PHARMACOLOGICAL PREVENTION OF SURGICAL STRESS IN PATIENTS WITH SPINAL CORD INJURY

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Objective. To evaluate the effectiveness of dalargin and polyoxidonium as neurovegetative protection components, when performing decompression and stabilization operations in patients in the late period of spine and spinal cord injury.

Material and Methods. Perioperative parameters of central hemodynamics and stress hormone levels were analyzed in 68 patients operated on using technology of multi-stage treatment in one surgical session under three variants of general anesthesia with mechanical ventilation: sevoflurane, fentanyl, and rocuronium bromide in Group I (n = 23); sevoflurane, fentanyl, dalargin, and rocuronium bromide – in Group II (n = 21); and sevoflurane, fentanyl, polyoxidonium, and rocuronium bromide – in Group III (n = 24).

Results. The duration of operation was: 385.7 ± 54.8 min in Group I, 391.5 ± 43.5 min in Group II, 399.2 ± 51.2 min in Group III, and blood loss was 1008.7 ± 89.2 ml, 968.3 ± 71.8 ml, 1001.4 ± 80.3 ml, respectively. Statistically significant differences in cardiac output parameter from initial values were recorded during anterior spinal fusion procedure and at the stage of spinal deformity correction. There were no significant differences in hemodynamics between the groups. The greatest deviations in stress hormone levels were recorded in Group I at stages of anterior spinal fusion, deformity correction, and on the first day after surgery. The level of endogenous intoxication in Group I corresponded to high severity, in Groups II and III – to moderate severity. The need for opioid analgesics was significantly lower in Groups II and III ($p < 0.05$).

Conclusion. Inclusion of dalargin and polyoxidonium into the anesthesia program allows achieving a required level of anesthetic protection of patients during operation, while maintaining adequate reactivity of the patient's body defenses.

Key Words: spine and spinal cord injury, multi-stage operations, hemodynamic monitoring, stress hormones.

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Damage to the spinal column with impaired spinal cord function is referred to severe types of injuries of the musculoskeletal system, which account for 3.3 % of total injuries. The injury often affects the thoracolumbar junction due to the spine anatomy. Such clinical events are associated with severe neurological symptoms in the form of motor and sensitive disorders [5, 9, 21]. The majority of these cases are working-age patients: about 80.0 % of them are under the age of 40 [5, 12, 14, 17]. A special place is occupied by the late period of spinal cord injury (SCI), which begins after 3–4 months after injury and is characterized by the development of disorders of almost all life support systems of the body [3, 9, 13].

To date, the goal of surgical treatment in the late period of SCI is to eliminate spinal cord compression and spinal deformity, stabilize the vertebral segment, and create conditions for optimal early rehabilitation of the patient [5, 15, 20]. In this regard, vertebral surgeons use the technology of multi-stage surgical treatment, which involves sequential stages of the surgery performed through different surgical approaches in one day [5, 9, 15, 23]. Such surgical tactics is reasonable in humane, economic, moral and social aspects [4, 14, 15]. At the same time, from the point of view of an intensivist, such surgeries are characterized by a high level of stress, significant duration and the risk of massive blood loss [3, 8, 15, 18, 22]. In this regard, reduction of the severity of surgical stress response becomes one of the leading tasks of anesthetic support for the performed surgeries.

The aim of the study is to evaluate the effectiveness of dalargin and polyoxidonium as neurovegetative protection components in decompression and stabilization operations in patients in the late period of SCI.

Material and Methods

The study is prospective and performed in the course of planned surgical treatment of 68 patients in the late period of SCI at Novosibirsk Research Institute of Traumatology and Orthopaedics in in the period of 2013 to 2016. The study included 31 (45.6 %) women and 37 (54.4 %) men.

All patients were admitted to hospital for neurological deficit of various severity. Furthermore, 23 (33.8 %) patients were referred to type A according to the ASIA classification [16]. Assessment of hemodynamics in all patients with ASIA A neurological deficit showed a reduced cardiac index (2.6 ± 0.3 L/min/m^2). A total of 28 (41.2 %) patients were initially diagnosed with BV deficit calculated using Moore's formula, which was 13.6 %. A total of 48 (70.6 %) patients were diagnosed with protein energy malnutrition of moderate severity confirmed by anthropometric and clinical and biochemical indices, while 33 (48.5 %) and 19 (27.9 %) patients had urinary system diseases and residual effects of post-thrombotic syndrome, respectively. The complex of organ dysfunctions in patients determined their physical status as ASA class II–III.

