THE ADVANTAGES OF CONTINUOUS EPIDURAL ANESTHESIA IN SPINAL DEFORMITY SURGERY

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The aim of the investigation was to assess the efficacy of epidural anesthesia and analgesia during the integrated anesthetic management in spinal deformity surgery.

Materials and Methods. The prospective randomized study involved 350 patients aged from 15 to 65 years, divided into two groups: group 1 (n=205) were given combined anesthesia — epidural and endotracheal anesthesia with sevoflurane and continuous epidural analgesia with ropivacaine, fentanyl and epinephrine after surgery; group 2 (n=145) had general anesthesia with sevoflurane and fentanyl, and systemic administration of opioids after surgery. We assessed systemic hemodynamics parameters (a non-invasive method), pain at rest and activities, parameters of hemostasis and fibrinolysis, plasma levels of stress hormones, cytokine levels at seven stages of the study (before, during and three days after surgery).

Results. Patients in group 1 with epidural anesthesia had significantly less pain both at rest and motion. The most blood saving effect (up to 60% of blood loss) was also found in group 1. Hemodynamic monitoring demonstrated epidural anesthesia not to lead to the life-threatening events of myocardial contractility, cardiac output, systemic vascular resistance and critical increasing of extravascular lung water. The impact of epidural anesthesia on hemostasis encompassed the activation of both coagulation and fibrinolysis. Furthermore, patients in group 1 compared to group 2 had significantly lower plasma levels of glucose, lactate, C-reactive protein, cortisol, and interleukins IL-1β, IL-6, IL-10.

Conclusion. Comprehensive anesthetic protection in spinal deformity surgery based on epidural anesthesia provides adequate antinociceptive effects, inhibition of endocrine and metabolic stress response and correction of hemostasis problems.

Key words: epidural anesthesia; spinal surgery; surgical stress response.

Spinal deformity surgeries of different etiology are highly traumatic and reflexogenic. They are characterized by significant perioperative blood loss and [1, 2]. Anesthetic management of correcting operations is the most difficult, and insufficiently solved problem in modern spinal surgery. The development of highly effective techniques of anesthetic protection, informative intraoperative monitoring of spinal functioning, the study of intraoperative blood loss control, and adequate choice of artificial respiration modes, intraoperative control of cardiohemodynamics and lungs hemodynamics still remain relevant [3].

Highly traumatic surgeries and related acute stress response cause significant immunological changes. Stress hormones (adrenaline and cortisol) play a key role in stress-induced suppression of adaptive immunity [4]. One of the most effective anesthetic approaches to stress response restriction is the use of regional anesthesia. A number of authors [5–9] have shown a beneficial effect of postoperative epidural analgesia on a patient`s body in the form of stress response weakening, reduced pain syndrome and immune alterations. Among the possible mechanisms of thoracic epidural analgesia effects, the limitation of stress hormones release which activates coagulation has been currently discussed. Moreover the systemic effect of local anesthetics, including their anticoagulant effect *in vitro*, has been demonstrated as well as the restriction of systemic inflammation processes closely related to hemostasis system, and the restriction of systemic inflammatory

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response accompanying highly traumatic surgeries has been shown [10–13]. However, an opinion has been widely spread that pathological changes of the spinal canal elements interfere usual anesthetic circulation in epidural space preventing from adequate analgesia [2].

Nowadays, there are no common approaches to intraoperative and postoperative epidural anesthesia in spinal pathologies that requires further studies in accordance with current knowledge of pain mechanisms and possible ways of its suppression at spinal level. At the same time there are some reports in literature on successfully used the epidural anesthesia in patients with spinal pathology and the diagnostics of endocrine and metabolic changes [14, 15].

The aim of the investigation was to assess the efficacy of epidural anesthesia/analgesia in complex anesthetic management in reconstructive surgery of spinal deformities.

