

## **ANALYSIS OF EFFICACY OF USING NONDEPOLARIZING MUSCLE RELAXANT ROCURONIUM BROMIDE AND SELECTIVE ANTIDOTE SUGAMMADEX WHILE PROVIDING GENERAL ANESTHESIA TO PATIENTS WITH DEGENERATIVE SPINAL CANAL STENOSIS OF THE CERVICAL SPINE**

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### **ABSTRACT**

*At present effective restoration of the life quality, full occupational and social rehabilitation are necessary conditions while providing medical care to surgical patients. Present study was aimed to analyze the efficacy of using nondepolarizing muscle relaxant Rocuronium bromide and selective antidote Sugammadex while providing general anesthesia to patients with degenerative spinal canal stenosis of the cervical spine.*

*The study included 96 patients who underwent single-level corpectomy with the installation of a telescopic prosthesis for stenosing processes in the cervical spine. Depending on the type of anesthesia patients were divided into 2 groups. In the main group (I group) anesthetic management was performed using antidepolarizing muscle relaxant Rocuronium bromide (Esmeron) and its selective antidote Sugammadex (Brydan). In the clinical comparison group (II group) muscle relaxants of peripheral action Arduan and Proserin were used for decurarization. Gender characteristics (sex, age), constitutional peculiarities (height, weight, body mass index), technical parameters of surgical interventions (extent of blood loss, anesthesia duration) and course of general anesthesia (speed of the onset and elimination of neuromuscular block) were assessed during the analysis. The effectiveness of neuromuscular block reversion was evaluated according to the clinical data.*

*No statistically significant differences were found during the comparative analysis between the groups by sex, age and constitutional peculiarities, as well as by the risks of anesthesia according to ASA. While studying the parameters of the anesthesia duration, extent of blood loss, activation time and length of hospital stay the absence of a statistically significant difference in intraoperative criteria was revealed, wherein the controlled reversion of neuromuscular block allowed realizing a safe early activation of patients and reducing the length of hospital stay in I group. It was also found that the mean time of onset of anesthesia in I group was statistically significantly lower according to the modified scale of Fuchs-Buder. Conditions while performing intubation after induction of anesthesia estimated 180 seconds after the onset were better in I group patients. Meanwhile, no correlation dependence of the speed of neuromuscular block reversion was revealed with the duration of general anesthesia, as well as anthropometric parameters and gender features of surgical patients. During the comparative statistical analysis fewer complications were detected in I group.*

**KEYWORDS:** *antidepolarizing muscle relaxants, selective antidotes of muscle relaxants, neuromuscular block reversion, cervical spine, decompressive-stabilizing interventions.*

### **INTRODUCTION**

At present effective restoration of the quality of life, full occupational and social rehabilitation are necessary conditions while providing medical care to surgical patients [Rihn J et al, 2013; Byvaltsev V et al., 2015; 2016]. To prevent the development of

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intra- and postoperative complications while performing surgical interventions the methods of neurophysiological monitoring are widely used for the anesthetic management [Grayling M, Sweeny B, 2007; Levina G et al., 2016].

Over the 2007 to 2015 period in the Department of Anesthesiology and Reanimation No 1, over 5000 general anesthesia has been carried out for various diseases and traumas of neurosurgical patients. The analysis of postoperative results showed that the vast majority of adverse effects of general anesthesia and the early postoperative period are associated with long-term of the neuromuscular block reversion and postanesthetic depression.

From modern positions in anesthesiology and reanimatology, one of the directions providing the safety of anesthesia duration with the ability to quickly control the restoration of the vital functions of patients in the early postoperative period is the use of a combination of nondepolarizing muscle relaxants and their selective antidotes [Chambers D et al., 2010; Gaszynski T et al., 2012].

The requirements for drugs in providing general anesthesia are: effective implementation of neuromuscular block and the onset of general anesthesia, easy controllability of the depth of anesthesia and rapid elimination with restoration of consciousness level in patients for timely diagnosis of pathological conditions requiring active measures for their elimination [Hemmerling T, Le N, 2007; Tran D et al., 2015]. This is a necessary condition for performing decompressive-stabilizing neurosurgical interventions, especially in the cervical spine. Prolonged stenosis of the spinal canal in the cervical region is accompanied by a significant rearrangement of the liquor- and blood circulation of the spinal cord, wherefore, after reconstruction of the spinal canal, it is necessary to control the restoration of functions and identification of neural structure dysfunctions, which is most important in the early postoperative period for the solution of the issue of urgent revision intervention [Byvaltsev V et al., 2013; Lee M et al., 2013].