All patients underwent multi-stage surgical treatment with sequential anterior and posterior intervention in one surgical session. The operations were performed under general anesthesia with mechanical ventilation. Three observation groups distinguished by a combination of pharmacological components used in general anesthesia have been selected:

Group I: 23 patients operated on under general anesthesia with sevoflurane and fentanyl;

Group II: 21 patients operated on under general anesthesia with sevoflurane, fentanyl and dalargin;

Group III: 24 patients operated on under general anesthesia with sevoflurane, fentanyl and polyoxidonium.

Anesthesia induction had no differences between the groups and was carried out by sequential intravenous administration of atropine (0.007–0.010 mg/kg), fentanyl (0.002 mg/kg), and propofol (2.0–2.5 mg/kg). Intubation of the trachea was performed 1 min after administration of rocuronium bromide at a dose of 0.6–1.0 mg/kg. For anesthesia maintenance, inhalation of sevoflurane was performed at a concentration of 1.8–2.0 vol % in a low-flow mechanical ventilation mode (1 L/min) in 40 % oxygen-air mixture with bolus administration of fentanyl (0.004–0.005 mg/kg). Rocuronium bromide (0.5–0.6 mg/kg/h) was used to maintain myoplegia. Mechanical ventilation was performed using the Fabius Plus in the PCV mode with the MV providing 32–37 mmHg $EtCO_2$.

Dalargin was administered in a form of continuous infusion after anesthesia induction at a dose of 40 mcg/kg/h, polyoxidonium was administered intravenously three times: in the evening before surgery, after anesthesia induction and on the first day after surgery at a dose of 0.012 g.

Mean age of patients in the groups was as follows: 38.8 ± 7.4 years (I), 40.0 ± 9.6 years (II), 35.7 ± 9.7 years (III). Body weight was as follows: 66.8 ± 14.7 kg (I), 70.5 ± 15.2 kg (II), 68.8 ± 16.6 kg (III).

Mandatory safety monitoring included registration of arterial blood pressure, heart rate, ECG, FiO_2, SaO_2, $FiCO_2$, $ETCO_2$, FiSev, EtSev, and hourly diuresis.

The depth of anesthesia and the state of myoplegia in the groups was assessed by registration of the bispectral index of the electroencephalogram (BIS) and electromyography using the Aspect BIS XP monitor with the target values of 45–50 %.

Infusion therapy included polyionic (sterofundin ISO, jonosteril) and colloidal solutions (gelofusine, tetraspan). Fresh frozen plasma and erythrocyte mass was transfused in indications for blood loss replacement.

Extended non-invasive monitoring of hemodynamic parameters was performed by the method of impedance cardiography (ICG) using the NICCOMO system (Germany) at the following stages: after premedication; during anesthesia induction; when turning the patient to lateral position; pneumothorax, anterior spinal fusion; when turning the patient to prone position; correction of spinal deformity; end of surgery. The following parameters were registered and evaluated: heart rate (HR), blood pressure (BP), stroke volume (SV), stroke index (SI), cardiac output (CO), cardiac index (CI), systemic vascular resistance (SVR), and systemic vascular resistance index (SVRI).

To assess the adequacy and effectiveness of anesthetic maintenance, the level of cortisol, thyroxine, insulin, and glucose was measured at the following stages: on the eve of surgery; during anesthesia induction; pneumothorax, anterior spinal fusion; correction of spinal deformity; in the evening on the day of surgery; on the first and the third days after surgery. General blood analysis and determination of the leukocyte index of intoxication (LII) were performed at the following stages: on the eve of surgery, on days 1, 3 and 5 after surgery.

The visual analogue scale (VAS) was used for assessment of analgesia level in the postoperative period: mild pain at rest (0–4 points), moderate pain (5–7 points), severe and intolerable pain (8–10 points).