Materials and Methods. The prospective randomized study involved 350 patients aged from 15 to 65 years, with degenerative diseases (osteochondrosis, multilevel spinal stenosis, spondylolisthesis, and hernias of intravertebral disk), and spinal injury. Among the patients there were 213 female (60.9%) and 137 male (39.1%) patients. Exclusion criteria were the following: thromboembolic episodes, coagulopathy, anemia, thrombocytopenia, and leukemia. During the period from August, 2007 to September, 2011 the patients underwent the following planned spinal surgeries: surgical correction of spinal deformities (1–2-stage operations — congenital, idiopathic, traumatic deformities); surgical treatment of degenerative diseases of vertebral column — stenosis with multilevel transpedicular fixation by different types of metallic constructions and spondylodesis, spondylolisthesis with decompression of spinal cord and nerve roots, and anterior thoracic and lumbar fusion.

The study complies with the declaration of Helsinki (adopted in June, 1964 (Helsinki, Finland) and revised in October, 2000 (Edinburg, Scotland)) and approved by the Ethics Committee of Nizhny Novgorod Research Institute of Traumatology and Orthopedics. Written informed consent was obtained from all patients.

Depending on the type of anesthesia all patients were randomly divided into two clinical groups, both groups were comparable in anthropometric characteristics. Anesthesia in all groups was induced by propofol IV (2–3 mg/kg) and fentanil IV (2 μg/kg). For muscle relaxation we used esmeronium bromide, at the dose of 0.6 mg/kg for trachea intubation, and 5 μg/kg/min — for continuous infusion intraoperatively, with TOF-Watch assessment. Patients in group 1 (n=205) were given combined anesthesia: epidural and endotracheal anesthesia with sevoflurane. After IV sedation or induction patients in group 1 underwent catheterization of epidural space up to the 2–4 segments higher than the alleged surgical wound level was, in the thoracic level. After the test-dose (2 ml 2% lidocaine) the bolus were given with 3 to 10 ml of 0.375–0.75% ropivacaine, and fentanil 50–100 μg followed by infusion of the mixture of 0.2% ropivacaine solution with fentanil 2 μg/ml and epinephrine 2 μg/ml at the rate of 5–10 ml/h. If the surgery exceeded more than 5–6 spinal segments two-level epidural anesthesia with ropivacaine and fentanil was performed. General anesthesia was maintained by sevoflurane in both groups.

In the postoperative period after neurological assessment in group 1 epidural anesthesia was continued by 0.2% ropivacaine with fentanil (2 μg/ml) and epinephrine (2 μg/ml), and when patients transferred to surgical department disposable elastomeric infusion pumps were used with controlled injection rate from 2 to 8 ml/h within 2–3 days using one or two epidural catheters.

Patients in group 2 (n=145) were given inhalation anesthesia with sevoflurane and continuous fentanil 0.002 mg/kg/h. Postoperative anesthesia included systemic administration of opioids (morphine IV). Patients in both groups had basic analgesia by IV paracetamol and ketorolac for 3 days during the postoperative period.

The investigations included the following stages: stage 1 — initial stage before surgery, stage 2 — incision, stage 3 – traumatic, 4 — the end of surgery, stage 5 — 4 h after the operation, stage 6 — 16 h after the operation, stage 7 — the third day after the surgery. During the surgery and anesthesia all patients underwent monitoring ECG in three leads, hemodynamics by a non-invasive method (apparatuses NICCOMO (Germany), NIHON COHDEN (Japan)). Coagulogram: activated partial thromboplastin time (APTT), thrombin clotting time (TCT), soluble fibrin-monomer complexes (SFMC), and XII-dependent fibrinolysis were measured preoperatively and twice postoperatively, at 4 and 5 stages. We studied complete blood count data, levels of glucose, lactate, cortisol, adrenaline, ACTH of blood serum, cytokines (n=125): IL-1β, IL-6, IL-10 and acute phase proteins (n=125) in blood serum. To measure cortisol concentration we used immunoenzymometric kit CORTISOL (Diagnostics Biochem Canada Inc.), the sensitivity of the technique was 0.4 μg/dl. Glucose was measured using a unified glucose oxidase test on “Exan-1” (Super GL ambulance, Germany).

Postoperative pain was assessed using 10-point Visual Analogue Scale (VAS). All numeric values were statistically analyzed using STATISTICA 6.0. Multiple one-sign comparison of the groups was carried out using ANOVA or Kruskal–Wallis test. We performed the one-sign comparison of two related groups using Student t-test or Wilcoxon criterion.

