring of central hemodynamic parameters was carried out on the basis of impedance cardiography data. The objective status of patients and data of X-ray diagnostics at the time of preoperative examination and during instrumental studies, as well as in 3–14 day intervals and in the mid-term (up to 4–6 months) postoperative period were analyzed.
Results. In the MPD group, 22 patients had ASIA type A neurological deficit, and an increase in ASIA grade was observed only in 4 (18 %) of them. There were 18 patients with incomplete injury in this group, and 9 of them (50 %) had a positive trend. In the MAP group, 38 patients had ASIA type A, out of them 11 (29 %) improved, and 28 patients had ASIA type B, C or D, out of them 17 (61 %) showed positive dynamics of neurological symptoms. No statistically significant differences were found. In the MPD group, complications such as nosocomial pneumonia and acute endobronchitis were observed three times more often, pulmonary embolism and decubital soft tissue ulcers – four times more often, and sepsis, acute respiratory distress syndrome and surgical site infection – two times more often. There were statistically significant differences in the incidence of nosocomial pneumonia and acute endobronchitis between MPD and MAP groups ($p = 0.004$ and $p = 0.002$, respectively.)
Conclusion. Maintaining mean arterial pressure at 85–90 mm Hg during the first 7–10 days after admission to the hospital allowed achieving a greater number of cases of improvement in the neurological status of patients, in contrast to the use of methylprednisolone. The use of methylprednisolone in patients with acute SCI increased the risk of nosocomial pneumonia or acute endobronchitis by 2.91 times ($p = 0.003$).

Key Words: spinal cord injury, methylprednisolone, neurological symptoms, blood pressure maintenance.
Please cite this paper as: *Rerikh VV, Pervukhin SA, Lukinov VL, Rerikh KV, Lebedeva MN. Comparative analysis of the effect of steroid therapy and blood pressure maintenance on the mid-term outcomes of spinal cord injury. Hir. Pozvonoc. 2020; 17(4):43–53. In Russian.*
DOI: http://dx.doi.org/10.14531/ss2020.4.43-53.

Spinal cord injury (SCI) is a serious social problem. Most patients with these injuries are the working-age population, and their treatment requires expensive resource-intensive surgical intervention followed by long-term rehabilitation [1, 2]. The incidence rate of SCI worldwide ranges from 15 to 40 per million population per year [3], and the prevalence rate is approximately 750 cases per million [4].

In SCI, there is a distinction between primary and secondary spinal cord injury [4]. The primary injury occurs immediately at the time of trauma and is a mechanical damage to the nervous tissue accompanied by death of neurons, disruption of axonal connections, and hemorrhage. A few minutes after primary injury, pathophysiological and biochemical reactions begin [5], which aggravate the injury and are called secondary injury. The literature describes dozens of secondary injury mechanisms: hemorrhage [6], ischemia, hypoxia, and endothelial damage [7], lipid peroxidation and oxidative stress [8], inflammation [9], immune cellular response cytokine effects [10], neuronal apoptosis [11], initialization of astroglial scar formation [12], etc.

One of the leading approaches for treating patients in the acute phase of SCI is to minimize the consequences of

secondary injury to the spinal cord by its urgent surgical decompression and timely initiation of neuroprotective therapy [13], the most common and long-used variant of which is administration of the so-called high doses of methylprednisolone on the first day after injury [14]. However, for several decades, this treatment option has divided clinicians and researchers around the world into its supporters and opponents because of the risks of infectious complications and the persisting contradictions regarding the efficacy of neuroprotective action of the drug, including different doses and time of administration [15–19]. The situation has not been changed even by large multicenter studies of methylprednisolone use in acute SCI (National Acute Spinal Cord Injury Study (NASCIS) I, II, and III) as well as repeated retrospective analyses of their results [20, 21].

According to the clinical guidelines of the AO Spine global community, which were developed on the basis of a systematic review of the literature and published in 2017, the use of methylprednisolone is not mandatory; it is just a therapeutic option [22]. Out of the methodological wordings of the strength of recommendations "we recommend" and "we suggest", Fehlings et al. [22] chose the latter: 24-hour infusion of methylprednisolone , starting no later than 8 h after injury, may lead to a slight increase in muscle strength assessed in patients using the American Spinal Injury Association (ASIA) scale in the long-term postoperative period [22].