To perform the assigned tasks antidepolarizing muscle relaxant Rocuronium bromide (Esmeron) and its selective antidote Sugammadex (Brydan) were used since September 2014, while providing general anesthesia in the Neurosurgery Center of

the Road Clinical Hospital at Irkutsk-Passenger station JSC "Russian Railways". The lack of information in the specialized literature on the results of using the abovementioned drugs in spinal surgery determined the purpose and objectives of present study.

Present study was aimed to analyze the efficacy of using nondepolarizing muscle relaxant Rocuronium bromide and selective antidote Sugammadex while providing general anesthesia to patients with degenerative spinal canal stenosis of the cervical spine.

#### MATERIAL AND METHODS

One-center prospective study was performed. The results of general anesthesia for 96 patients with degenerative spinal canal stenosis of the cervical spine due to herniated intervertebral discs, ossification of the posterior longitudinal ligament, hypertrophy of the yellow ligament and arthrosis of the facet joints were retrospectively analyzed. According to the neuroimaging data, the localization at the level of C<sub>III</sub>-C<sub>IV</sub>, C<sub>IV</sub>-C<sub>V</sub> was detected in 9 (9%) cases, C<sub>IV</sub>-C<sub>V</sub>, C<sub>V</sub>-C<sub>VI</sub> in 24 (25%), C<sub>V</sub>-C<sub>VI</sub>, C<sub>VI</sub>-C<sub>VII</sub> in 57 (60%), C<sub>VI</sub>-C<sub>VII</sub>, C<sub>VII</sub>-Th<sub>I</sub> – in 6 (6%) patients.

Surgical approach, direct decompression of nerve structures were performed according to generally accepted neurosurgery standards using the OPMI Pentero (Carl Zeiss, Germany) surgical microscope, specialized power tools, high-speed drill (Anspach Effort Inc., USA) and retractor systems ADD-plus (Ulrich, Germany) with implantation of the distraction endoprosthesis of vertebral body after a single-level corpectomy.

Depending on the type of anesthesia, patients were divided into 2 groups: I group (main group, n=50) consisted of patients operated with non-depolarizing muscle relaxant Rocuronium bromide (Esmeron) 0.6-1 mg/kg, Diprivan (Propofol) 4-12 mg/kg/h, followed by the introduction of selective antidote Sugammadex (Brydan) 4 mg/kg for rapid reversion of the neuromuscular block. The II Group (clinical comparison group, n=46) included patients retrospectively selected in a random sample. Patients corresponded to all the inclusion and exclusion criteria and were operated earlier for the same indications, but for the general anesthesia, nondepolarizing muscle relaxant Pipecuronium

bromide (Arduan) 80-100  $\mu\text{g}/\text{kg}$ , Diprivan (Propofol) 4-12  $\text{mg}/\text{kg}/\text{h}$  were used, for decurarization – Neostigmine methyl sulfate (Proserin) 2  $\text{mg}$ .

All operations were performed in the patient's supine position with the use of total intravenous anesthesia and artificial lung ventilation, the use of drugs to eliminate neuromuscular block was carried out after layered closure of the postoperative wound.

Gender characteristics (sex, age), constitutional peculiarities (height, weight, body mass index), technical parameters of surgical interventions (extent of blood loss, duration of anesthesia) and the course of general anesthesia (the speed of onset and elimination of neuromuscular block) were assessed for the comparative analysis. The effectiveness of the neuromuscular block reversion was evaluated by the recovery of spontaneous breathing, extremity active range of motion, the ability to self-hold the head and perform simple commands.

Statistical analysis of the study results was performed using Microsoft Excel and Statistica 8.0 software. To assess the significance of differences in sample populations, the criteria for nonparametric statistics were used, and the level of  $p < 0.05$  was considered as the lower limit for reliability. The data are presented in median and interquartile range as Me (25%; 75%). Criteria for nonparamet-

ric statistics were used: Mann-Whitney for intergroup comparison, Wilcoxon criterion for dependent samples, Pearson's chi-squared test ( $\chi^2$ ) for binomial signs.