Statistical analysis of the obtained results was performed using Statistica 6.0 software with the calculation of the mean arithmetic values (M) and standard deviation (σ). For intergroup comparisons, the Mann-Whitney test was used. Differences were considered reliable at $p < 0.05$.

Results and Discussion

The duration of surgical intervention was 385.7 ± 54.8 min in Group I, 391.5 ± 43.5 min in Group II, and 399.2 ± 51.2 min in Group III ($p > 0.05$). The volume of intraoperative blood loss was 1008.7 ± 89.2 ml in Group I, 968.3 ± 71.8 ml in Group II, and1001.4 ± 80.3 ml in Group III ($p > 0.05$).

Extended non-invasive monitoring of hemodynamic parameters was applied in all patients. Table 1 presents data obtained at different stages of the study.

The initial indices in the selected groups were within the conventionally normal values. Unidirectional changes in the studied parameters were observed at the stages of the operational period: an increase in HR, a decrease in the mean BP, SV (SI), CO (CI), SVR (SVRI). Statistically significant differences (as compared to baseline values) in the parameters associated with the cardiac output were registered during anterior spinal fusion (under conditions of surgical pneumothorax) and at the stage of spinal deformity correction. The registered decrease in SV, SI, CO, and CI was undoubtedly determined by a combination of factors: impede venous return of blood due to the patient's position (lateral and prone positions), negative effects of open pneumothorax, spine hyperextension (on the roll of the surgical table), severity of the dose-dependent vasodilator and cardiodepressant effects, administration of anesthetics and opioid analgesics. SVR and SVRI dynamics were determined by the vasoplegic effect of sevoflurane. Furthermore, all registered abnormalities were within the permissible physiological limits. There were no significant differences in the studied parameters between the groups at any stage of the study.

Based on the analysis of hemodynamic parameters, one can conclude that all of the applied types of anesthesia provided an adequate antinociceptive protection of the operated patients, since unstable hemodynamic profile implementing through the stress response to surgical aggression in a patient is known to be one of the most accessible indicators of the unfavorable course of anesthesia [7, 19].

Afferent activity from the area of surgery is known to result in activation of not only hypothalamic-hypophyseal adrenal axis but also the release of cytokines, which are involved in the development of surgical stress, from damaged tissues [1, 24]. An increased concentration of inflammatory mediators in injured area leads to persistent excitation of not only existing nociceptors but also to formation of new ones. As a result of such multifaceted stimulation, neurohumoral response is formed in the form of a release of stress hormones [2, 6, 8, 11]. Plasma concentration level of cortisol, thyroxine, glucose, insulin, and a secondary marker of surgical stress LII are the common biochemical markers of the severity of surgical stress.

Analysis of the obtained data allowed us to determine that the initial indices of stress hormones in the groups did not exceed the limits of the mean-age standard indices and did not have statistically significant differences between the groups, which allowed their comparison at subsequent stages. The dynamics of changes in the blood plasma levels of stress hormones at the study stages is presented in Table 2. Analysis of the obtained data revealed an increase in cortisol level in all groups at all stages of the study compared to baseline values. However, it was more significant in Group I in the evening on the day of surgery and on the first day of the postoperative period ($p < 0.05$). Increase in cortisol level was less pronounced in Group II and III patients and did not exceed the permissible physiological limits at any stage. Hormoneemia level remained higher than the baseline in all groups by the third day of observation; no statistically significant differences were noted between the groups.

A statistically significant increase in the level of thyroxine was noted in Group I compared to baseline values and other groups at the main stages of operation and postoperative period. Thyroxin level was approaching baseline values in Group II and III patients by the first day of the postoperative period. On day 1 after surgery, the level of thyroxine in Group I patients remained higher than the baseline and significantly differed from the values for the Groups II and III ($p < 0.05$). This circumstance confirmed the positive effect of additional anesthesia components (dalargin and polyoxidonium) on the functional state of the thyroid gland, the hormones of which are known to serve as markers of stress development in response to surgical intervention.