The literature reports a number of neuroprotective techniques that have demonstrated encouraging results in experimental studies, but a very limited effect in clinical trials [23]. The neuroprotective techniques that, according to some authors [24, 25], have prospects in clinical practice include maintenance of adequate blood pressure by constant infusion of vasopressors and instrumental control of the target hemodynamic parameters (85–90 mm Hg), which can limit secondary spinal cord injury and potentially improve neurological symptoms.

The study, the results of which we partially reported in [26], was based on the existing controversies between the use of methylprednisolone for SCI and a relatively small number [27] of publications on the results of clinical application of adequate blood pressure maintenance.

The study purpose was to analyze changes in neurological symptoms and type of complications associated with the use of methylprednisolone and a technique for maintaining target mean arterial pressure during surgical treatment of patients in the acute phase of SCI.

The study objectives were as follows:

1) to determine the severity of neurological disorders in patients in the acute phase of SCI by using the ASIA scale and reveal the differences in their changes during the follow-up period in groups using various neuroprotective techniques;

2) to determine the nosological forms of complications associated with the treatment of patients and compare their rate in the study groups.

Material and Methods

The study was a retrospective analysis of a prospective study conducted between January 2012 and March 2018. We analyzed medical history, radiographs, and outpatient medical records of 262 patients hospitalized in the acute phase of SCI. Of these, we selected 174 patients with neurological deficits of ASIA (American Spinal Injury Association) grade A to D and persistent compression of the spinal cord segments. After excluding patients with drowning and pulmonary contusion, data of 110 patients were finally included in the study.

Patients included in the study at different times after injury underwent urgent decompression and stabilization surgery 2–3 h after admission to the hospital.

We analyzed the data of objective patient examination and radiographs obtained at preoperative examination, during instrumental studies, at day 3–14, and in the mid-term (up to 4–6 months) postoperative period.

The neurological status of patients was assessed using the ASIA scale. The neurological status was considered favorable if it improved by one or more grade compared with the baseline neurological grade.

After admission to the hospital, all patients required intensive therapy aimed at monitoring and correcting hemodynamics and respiratory disorders, which continued in the postoperative period in the intensive care unit. The criterion for group formation was inclusion of methylprednisolone in intensive therapy.

Until December 2014, patients included in the study received methylprednisolone as a neuroprotective agent at a dose of 30 mg/kg bolus within the first hour after admission to the hospital, followed by infusion at a dose of 5.4 mg/kg/h for 23 h. These patients constituted the MPD study group (n = 43).

Since January 2015, patients did not receive methylprednisolone. These patients constituted the MAP group (n = 67). Maintenance of adequate perfusion pressure was the main goal of intensive therapy in the selected groups to improve blood supply to the damaged segments of the spinal cord and prevent multiple organ failure. Central hemodynamic parameters were non-invasively monitored based on impedance cardiography data (NICCOMO monitor, Medis Medizinische Messtechnik GmbH, Germany).

Drugs of choice to ensure adequate perfusion pressure with target mean blood pressure (MBP) 85–90 mm Hg were 0.02 % noradrenaline (norepinephrine) 0.05–0.5 μg/kg/min; 0.5% dopamine at a dose of 1.0–10.0 μg/kg/min; 0.5 % dobutamine at a dose of 1.0–10.0 μg/kg/min. Norepinephrine was the drug of choice for the normal range of the cardiac index (3.5–4 L/min/m2). Dobutamine was used for cardiac index values <3.5 L/min/m2 [28, 29]. Hemodynamic support was performed for 7–10 days.

All complications were taken into account in patients of both groups; after relief of the complications, they were discharged for outpatient treatment

or transferred to specialized centers of SCI care for further rehabilitation. The groups were divided into subgroups 1, 2, and 3 according to the time between injury and spinal cord decompression: up to 8 h (subgroup 1), 8 through 24 h (subgroup 2), and 24 h or more (subgroup 3).

The baseline neurological status in the subgroups is shown in Table 1.

There were significant differences only in the severity of ASIA grade B neurological deficit in subgroup 3, which was taken into account in the subsequent analysis (Table 1).

We suggested that the refusal to use methylprednisolone in the acute phase of SCI would not reduce the number of complications during treatment of patients and would not compromise possible improvement of neurological symptoms. On the basis of this suggestion, null hypotheses of the study were accepted:

1) the rate of improvement in the neurological status in patients of the study groups will not differ;

2) the rate of complications in the study groups will be the same.