Results and Discussion

Blood loss. The study has revealed statistically significant intraoperative blood loss reduction by 60% in patients of group 1 compared to group 2 (423.6±24.4 ml versus 1045.3±16.5 ml). No differences have been

Table 1

Dynamics of hemodynamic parameters at surgery stages (M±m)

Stages	Groups	SBP, mm Hg	MAP, mm Hg	HR, bpm	CI, L/min/m^2	CVRI, dyne·s·cm^{-5}
1	1	115.9±6.8$^{\#}$	87.5±1.2$^{\#}$	88.7±3.9$^{\#}$	3.7±0.3$^{\#}$	1567.5±102.3$^{\#}$
	2	120.1±9.1$^{\#}$	85.4±2.8$^{\#}$	90.1±4.2$^{\#}$	3.6±0.1	1685.6±97.9$^{\#}$
2	1	93.1±7.4$^{*\#}$	66.4±5.3$^{\#*}$	72.2±5.3$^{\#*}$	2.8±0.2*	1348.3±87.3$^{\#*}$
	2	110.7±5.8$^{\#}$	75.3±1.9$^{\#*}$	82.4±4.7	3.2±0.1	1755.4±104.4*
3	1	88.6±5.7$^{*\#}$	65.6±8.8$^{\#*}$	69.2±4.3$^{\#}$	2.8±0.6$^{\#*}$	1765.9±114.1$^{\#*}$
	2	98.8±9.2$^{\#}$	70.4±7.3$^{\#}$	78.6±5.4$^{\#}$	3.0±0.4$^{\#}$	2200.2±124.7$^{\#}$
4	1	107.6±5.9$^{\#}$	87.9±5.4	88.6±9.3	3.3±0.3	1896.5±79.6
	2	110.3±4.5	80.3±8.3	92.2±8.5	3.8±0.1	2104.3±69.5*

* — statistically significant differences between the groups, $p<0.05$; # —compared to an initial value, $p<0.05$.

found between groups in postoperative blood loss. The effects of hypotensive epidural anesthesia on intraoperative blood loss were shown by some authors in orthopedic operations on knee and hip joints [16]. Intraoperative blood loss decreased down to 50% compared to general anesthesia. However, there was no information on postoperative blood loss. The main cause of such effective blood loss reduction in spinal surgeries must have been blood flow redistribution and pressure decrease in vertebral bodies and epidural veins.

Hemodynamics. Anesthesia course has been characterized by stability of hemodynamics parameters, which have had no significant changes from normal physiological values. However, in patients of group 2 at the most traumatic stage such parameters as heart rate (HR), mean blood pressure (MBP), cardiac index (CI) appeared to be significantly (by 15–20%) higher (Table 1). Patients in group 1 have had significant decrease of hemodynamic parameters (MAP, CI, cardiovascular resistance index (CVRI)) at the stages 2 and 3 compared to initial values that is related to sympathetic block development. In addition, vasopressor agents (ephedrine by bolus or adrenaline IV, 2–4 μg/min) were used in 20% of patients in group 1. Non-invasive monitoring of hemodynamics has shown that epidural anesthesia do not cause a life-threatening disorders of myocardial contractility, cardiac output, systemic vascular resistance and critical increased concentration of extravascular lung water.

Pain syndrome. The study of postoperative pain syndrome has shown that pain intensity in group 1 was significantly lower, and patients required no additional administration of opioids (Table 2). The patients could get up and walk with infusion pumps on the first and the second days after surgery. Patients of group 1 assessed analgesia quality as excellent.