Glycemic level is known to be considered as one of the indirect indicators used in assessing anesthesia adequacy. In particular, the intraoperative increase in blood glucose level is a consequence of the release of catecholamines, which indicate body responce to surgical injury [8, 10, 11]. Analysis of glycemic level revealed that it did not exceed the standard values before surgery, its increase was noted during the stages of surgery with its level reaching the maximal value at the end of surgical intervention. In Groups II and III, the glycemic index did not exceed the limits of the stress norm at the study stages; glucose level in Group I was significantly higher than baseline and glycemic levels in Groups II and III. For instance, glycemic level in Group I exceeded the initial values by 36.9 % at the stage of anterior spinal fusion and by 42.1 % at the stage of posterior fixation of the spine. An increase in glycemic level was noted in Group II: 25.5 % increase at the stage of anterior spinal fusion, 26.5 % increase at the stage of spine deformity correction; in Group III, glycemic level was increased by 18.2 % and 19.9 %, at the stages of anterior spinal fusion and spine deformity correction, respectively. A tendency to normalization of glycemic level was noted in Groups II and III on the first day of the postoperative period with achievement of the initial values on the third day; minor hyperglycemia was preserved in Group I.

The study of serum insulin level showed its decrease in Group I (compared to the baseline values) by 19.6 % at the stage of anterior spinal fusion and by 28.2 % at the stage of spinal deformity correction ($p < 0.05$). Moreover, no patient had insulin value less than 2.7 μIU/ml, which is a critical indicator. Significant differences between the groups in the serum insulin levels were found at the main stages of surgical intervention. Despite the absence of any statistically significant differences between the groups, serum level of insulin was higher in Groups II and III on the day of surgery, which was associated with a lower glycemic level.

Evaluation of the level of postoperative endogenous intoxication, which contributes to the development of immunosuppression and reduction of body resistance, plays an important role in assessing the adequacy of anesthetic maintenance [4, 6]. Taking into account the labor intensity, duration of implementation and low availability of special immunological studies in the common practice, we used the available data based on the analysis of the leukocyte blood count and LII calculation (Table 3).

The initial indices of the number of leukocytes in the groups were within standard values. An increase in leukocyte number (compared to the initial values)