Statistical methods. Continuous data on the age and stenosis percentage were tested for normality using the Kolmogorov – Smirnov type test [30] (Table 2) and for equality of variances using the Fisher's F test. According to the test results presented in Table 1, the distributions of continuous data were compared using the nonparametric unpaired Mann – Whitney U test with evaluation of the distribution bias between the MPD and MAP groups and generation of a 95 % confidence interval for the bias (95 % CI) designated as the difference in the tables. Continuous data are presented as median [first quartile; third quartile] (MED [IQR]).

Binary data are presented as follows: number, percentage [lower limit of the 95% CI; upper limit of the 95 % CI], with the 95 % CI limits being calculated using the Wilson formula. The number of patients (%) in each category was calculated in categorical data. The unpaired two-tailed Fisher's exact test was used to compare binary and categorical parameters between the MPD and MAP groups. The Benjamini–Hochberg method was used to correct the errors of an achieved significance level p due to multiple comparisons. The difference between binary data was calculated as the odds ratio and the risk difference with generation of 95 % CI for each value. The paired McNemar test was used to compare categorical data on changes in the neurological status of patients within the MPD and MAP groups.

Statistical hypotheses were tested at a critical significance level $p = 0.05$, i.e. the difference was considered statistically significant if $p < 0.05$. All statistical calculations were performed in the RStudio software (version 1.2.5001) using R language (version 3.6.1).

Results

The time interval, which was spent for decompression and served the basis to compose the subgroups, included the time required for the call and the arrival of the ambulance, primary diagnosis at the site of injury, coordination and transportation of the patient to the emergency department (in particular, from the hospital where the patient was initially admitted), examination of the patient, making a diagnosis, preparation of the patient for urgent surgery, starting surgery, and decompression of the spinal cord (reduction of the vertebra, resection of a displaced vertebral body fragment, etc.). Males accounted for a significant proportion (over 80 %) of patients with SCI. The mean age was 34.3 ± 12.3 years. There were no significant differences in gender and age between the groups (Table 3).

Falls, including diving accidents (diving into shallow water, followed by striking the driver's head on the bottom), fall from height, and road traffic accidents were the most common causes of spinal cord injury. Drowning cases were excluded from the study. The differences between the groups in terms of the trauma circumstances and the level of injury to the spine and spinal cord were insignificant (Table 4). Improvements in the neurological status of patients, from the time of their admission to the moment of the first control 3–14 days after surgical treatment, occurred only in cases of baseline incomplete neurological deficit in 3 (16.6 %) and 5 (17.8 %) patients in the MPD and MAP groups, respectively. There were no significant differences ($p > 0.05$). Changes in the neurological status of patients, from the time of their admission to the time of control in the long-term postoperative period, are shown in Table 5.

The neurological status with type B deficit was significantly more common in the MPD group. These differences remained without changes in the neurological status within 4–6 months. In the other cases, there were no significant differences in regression of pathological neurological symptoms in the groups. Therefore, almost 33 % of patients in the MPD group and 42 % of patients in the MAP group had an improvement in the form of a transition from the baseline ASIA grade to a milder one.

In the MPD group, 22 patients had ASIA grade A; of these, only 4 (18 %) patients had an increase in the ASIA grade. There were 18 patients with incomplete spinal cord injury in the same group, 9 (50 %) of them had an improvement. In the MAP group, there were 38 patients with ASIA grade A, of whom 11 (29 %) patients improved; 28 patients with ASIA grade B, C, or D, of whom 17 (61 %) patients improved neurological symptoms. However, statistical analysis did not reveal significant differences.

An analysis of the changes in neurological deficits in the subgroups allocated on the basis of the time from injury to the end of decompression revealed more improvements in the MAP group, but no significant differences were found (Table 6).

In the same group, there were fewer cases of pulmonary artery thromboembolism, decubitus ulcers, sepsis, acute respiratory distress syndrome, and surgical site infections. The type of complications and mortality in the groups are presented in Table 7.

There was a statistically significant difference in the rate of complications at a combined point to which any of the events, nosocomial pneumonia or acute endobronchitis, was attributed.