## RESULTS

General information about the study group patients is presented in table 1: mainly males of middle age (35-60 years) with supernutrition (body mass index  $>25 \text{ kg}/\text{m}^2$ ) predominated. No statistically significant differences were found during the comparative analysis between the groups of studied patients by sex ( $p=0.62$ ), age ( $p=0.45$ ) and constitutional peculiarities ( $p=0.34$ ), as well as by the risks of anesthesia according to ASA (0.76) (Table 1).

Summary data on the duration of anesthesia, extent of blood loss, activation time and the length of hospital stay are presented in table 2. Comparative analysis established that the studied intraoperative parameters did not have a statistically significant difference ( $p > 0.05$ ), wherein, the controlled reversion of neuromuscular block allowed realizing a safe early activation of patients and reducing the length of hospital stay (Table 2).

While analyzing the data on the course of general anesthesia, it was found that the mean time of the onset of anesthesia in I group was statistically

TABLE 1

Distribution of studied patients by groups depending on the type of anesthesia

Indicators	I group, n=50	II group, n=46	p
Age, years, Me	39 (35; 52)	38 (35; 51)	0.45
Sex	Male n (%)	33 (73)	0.62
	Female, n (%)	12 (27)	
Body mass index $\text{kg}/\text{m}^2$ , Me	26.4 (23.1; 29.4)	26.8 (23.5; 29.7)	0.34
Risks of anesthesia by ASA, Me	2 (2; 3)	2 (2; 3)	0.76

TABLE 2

Characteristics of patients by surgical criteria and peculiarities of postoperative management

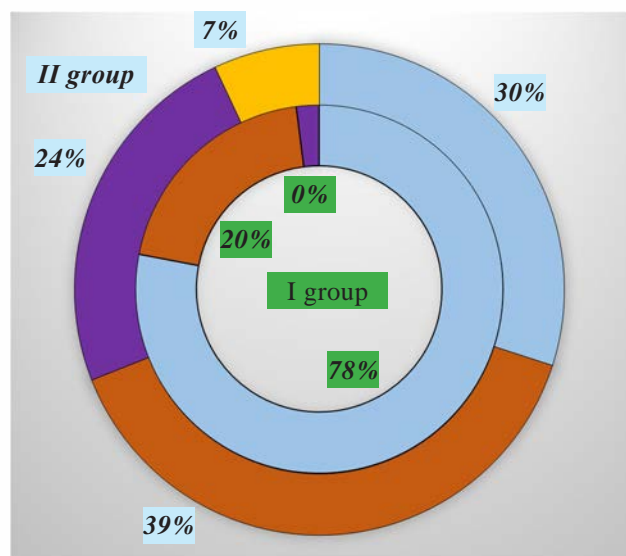
Parameters	I group, n=50	II group, n=46	p*
Duration of general anesthesia (min)	145 (90; 160)	150 (90; 175)	0.51
Extent of blood loss (ml).	120 (90; 165)	135 (95; 170)	0.48
Activation time (days).	1 (1; 2)	2 (1; 2)	0.04
Length of hospital stay (days)	8 (7; 8)	10 (9; 10)	0.02

significantly lower: for I group, 46 (44; 50) seconds; for II – 80 (68; 86) (p=0.015). It was also established that the conditions for intubation after induction of anesthesia, estimated 180 seconds after its onset, were better in I group of patients according to the modified scale of Fuchs-Buder [Fuchs-Buder T et al., 2007] compared to II group (p=0.008 ) (Fig. 1).

The study of the speed of neuromuscular block reversion allowed establishing smaller time index in I group than in II group – 135 (115; 175) seconds and 575 (515; 630) seconds, respectively (p<0.0001). No correlation was revealed between the speed of neuromuscular block reversion and duration of general anesthesia (R>0.05, p>0.05), as well as anthropometric parameters and gender characteristics of operated patients (R>0.05, p>0.05).

The incidence of registered complications after general anesthesia is shown in figure 2. During the comparative analysis, statistically significantly smaller number of them was found in I group of patients in comparison with II group (p<0.05).

No complications or side effects associated with their pharmacokinetics and pharmacodynamics were registered in the conducted study with the use of Esmeron and Brydan drugs.