Table 1

Hemodynamic parameters in observation groups at the study stages, M ± σ

Parameter	Group	After premedication	Anesthesia induction	Turn of the patient to lateral position	Pneumothorax, ventral spinal fusion	Turn of the patient to prone position	Correction of spinal deformity	End of surgery
Heart rate, bpm	I	69.8 ± 6.1	96.1 ± 5.8*	78.6 ± 5.2	80.1 ± 5.7	82.9 ± 4.8*	91.6 ± 4.4*	78.4 ± 5.2
	II	65.3 ± 5.3	89.4 ± 6.0*	76.9 ± 4.9	75.4 ±5.6	79.4 ± 5.2*	88.4 ± 4.7*	74.3 ± 4.8
	III	71.4 ± 5.7	91.2 ±6.3*	79.2 ± 4.6	77.9 ± 5.1	81.7 ± 4.6*	90.1 ± 5.1*	75.1 ± 5.6
Mean arterial pressure, mm Hg	I	90.3 ± 4.6	82.5 ± 3.9	84.3 ± 5.2	82.8 ± 5.5	78.9 ± 5.1	73.1 ± 4.9*	81.1 ± 4.5
	II	87.6 ± 4.2	82.1 ± 4.0	83.5 ± 4.7	81.1 ± 4.7	76.7 ± 4.2	73.5 ± 5.0*	82.0 ± 4.8
	III	89.1 ± 4.4	83.9 ± 4.8	86.1 ± 4.3	82.3 ± 5.1	78.1 ± 4.6	74.2 ± 4.5*	79.4 ± 4.7
Stroke volume, ml	I	75.1 ± 6.2	64.3 ± 6.0	61.8 ± 5.4	50.9 ± 5.0*	55.4 ± 5.1	51.4 ± 6.8*	61.0 ± 8.4
	II	73.9 ± 7.3	61.5 ± 5.4	58.1 ± 6.0	49.6 ± 4.8*	53.5 ± 5.4	52.1 ± 7.1*	59.8 ± 7.1
	III	73.2 ± 6.8	60.5 ± 5.1	59.8 ± 4.8	48.9 ± 4.5*	54.3 ± 4.9	51.4 ± 6.0*	62.3 ± 7.3
Stroke index	I	40.2 ± 3.2	38.1 ± 2.9	38.9 ± 3.0	30.5 ± 3.4*	36.1 ± 2.9	30.8 ± 2.8*	34.3 ± 3.0
	II	41.8 ± 2.9	36.7 ± 2.7	37.1 ± 2.8	28.3 ± 3.1*	34.4 ± 3.1	32.8 ± 2.8*	33.6 ± 2.9
	III	40.7 ± 2.8	39.6 ± 2.7	38.4 ± 2.9	26.8 ± 3.5*	33.2 ± 3.2	29.9 ± 3.0*	33.8 ± 2.8
Cardiac output, l/min	I	5.4 ± 0.4	5.7 ± 0.5	5.1 ± 0.4	4.2 ± 0.6*	5.0 ± 0.5	4.5 ± 0.4*	4.8 ± 0.5
	II	5.5 ± 0.6	5.9 ± 0.4	4.9 ± 0.3	4.5 ± 0.3*	5.1 ± 0.4	4.7 ± 0.4	5.1 ± 0.3
	III	5.5 ± 0.3	5.8 ± 0.4	5.2 ± 0.3	4.3 ± 0.5*	5.0 ± 0.5	4.6 ± 0.6	4.9 ± 0.4
Cardiac index, l/min/m^2	I	3.4 ± 0.3	3.6 ± 0.3	2.9 ± 0.5	2.5 ± 0.5*	2.8 ± 0.4	2.5 ± 0.4*	2.5 ± 0.4*
	II	3.6 ± 0.4	3.7 ± 0.4	3.0 ± 0.4	2.4 ± 0.5*	2.7 ± 0.4*	2.6 ± 0.3*	2.6 ± 0.4*
	III	3.3 ± 0.3	3.5 ±0.4	2.8 ± 0.5	2.3 ± 0.4*	2.8 ± 0.5	2.4 ± 0.3*	2.6 ± 0.3*
Systemic vascular resistance index	I	2150.8 ± 179.6	1779.5± 161.9*	1516.4 ± 215.8*	2214.6 ± 234.4	1688.1 ± 179.1	1824.3 ± 171.5	1975.6 ± 188.9
	II	2218.5 ± 169.4	1759.6 ± 158.4*	1608.9 ± 207.4*	2280.6 ± 218.8	1736.5 ± 164.8	1854.3 ± 158.9*	2047.9 ± 174.1
	III	2198.4 ± 169.8	1815.8 ± 169.5*	1575.4 ± 194.8*	2198.5 ± 209.1	1641.9 ± 174.5	1751.3 ± 164.4*	1934.7 ± 169.9

*$p < 0.05$ — reliability of differences compared to the initial values.

by 113.5 % (Group I), 70.8 % (II), and 41.7 % (III) ($p < 0.05$) was noted on the first day of the postoperative period. The degree of leukocytosis severity in patients of the Group I established statistically significant intergroup differences at this stage. Analysis of the number of stab neutrophils allowed establishing a similar tendency. Analysis of the results of LII measurements showed that LII was significantly higher than the baseline values in the groups on the first day after surgery. Statistically significant differences between the groups were obtained at the same stage. Moreover, LII values corresponded to the high severity of endogenous intoxication in Group I and moderate severity in Groups II and III. A gradual decrease in the index was noted on the third day. However, LII reached the initial value on day 5 only in Group III. The dynamics of the number of leukocytes in the blood, the severity of the shift in the haematologic state and LII value completely corresponded to the severity of the applied surgical stress.

Postanesthesia respiratory depression was noted in all patients in the early postoperative period, which determined the need for prolonged mechanical ventilation. The mean duration of mechanical ventilation in the postoperative period was as follows: 63.2 ± 11.1 min (I), 89.7 ± 12.1 min (II), and 95.2 ± 14.8 min (III). The periods of consciousness restoration were the following: 68.1 ± 9.8 min (I), 96.7 ± 11.4 min (II), and 102.3 ± 16.7 min (III). Extubation of the trachea was performed after 72.7 ± 12.7 min in Group I, after 101.3 ± 9.6 min in Group II, and after 104.7 ± 15.4 min in Group III ($p < 0.05$). The persistent sufficient level of analgesia in the immediate postoperative period contributed to a slight increase in the awakening time in Groups II and III. However, it ensured calm recovery of consciousness without signs of increased psychomotor activity. The need for opioid analgesics in the early postoperative period was statistically significantly lower in patients of the Groups II and III. The data are presented in Table 4.