Table 1
Baseline neurological status (ASIA) of patients in study subgroups

Subgroup	MPD, n (%)	MAP, n (%)	Two-tailed Fisher's exact test, p-level
1st (n = 43)	A – 13 (56.5) B – 2 (8.7) C – 4 (17.4) D – 4 (17.4)	A – 12 (60.0) B – 0 (0.0) C – 6 (30.0) D – 2 (10.0)	General comparison: 0.513 Category: p; correction p A > 0.999; > 0.999 B – 0.491; 0.892 C – 0.473; 0.892 D – 0.669; 0.892
2nd (n = 26)	A – 7 (70.0) B – 2 (20.0) C – 0 (0.0) D – 1 (10.0)	A – 14 (87.5) B – 0 (0.0) C – 1 (6.2) D – 1 (6.2)	General comparison: 0.271 Category: p; correction p A – 0.340; 0.680 B – 0.138; 0.554 C > 0.999; > 0.999 D > 0.999; > 0.999
3rd (n = 41)	A – 5 (50.0) B – 5 (50.0) C – 0 (0.0) D – 0 (0.0)	A – 13 (41.9) B – 3 (9.7) C – 4 (12.9) D – 11 (35.5)	General comparison: 0.010 Category: p; correction p A – 0.724; 0.724 B – 0.013; 0.050 C – 0.556; 0.724 D – 0.039; 0.079

MPD – patients receiving methylprednisolone; MAP – patients not receiving methylprednisolone.

The risks of these complications in the methylprednisolone group were 2.91-fold [1.38; 6.33] higher than in the MAP group (p = 0.003). After surgery, nosocomial pneumonia or acute endobronchitis was detected within 3 to 12 days (5.35 ± 4.9) in the MPD group and within 3 to 26 (9.36 ± 10.1) days in the MAP group. It should be noted that in a period of 3–14 days, these complications were diagnosed in 88 % of cases in the first group, in 63 % cases in the second group, and in 43.5 % and 25.0 %, respectively, in patients who underwent surgical treatment within 8 h after injury. These complications developed significantly earlier in patients operated on at longer times after injury in the MPD group (p = 0.018) as well as more often in subgroup 3 (Table 8).

Discussion

Secondary spinal cord changes developing shortly after trauma are the main target for treatment of the patient as early as in the acute phase when neuroprotective therapy and surgical treatment are used [20, 21, 32–35]. Maintenance of mean blood pressure of more than 85 mm Hg in the first 7 days after spinal cord injury provides the best outcomes in recovery of lost neurological functions [35, 36]. The mechanism of this influence is currently being studied and, apparently, is implemented through perfusion pressure in the spinal cord segments, but its optimal value and correlation with mean arterial pressure have not been determined [37–40]. According to the results of studies of NASCIS II therapeutic protocols, in the treatment of SCI, there is a discrepancy of arguments about the efficacy of early, short-, and long-term use of methylprednisolone in reducing neurological effects [41–43].

In our study, in both groups, the prerequisite of maintaining the target blood pressure was observed during the period from admission of patients to the hospital to surgery as well as during surgery and within 7–10 days after surgery. In this setting, methylprednisolone therapy was performed.

Table 2
Testing the normality of continuous parameters using the Kolmogorov–Smirnov type test and homoscedasticity using the Fisher F-test

Parameter	Kolmogorov – Smirnov normality test, p-level		Variance [95 % CI]		Fisher's test for equality of variances	
	MPD	MAP	MPD	MAP	ratio of variances [95 % CI]	p-level
Age	0.050	0.003	151.5 [103.0; 244.7]	148.1 [108.2; 215.1]	1.0 [0.6; 1.8]	0.918
Stenosis	0.948	0.705	222.8 [147.4; 376.0]	416.8 [303.1; 609.4]	0.5 [0.3; 1.0]	0.044*

MPD – patients receiving methylprednisolone; MAP – patients not receiving methylprednisolone;
*cases of statistically significantly different variances. Data with p-value > 0.05 are considered to be normally distributed.

Table 3
Age and gender of patients with spinal cord injury (n = 110)

Parameter	MPD (n = 43)	MAP (n = 67)	Difference [95 % CI]	p-level
Age at injury	29 [21.5; 41.0]	34 [26.5; 41.0]	3 [-2.0; 7.0]	0.226
Gender	F – 6 (14.0 %) M – 37 (86.0 %)	F – 13 (19.4 %) M – 54 (80.6 %)	–	0.607

MPD – patients receiving methylprednisolone; MAP – patients not receiving methylprednisolone.

No studies focused on the efficacy of simultaneous action of these two factors in the treatment of spinal cord injury were found in the literature.