**FIGURE 1.** Characteristics of patients by the conditions for performing intubation according to the modified scale of Fuchs-Buder  
 Note: Excellent (■), good (■), satisfying (■), unsatisfying (■)

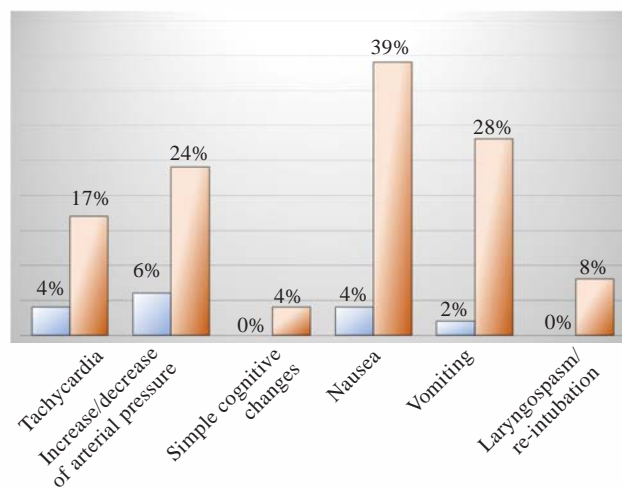
**DISCUSSION**

In modern anesthesiology, muscle relaxants are an integral part of providing general anesthesia in most surgical interventions [Shukla A, Misra S, 2016].

Rocuronium bromide (Esmeron) is a nondepolarizing muscle relaxant, which has a high rate of neuromuscular block development with non-significant effect on the functioning of the cardiovascular system [Naguib M et al., 1995].

High efficacy of anesthesia with low risks of complications of using Rocuronium derivatives has been proved by a number of studies [Chatrath V et al., 2010; Kwon M et al., 2013; Oh A et al., 2013]. However, in specialized literature, the effectiveness of their use in surgical interventions on the cervical spine is not fully illuminated.

Since the appearance of Sugammadex (Brydan) drug for the neuromuscular block reversion, the new era of efficacy and safety of surgical interventions has been developed in anesthesiology and re-animation [Belekar V, Shubhangi K, 2013]. However, neurophysiological monitoring is necessary for an effective dosing regimen [Della Rocca G et al., 2012; Dogan E et al., 2014]. A number of studies have shown that the use of Sugammadex can reduce the time of anesthesia and extubation without increasing the incidence of adverse effects of anesthesia [Gaszynski T et al., 2012; Carron M et al., 2013; Park E et al., 2016]. The use of selective antidote Rocuronium also helps to reduce the risk of developing early postoperative complications, improves the overall condition of patients, reduces the duration of observation in the intensive care



**FIGURE 2.** Registered complications in study group patients  
 Note: I group (■), II group (■)

unit and the overall duration of inpatient treatment, as well as prevents the development of incomplete reversion of neuromuscular block and re-intubation of patients [Srivastava A, Hunter J, 2009; Varadhan K et al., 2010].

It has been shown that the means used to control neuromuscular block reversion while performing surgical interventions in spinal surgery (neurophysiological monitoring, TOF Watch neurostimulants, etc.) proved to be quite effective [Lieberman J et al., 2008; Gonzalez A et al., 2009; Adamus M et al., 2011]. But even the application of the abovementioned methods does not allow to avoid the risks of development of complications associated with insufficient recovery of neuromuscular transmission in all cases, as well as the presence in the arsenal of high-tech equipment requires significant economic costs, on the acquisition, maintenance and training of medical staff. In connection with this, the need to study the clinical parameters of patient monitoring in the early postoperative period is topical.

In present study, we confirmed the effectiveness of using nondepolarizing muscle relaxant Ro-

curonium bromide (Esmeron) before Pipecuronium bromide (Arduan). We also focused on the importance of using the selective antidote Sugammadex (Brydan) while performing general anesthesia during neurosurgical interventions on the cervical spine.

#### CONCLUSION

Present study showed a high efficiency of simultaneous use of antidepolarizing muscle relaxant Rocuronium bromide (Esmeron) and its selective antidote Sugammadex (Brydan) while performing decompressive-stabilizing interventions on the cervical spine. Rapid recovery of neuromuscular transmission and productive contact with the patient was established to assess the functional state of the cervical spinal cord in the early postoperative period, as well as fewer complications compared to traditional methods of providing general anesthesia.

Further researches are required to study the effectiveness of neuromuscular block elimination in the provision of general anesthesia for various nosological forms of neurosurgical diseases and traumas.

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