Conclusion

Analysis of the obtained information is based on the perioperative assessment of hemodynamic status, markers of surgical stress, and features of postoperative course in patients with SCI in the late period of injury led to the conclusion that inclusion of dalargin

Table 2

Stress hormone levels in observation groups at the study stages, M ±σ

Stage of the study	Group	Cortisol	Thyroxine	Glucose	Insulin
On the eve of surgery	I	265.8 ± 64.0	112.1 ± 10.1	5.8 ± 0.9	9.9 ± 1.0
	II	253.8 ± 64.9	114.1 ± 10.5	5.6 ± 0.7	10.3 ± 1.1
	III	243.5 ± 56.0	109.4 ± 11.2	5.6 ± 0.7	9.9 ± 1.2
Anesthesia induction	I	317.0 ± 66.0	108.2 ± 14.2	6.0 ± 0.6	9.9 ± 1.1
	II	239.8 ± 76.9	111.0 ± 13.1	6.2 ± 0.7	10.1 ± 1.0
	III	261.8 ± 49.3	100.1 ±10.6	6.5 ± 0.8	9.9 ± 1.1
Pneumothorax, ventral spinal fusion	I	573.4 ± 58.1* PI–II < 0.05 PI–III < 0.05	141.9 ± 14.0* PI–II < 0.05 PI–III < 0.05	9.2 ± 0.8* PI–II < 0.05 PI–III < 0.05	8.0 ± 1.1* PI–II < 0.05 PI–III < 0.05
	II	399.0 ± 84.9*	113.1 ± 12.4	6.8 ± 0.7	9.9 ± 1.1
	III	398.6 ± 66.5*	110.9 ± 9.6	7.5 ± 0.7	11.0 ± 1.1
Deformity correction	I	658.3 ± 61.3* PI–II < 0.05 PI–III < 0.05	144.9 ± 12.3* PI–II < 0.05 PI–III < 0.05	10.0 ± 0.9* PI–II < 0.05 PI–III < 0.05	7.1 ± 1.1* PI–II < 0.05 PI–III < 0.05
	II	478.3 ± 78.0*	107.6 ± 11.4	7.4 ± 0.7	9.2 ± 0.9
	III	482.9 ± 64.8*	112.6 ± 10.6	8.0 ± 0.8	10.2 ± 1.1
In the evening at the day of surgery	I	789.4 ± 88.4* PI–II < 0.05 PI–III < 0.05	145.9 ± 12.3* PI–II < 0.05 PI–III < 0.05	9.7 ± 1.3	8.4 ± 1.2
	II	598.9 ± 81.3*	105.6 ± 13.4	7.2 ± 1.1	9.8 ± 1.0
	III	572.4 ± 69.2*	113.9 ± 10.9	7.6 ± 1.2	11.3 ± 1.2
Day 1 after surgery	I	876.4 ± 79.4* PI–III < 0.05	143.4 ± 11.0* PI–II < 0.05 PI–III < 0.05	8.2 ± 1.2	10.2 ±1.2
	II	723.9 ± 92.7*	103.4 ± 16.2	6.0 ± 0.9	11.3 ± 1.1
	III	643.2 ± 88.5*	115.4 ± 10.9	6.2 ± 1.0	12.0 ± 1.2
Day 3 after surgery	I	542.1 ± 93.9*	132.3 ± 10.3	6.6 ± 0.7	11.2 ± 1.1
	II	506.4 ± 94.8*	107.9 ± 14.0	5.3 ± 0.5	10.4 ±1.1
	III	477.4 ± 94.0*	116.0 ± 9.8	5.6 ± 0.5	11.6 ± 1.1

*p < 0.05 — reliability of differences compared to the initial values;
P — reliability of intergroup differences.

and polyoxidonium as neurovegetative protection components in the program of general anesthesia allows reducing the stress effect of surgical intervention while maintaining adequate reactivity of the patient’s body.