Among the patients of both groups, regression of neurological symptoms at the first checkpoint after surgery (3–14 days) was detected in 8 (7.3 %) patients with incomplete neurological deficits (D and C): in 3 (7.0 %) patients in the MPD group and in 5 (7.5 %) patients in the MAP group; no significant differences were found ($p < 0.05$). These differences were determined at the second control point in patients with ASIA grade B: there were more patients in the MPD group without any changes in the neurological status. Decompression and stabilization surgery within the first 8 h after injury was performed in 43 patients (MPD, 23; MAP, 20). Despite the fact that incomplete neurological deficit prevailed in the MPD group, it decreased in only 2 (8.7 %) patients in the first control point, and in the MAP group – in 3 (15.0 %) patients. Marked regression of neurological symptoms occurred in the delayed period. By the second control point, there was improvement in 13 (56.5 %) and 11 (57.9 %) patients, respectively, without significant differences in the groups ($p < 0.05$). The changes did not make much difference in the baseline neurological status in the first control point relative to a period of 4–6 months. This casts doubt on a significant effect of short-term use of methylprednisolone in the first hours after spinal cord injury on the changes in neurological deficit, which is currently reflected in other studies [44]. However, one should agree with many authors that analysis of the effect of conservative and surgical treatment of SCI on neurological outcomes should take into account not only the duration of compression, injury level, and severity of neurological deficit but also syndromic manifestations reflecting morphological destruction of the anatomical parts of the spinal cord [45, 46]. Complications in SCI also develop in methylprednisolone neuroprotective therapy [22, 44]. There was a significant difference in the number of complications in the MPD group for nosocomial pneumonia and endobronchitis. They were found to occur not only in a larger number of patients in this group but also earlier ($p < 0.05$). In this study, the number of complications developed in patients with acute SCI decreased after withdrawal of hormone therapy but with medical support aimed at maintaining mean arterial pressure in a range of 85–90 mm Hg. Given the fact that the outcomes were followed-up for 6 months after surgical treatment, there may be a possible change in regression of neurological deficit in patients of both groups in a more delayed period. The data of many studies and our work do not provide grounds for introducing methylprednisolone into drug therapy of spinal cord injury in the form of recommendations.

Limitations. The limitation of this study was an insufficient sample of patients to determine significance of the effect of these factors on complications and changes in neurological defi-

Table 4
Distribution of patients by the level of spine and spinal cord injury (n = 110), n (%)

Parameter	MPD (n = 43)	MAP (n = 67)	Difference [95 % CI]	Two-tailed Fisher's exact test, p-level
Injured spine region	Thoracic: 11 (25.6); lumbar: 8 (18.6); cervical: 24 (55.8)	Thoracic: 17 (25.4); lumbar: 15 (22.4); cervical: 35 (52.2)	–	General comparison: 0.933 Category: p; correction p thoracic: > 0.999; >0.999; lumbar: 0.811; >0.999; cervical: 0.845; >0.999
Spinal canal stenosis	MED [IKI]	MED [IKI]	Difference [95 % CI]	Mann – Whitney U-test, p-level
	52.38 [40.74; 62.50]	52.94 [37.5; 68.0]	0.93 [-6.67; 8.99]	0.826

MPD – patients receiving methylprednisolone; MAP – patients not receiving methylprednisolone.

Table 5

Changes in the neurological status (ASIA) of patients within 4–6 months after surgery