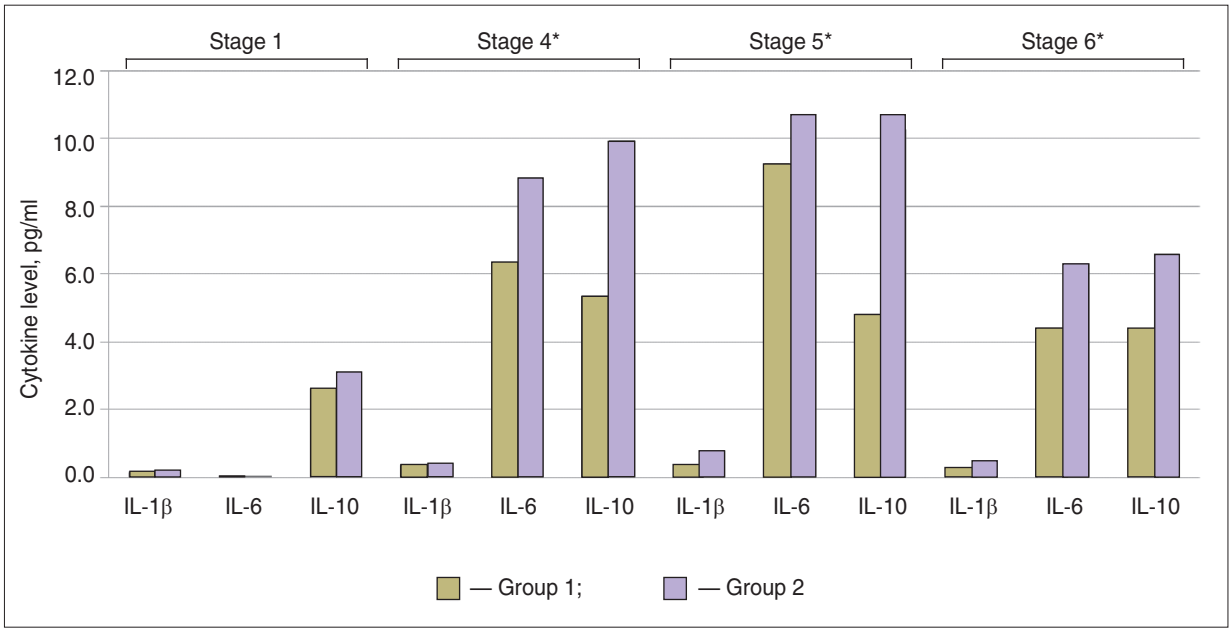
Table 2

An average value of pain syndrome in a early postoperative period according to VAS (M±m)

Postoperative pain intensity	Group 1 (n=205)	Group 2 (n=145)	p
Per 48 h at rest			
0 h	8.2±0.8	52.4±4.5	0.001
2 h	12.1±2.9	46.5±7.2	0.001
3 h	18.3±1.0	42.3±6.8	0.002
6 h	15.2±1.8	39.5±2.9	0.003
12 h	17.4±3.9	47.6±8.4	0.005
16 h	18.3±4.3	46.4±8.1	0.002
24 h	26.6±6.5	42.4±3.8	0.01
36 h	17.7±6.4	38.5±4.7	0.13
Per 48 h in motion			
0 h	18.3±1.6	66.4±2.1	0.003
2 h	35.2±1.2	72.5±1.9	0.01
3 h	32.6±3.3	58.3±1.6	0.01
6 h	29.4±6.9	46.2±2.2	0.06
12 h	26.7±3.6	57.8±2.3	0.01
16 h	28.8±2.3	56.4±2.0	0.02
24 h	34.6±1.8	58.2±5.7	0.07
36 h	25.7±6.8	49.1±2.6	0.04

Patients of group 2 complained of moderate and sometimes severe pain, their daily consumption of morphine was 45.4±15.3 mg. On the first postoperative day, as a rule, they could not turn and lie of their side or pronate unassisted, and were not completely satisfied by analgesia estimating it as satisfactory.

Stress-response. The study of standard markers of surgical stress — the level of glucose and blood serum lactate at three stages of the research (during the surgery) has not revealed significant differences in glycemia dynamics in both groups that indicates adequate anesthesia. By the end of the operation and 4 h later glucose and lactate content in blood serum in group 2 has increased (6.4±0.5 and 1.2±0.01 mmol; $p=0.0001$) and exceeded normal values (3.4–6.6 and 0.5–1.5) compared



Plasma concentrations of cytokines (M±m); * — statistically significant difference of values between the groups, p<0.05

to group 1 (5.2±0.2 and 2.5±0.06 mmol; p=0.0002) that means the importance of adequate sympathetic adrenergic blockade.