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Table 3

Dynamics of the leukocyte index of intoxication in observation groups at the study stages, $M \pm \sigma$

Stage of the study	Group	Leukocytes, *109/l	Stab neutrophils, %	LII, U
Prior to surgery	I	6.33 ± 17.00	2.60 ± 0.90	1.41 ± 0.50
	II	5.78 ± 1.60	2.29 ± 0.70	1.16 ± 0.50
	III	6.18 ± 1.50	1.62 ± 0.80	1.48 ± 0.60
Day 1 after surgery	I	13.50 ± 2.20* PI—II < 0.05 PI—III < 0.05	13.70 ± 4.10*	8.85 ± 2.00* PI—II < 0.05 PI—III < 0.05
	II	9.87 ± 1.30*	12.80 ± 3.20*	4.32 ± 1.60*
	III	8.76 ± 1.50	10.10 ± 3.80*	4.75 ± 0.80*
Day 3 after surgery	I	9.06 ± 2.50	5.80 ± 2.50	3.62 ± 1.60
	II	9.28 ± 3.40	4.00 ± 2.10	3.29 ± 1.70
	III	7.67 ± 2.00	3.60 ± 1.80	2.55 ± 1.00
Day 5 after surgery	I	7.86 ± 2.70	6.50 ± 3.10	2.26 ± 0.90
	II	7.70 ± 2.80	6.50 ± 2.60	1.86 ± 0.70
	III	6.50 ± 1.90	4.20 ± 1.90	1.84 ± 0.50

*p < 0.05 — reliability of differences compared to the initial values;
P — reliability of intergroup differences.

Table 4

Intensity of postoperative pain syndrome and the need for opioid analgesics in the patients of the studied groups, $M \pm \sigma$

Postoperative pain intensity criteria	I	II	III
Interval to the first requirement of an analgesic, min	76.70 ± 15.80 PI—II < 0.05 PI—III < 0.05	110.70 ± 17.10	116.90 ± 16.50
Average postoperative pain intensity, points	5.10 ± 0.50 PI—II < 0.05 PI—III < 0.05	3.10 ± 0.40	3.60 ± 0.60
Average daily dose of promedol, mg/kg/day	1.26 ± 0.05 PI—II < 0.05 PI—III < 0.05	1.08 ± 0.05	1.10 ± 0.06