Variable	MPD (n = 40), n [95 % CI]	MAP (n = 66), n [95 % CI]	Odds ratios [95 % CI]; risk difference [95 % CI]	p-level
A → B	1.20 [0; 13]	3.50 [2; 13]	0.55 [0.01; 7.15]; -2 [-9; 5]	>0.999
A → C	1.20 [0; 13]	6.90 [4; 18]	0.28 [0.01; 2.42]; -7 [-15; 2]	0.419
A → D	1.20 [0; 13]	1.20 [0; 8]	1.64 [0.02; 131.31]; 1[-5; 7]	>0.999
A → E	1.20 [0; 13]	1.20 [0; 8]	1.64 [0.02; 131.31]; 1[-5; 7]	>0.999
All improvements in complete injury (ASIA A)	4.10 [4; 23]	11.17 [10; 27]	0.60 [0.13; 2.21]; -7 [-20; 6]	0.568
B → C	2.50 [1; 17]	1.20 [0; 8]	3.26 [0.16; 197.33]; 3 [-4; 11]	0.558
B → D	2.50 [1; 17]	0.00 [0; 6]	+∞[0.3; +∞]; 5 [-2; 12]	0.149
B → E	0.00 [0; 9]	1.20 [0; 8]	0.00 [0; 65.26]; -2 [-4; 1]	>0.999
C → D	0.00 [0; 9]	8.12 [6; 22]	0.00 [0; 1.03]; -12 [-20; -4]	0.049*
C → E	2.50 [1; 17]	2.30 [1; 10]	1.64 [0.11; 23.49]; 2 [-6; 10]	0.635
D → E	3.80 [3; 20]	5.80 [3; 17]	0.99 [0.15; 5.41]; 0 [-10; 10]	>0.999
All improvements in incomplete injury (ASIA B, C, D)	9.22 [12; 38]	17.26 [17; 37]	0.87 [0.31; 2.31]; -3 [-20; 13]	0.824
A (no changes)	18.45 [31; 60]	27.41 [30; 53]	1.10 [0.5; 2.37]; 4 [-15; 24]	0.856
B (no changes)	5.12 [5; 26]	1.20 [0; 8]	8.11 [0.86; 395.13]; 11 [0; 22]	0.038*
C (no changes)	2.50 [1; 17]	2.30 [1; 10]	1.64 [0.11; 23.49]; 2 [-6; 10]	0.635
D (no changes)	2.50 [1; 17]	8.12 [6; 22]	0.42 [0.04; 2.23]; -7 [-17; 3]	0.325
Lethal outcome	3.80 [3; 20]	1.20 [0; 8]	4.88 [0.38; 263.30]; 6 [-3; 15]	0.297
No changes in neurological status	27.68 [52. 80]	38.58 [46; 69]	1.17 [0.59; 2.31]; 10 [-9; 29]	0.632

MPD – patients receiving methylprednisolone; MAP – patients not receiving methylprednisolone; The number of cases in the study groups is less than that indicated in the Materials and methods due to lethal outcomes (n = 4) that could not be taken into account at the late stage of postoperative follow-up.

Table 6

Changes in the neurological status (ASIA) in subgroups 1, 2, and 3 within 4–6 months after surgery

Subgroup	Variable	MPD, n (%) [95 % CI]	MAP, n (%) [95 % CI]	Odds ratio [95 % CI]	p-level
1 (n = 41: MPD – 21*; MAP – 20)	All improvements	8 (38) [21; 59]	9 (45) [26; 66]	1.3 [0.3; 5.5]	0.756
	Improvements in complete injury	2 (18) [5; 48]	3 (25) [9; 53]	1.5 [0.1; 21.7]	>0.999
	Improvements in incomplete injury	6 (60) [31; 83]	6 (75) [41; 93]	1.9 [0.2; 29.2]	0.638
	No changes	13 (62) [41; 79]	11(55) [34; 74]	0.8 [0.2; 3.1]	0.756
2 (n = 26: MPD – 10; MAP – 15*)	All improvements	2 (20) [6; 51]	8 (50) [28; 72]	3.8 [0.5; 47.8]	0.218
	Improvements in complete injury	1 (14) [3; 51]	6 (43) [21; 67]	4.2 [0.3; 240.5]	0.337
	Improvements in incomplete injury	1 (33) [6; 79]	NA	–	–
	No changes	8 (80) [49; 94]	8 (50) [28; 72]	0.3 [0; 1.9]	0.218
3 (n = 40: MPD – 9*; MAP – 31)	All improvements	3 (33) [12; 65]	13 (45) [28; 62]	1.6 [0.3; 11.9]	0.706
	Improvements in complete injury	1 (20) [4; 62]	4 (36) [15; 65]	2.2 [0.1; 140.1]	>0.999
	Improvements in incomplete injury	2 (50) [15; 85]	9 (50) [29; 71]	1.0 [0.1; 16.7]	>0.999
	No changes	6 (67) [35; 88]	15 (52) [34; 69]	0.5 [0.1; 3.2]	0.476

MPD – patients receiving methylprednisolone; MAP – patients not receiving methylprednisolone; the number of cases in the study groups is less than that indicated in the Materials and methods due to lethal outcomes that could not be taken into account to the date of postoperative follow-up.