Cortisol levels were increasing in both groups with the start of the surgery. However, by the end of the operation and postoperatively it was significantly lower in patients of group 1 (26.9±2.4 versus 18.7±4.2 μg/dl; p=0.00001). Moreover, cortisol concentration in group 1 has returned to normal by the next morning after surgery.

Inadequate analgesia after surgery causes a variety of metabolic disorders which can have negative effects on postoperative recovery. Pain directly induces raise of sympathetic activity manifested by increased levels of adrenaline and noradrenalin in plasma. It also stimulates disbalance of glucose and cortisol metabolism. At the same time, postoperative pain can cause increased thrombogenesis, intestinal obstruction, myocardial ischemia and pneumonia [12].

In addition to metabolic imbalance, postoperative pain can trigger systemic anti-inflammatory response. P. Marz et al. [17] in their study showed the stimulation of sympathetic neurons to promote proinflammatory cytokine production. Stress-induced hyperglycemia can also increase the release of proinflammatory cytokines by leukocytes and endothelial cells. Moreover, glucose controlled by insulin, as well as low doses of local anesthetics are known to limit systemic inflammatory response [18].

The present study has demonstrated that combined general and epidural anesthesia during and after reconstructive spinal operations provides better anesthesia, early mobility of patients, less blood loss, a reduced number of postoperative nausea and vomiting episodes, improved action of a bowel, as well as increased anesthesia satisfaction of patients compared to general anesthesia combined with systemic administration of opioids. Moreover, epidural anesthesia/analgesia has been found to be accompanied by less intense increase of pro- and anti-inflammatory cytokines IL-1β, IL-6 and IL-10 (See Figure).

Hemostasis system. The study of hemostasis system during the first 6 h after surgery in both groups has revealed the prevalence of hypercoagulation changes characterized by APTT with the range of normal values, increased concentration of fibrinogen, SFMC. By the stage 6 APTT has returned to the initial value in all groups with preventive use of low molecular weight heparin. However, in group 2 APTT has remained significantly lower. Moreover, the moderate activation of fibrinolysis has been found in group 2, significantly more intense in the increase of SFMC and XII-dependent fibrinolysis time by 14 and 27% respectively (Table 3). We have not found episodes of thromboembolism during the hospital stay and the study.

One of the most important factors capable of stress response inhibition is the stage when epidural anesthesia/analgesia is used. T. Volk et al. [8] used epidural anesthesia only postoperatively and revealed no differences in the content of circulating cytokines, C-reactive protein or cortisol. Thus, we can suggest a preventive effect of epidural anesthesia on surgical stress response.

The present study has shown that the major blood saving (up to 50% of blood loss volume) is clearly observed when using epidural anesthesia as a component of general anesthesia in spine deformity surgery. In addition, the data of extended researches indicating the capability of epidural anesthesia to

Table 3

Main indicators of hemostasis system at study stages, n=200 (M±m)

Stages	Groups	Indices		
		APTT	SFMC	XII-a-dependent fibrinolysis
1	1	38.7±7.6	37.5±3.8	6.4±0.2
	2	37.9±8.2	40.7±7.4	7.1±0.4
5	1	33.4±2.6#	36.4±3.7	—
	2	28.5±1.8#	37.6±2.9	—
6	1	40.3±5.5*	58.5±6.5*#	13.8±0.7*#
	2	33.4±4.7*#	97.3±3.9*#	20.9±0.2*#

* — statistically significant differences between the groups, p<0.05; # — compared to an initial value, p<0.05.

reduce both thromboembolic complications, and also postoperative blood loss seem to be contradictory [19, 20]. The role of epidural anesthesia seems to consist in the limited activation of hemostasis/fibrinolysis system as one of the components of surgical stress response.

Conclusion. Spinal deformity surgery is accompanied by intense nociceptive stimulation, both intraoperative and postoperative, as well as significant increase of surgical stress response markers. Integrated anesthetic protection based on epidural anesthesia used in spinal deformity surgery provides an adequate antinociceptive effect, inhibition of endocrine and metabolic stress response and correction of hemostasis disorders.

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