References

1. **Bunyatyan KA, Vyzhigina MA, Inviyaeva EV, Vinnitsky LI.** Use of polyoxidonium as a component of neurovegetative protection in patients with surgical diseases of lungs an trachea. Allergologia I immunologia. 2009;10(3): 369–370. In Russian.
2. **Voloshenko EV.** Anti-stress protection from surgical aggression using adren-gangliooplegics and clonidine: Abstract of DMSc Thesis. Krasnoyarsk, 2000. In Russian.
3. **Golikov RI, Lukyanov DS.** Modern approaches to anesthetic management during surgical treatment for spinal cord injury in the late period. Hir. Pozvonoc. 2015;12(3):89–96. In Russian. DOI: http://dx.doi.org/10.14531/ss2015.3.89-96.
4. **Golub IE, Chizhova EO, Usachev OYu**. New aspects of improving the quality of anesthetic protection in patients with acute cholecystitis. Siberian Medical Journal (Irkutsk). 2003;31(2):17–18. In Russian.
5. **Dulaev AK, Usikov VD, Ptashnikov DA, Fadeev EM, Dadykin AV, Alikov ZYu**, **Dulaeva NM.** Surgical treatment of patients with unfavorable consequences of vertebral-spinal injuries. Traumatology and Orthopedics of Russia. 2010;(2):51–54. In Russian.
6. **Yezhevskaya AA, Akulov MS, Prusakova GB.** Multimodal Perioperative Management of Scoliosis Surgical Correction. Hir. Pozvonoc. 2010;1:62–67. In Russian. DOI: http://dx.doi.org/10.14531/ss2010.1.62-67.
7. **Kirov MYu, Kuzkov VV.** Optimization of hemodynamics in the perioperative period. Messenger of Anesthesiology and Resuscitation. 2012;9(5):56–66. In Russian.
8. **Lebedeva MN.** Anesthetic protection at stages of surgical treatment of patients with severe spinal deformities: Abstract of DMSc Thesis. Novosibirsk, 2010. In Russian.
9. **Lutsik AA, Rerikh VV, Ratkin IK, Bondarenko GYu**. Decompression and Stabilization Surgical Technique in Spine and Spinal Cord Injury: Manual. Novokuznetsk, 2011. In Russian.
10. **Nazarov IP.** Anaesthesiology and Reanimation: Selected lectures. Vol. 1. Krasnoyarsk, 2005. In Russian.
11. **Ovechkin AM.** Clinical pathophysiology and anatomy of acute pain. Regional Anesthesia and Acute Pain Management Journal. 2012;6(1):32–40. In Russian.
12. **Polishchuk NE, Korzh NA, Fishchenko VYa**. Injuries of the Spine and Spinal Cord (Mechanisms, Clinical Picture, Diagnosis, Treatment). Kiev, 2001. In Russian.
13. **Razdolsky IYa**. General questions of diagnosis of traumatic injuries and diseases of the spinal cord and spine. In: Multivolume Guidance in Surgery. Vol. 4. Moscow, 1963:181. In Russian.
14. **Ramikh EA.** Injuries of the thoracic and lumbar spine. Hir. Pozvonoc. 2008;(1):86–106. In Russian. DOI: http://dx.doi.org/10.14531/ss2008.1.86-106.
15. **Rerikh VV, Borzykh KO.** Post-traumatic deformities of the thoracic and lumbar spine in patients in the late period of the spinal trauma after previously performed surgical interventions. Proceedings of the 6th Congress of Association of Spine Surgeons «Vertebrology in Russia: Prospects, Problems and Ways of Solution». Krasnodar, 2015. Vol. 1. P. 207–212. In Russian.
16. American Spinal Injury Association Reference Manual for the International Standards for Neurological Classification of Spinal Cord Injury. Chicago, IL: American Spinal Injury Association, 2003.
17. **Asouhidou I, Katsaridis V, Vaidis G, Ioannou P, Givissis P, Christodoulou A, Georgiadis G.** Somatosensory Evoked Potentials suppression due to remifentanil during spinal operations; a prospective clinical study. Scoliosis. 2010;5:8. DOI: 10.1186/1748-7161-5-8.
18. **Borghi B, Frugiuele J, Adduci A.** Anaesthesia in orthopaedic surgery. In: Gullo A. (ed), Anaesthesia, Pain, Intensive Care and Emergency A. P. I. C.E. Springer, Milano, 2006:677–684. DOI: 10.1007/88-470-0407-1_61.
19. **Hofer CK, Cecconi M, Marx G, della Rocca G.** Minimally invasive haemodynamic monitoring. Eur J Anaesthesiol. 2009;26:996–1002. DOI: 10.1097/EJA.0b013e3283300d55.
20. **Kaneda K, Asano S, Hashimoto T, Satoh S, Fujiya M.** The treatment of osteoporotic-posttraumatic vertebral collapse using the Kaneda device and a bioactive ceramic vertebral prosthesis. Spine. 1992;17(8 Suppl):295–303. DOI: 10.1097/00007632-199208001-00015.
21. **Parizel PM, van der Zijden T, Gaudino S, Spaepen M, Voormolen MH, Venstermans C, De Belder F, van den Hauwe L, Van Goethem J.** Trauma of the spine and spinal cord: imaging strategies. Eur Spine J. 2010;19 Suppl l:S8–S17. DOI: 10.1007/s00586-009-1123-5.
22. **Steven HR, Elliot BA, Horloker TT.** Anesthesia, positioning and postoperative pain management for spine surgery. In: Frymoyer JW, ed. The Adult Spine: Principles and Practice, 2nd ed. Philadelphia, 1997:703–718.
23. **Patel VV, Burger E, Brown CW, eds.** Spine Trauma: Surgical Techniques. Berlin/Heidelberg: Springer-Verlag, 2010.
24. **Weledji EP.** Cytokines and postoperative hyperglycaemia: from Claude Bernard to enhanced recovery after surgery. Int J Surg Res. 2014;3:1–6. DOI: 10.5923/j.surgery.20140301.01.

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