Table 7

Complications and mortality in the MPD and MAP groups

ICD10	Nosological forms	MPD (n = 43), n (%) [95 % CI]	MAP (n = 67), n (%) [95 % CI]	Odds ratio [95 % CI]; risk difference [95 % CI]	p-level
J13–J18 + J20	Nosocomial pneumonia + acute endobronchitis	32 (74) [60; 85]	17 (25) [16; 37]	2.91 [1.38; 6.33]; 49.00 [32.00; 66.00]	0.003*
N30 + N10 + N34	Acute cystitis + acute tubulointerstitial nephritis + urethritis	14 (33) [20; 47]	14 (21) [13; 32]	1.55 [0.62; 3.91]; 12.00 [-5.00; 29.00]	0.390
I26	Thromboembolism of the pulmonary artery	3 (7) [2; 19]	1 (1) [0; 8]	4.61 [0.36; 248.62]; 5.00 [-3.00; 14.00]	0.301
I80	Peripheral intravenous catheter-related thrombophlebitis	0 (0) [0; 8]	5 (7) [3; 16]	0.00 [0.00; 1.80]; -7.00 [-14.00; -1.00]	0.155
I82	Acute peripheral venous thrombosis	2 (5) [1; 15]	1 (1) [0; 8]	3.08 [0.16; 186.32]; 3.00 [-4.00; 10.00]	0.562
A41	Sepsis	2 (5) [1; 15]	1 (1) [0; 8]	3.08 [0.16; 186.32]; 3.00 [-4.00; 10.00]	0.562
L89	Decubitus ulcer	3 (7) [2; 19]	1 (1) [0; 8]	4.61 [0.36; 248.62]; 5.00 [-3.00; 14.00]	0.301
J80	Adult acute respiratory distress syndrome	2 (5) [1; 15]	1 (1) [0; 8]	3.08 [0.16; 186.32]; 3.00 [-4.00; 10.00]	0.562
T84.6	Surgical site infection	2 (5) [1; 15]	1 (1) [0; 8]	3.08 [0.16; 186.32]; 3.00 [-4.00; 10.00]	0.562
E89	Hypercatabolic syndrome	1 (2) [0; 12]	0 (0) [0; 5]	+∞ [0.04; +∞]; 2.00 [-2.00; 7.00]	0.396
R65.3	Multiple organ failure	2 (5) [1; 15]	0 (0) [0; 5]	+∞ [0.28; +∞]; 5.00 [-2.00; 11.00]	0.159
R04.8	Hemorrhage in respiratory passages	1 (2) [0; 12]	0 (0) [0; 5]	+∞ [0.04; +∞]; 2.00 [-2.00; 7.00]	0.396
Lethal outcome		3 (7) [2; 19]	1 (1) [0; 8]	4.61 [0.36; 248.62]; 5.00 [-3.00; 14.00]	0.301

MPD — patients receiving methylprednisolone; MAP — patients not receiving methylprednisolone.

Table 8

Timing of the development of nosocomial pneumonia and/or endobronchitis in subgroups after surgery

Subgroup	Development of complications, days		Difference [95 % CI]	Mann — Whitney U-test (p-level)
	MPD [95 % CI]	MAP [95 % CI]		
1	5.0 [3.25; 6.50]	4 [3.50; 6.50]	0 [-2; 2]	0.921
2	4.5 [4.00; 5.75]	8 [8.00; 11.75]	4 [1; 14]	0.028*
3	5.0 [4.00; 6.00]	8 [8.00; 9.00]	3 [1; 9]	0.049*

MPD — patients receiving methylprednisolone; MAP — patients not receiving methylprednisolone.

cit depending on the level of injury to the spine and spinal cord. Accumulation of experience in the treatment of these patients and further in-depth analysis of the obtained results are necessary.

Conclusions

1. The use of methylprednisolone in acute SCI significantly increased risks of nosocomial pneumonia or acute endobronchitis in patients 2.91-fold [1.38; 6.33] ($p = 0.003$).

2. Maintenance of mean arterial pressure using vasopressors (norepinephrine, dobutamine) at 85–90 mm Hg during the first 7–10 days after admission to the hospital resulted in a greater number of improvements in the neurological status of patients in contrast to the use of methylprednisolone under the same conditions. However, no statistically significant differences were found.

The study was conducted without financial support.
The authors declare no conflict of interest.

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Received 23.04.2019
Review completed 25.11.2020
Passed for printing 28.11.2020

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