

The condition of newborns after the conversion of epidural analgesia to anesthesia during cesarean section: a prospective randomized study

Yu.S. Alexandrovich¹, O.V. Ryazanova^{2,*}, D.I. Karabaev³,
S.N. Nezabudkin¹, A.M. Ioskovich^{4,5}

¹ Saint Petersburg State Pediatric Medical University,
St. Petersburg, Russia

² D.O. Ott Research Institute of Obstetrics and Gynecology RAMS,
St. Petersburg, Russia

³ Municipal Maternity Hospital No. 1, Dushanbe,
Republic of Tajikistan

⁴ Shaare Zedek Medical Center, Jerusalem, Israel

⁵ Hebrew University, Jerusalem, Israel

Abstract

INTRODUCTION: When performing epidural analgesia in childbirth, if surgical delivery is necessary, the question arises about the choice of further tactics of regional anesthesia. The article discusses the peculiarities of the effect of local anesthetics on the condition of a newborn during the conversion of epidural analgesia into anesthesia when caesarean section is necessary, depending on the local anesthetic used. **OBJECTIVE:** To assess the condition of a newborn baby during the conversion of epidural analgesia in childbirth through the natural birth canal into anesthesia during cesarean section, depending on the local anesthetic used. **MATERIALS AND METHODS:** A prospective randomized study of 143 children born to mothers who underwent the conversion of epidural analgesia into anesthesia for operative delivery by caesarean section was conducted. Depending on the local anesthetic used, the patients were divided into three groups, in the first group 20.0 ml of 2 % lidocaine in combination with 0.1 mg of epinephrine was injected into the epidural space, in the second group — 20.0 ml of 0.5 % bupivacaine, in the third — 20.0 ml of 0.75 % ropivacaine. The assessment of the condition of newborns was carried out on the Apgar scale at the 1st and 5th minutes

Состояние новорожденных после конверсии эпидуральной анальгезии в анестезию при кесаревом сечении: проспективное рандомизированное исследование

Ю.С. Александрович¹, О.В. Рязанова^{2,*}, Д.И. Карабаев³,
С.Н. Незабудкин¹, А.М. Иоскович^{4,5}

¹ ФГБОУ ВО «Санкт-Петербургский государственный
педиатрический медицинский университет»,
Санкт-Петербург, Россия

² ФГБНУ «Научно-исследовательский институт
акушерства, гинекологии и репродуктологии
им. Д.О. Отта», Санкт-Петербург, Россия

³ Городской родильный дом № 1, Душанбе,
Республика Таджикистан

⁴ Медицинский центр Шаарей Цедек, Иерусалим, Израиль

⁵ Еврейский университет, Иерусалим, Израиль

Реферат

АКТУАЛЬНОСТЬ: При проведении эпидуральной анальгезии (ЭА) в родах в случае необходимости оперативного родоразрешения встает вопрос о выборе дальнейшей тактики регионарной анестезии. В статье рассмотрены особенности влияния местных анестетиков на состояние новорожденного при проведении конверсии ЭА в анестезию при необходимости выполнения операции кесарева сечения в зависимости от используемого местного анестетика. **ЦЕЛЬ ИССЛЕДОВАНИЯ:** Оценить состояние новорожденного при проведении конверсии ЭА в родах через естественные родовые пути в анестезию при кесаревом сечении в зависимости от применяемого местного анестетика. **МАТЕРИАЛЫ И МЕТОДЫ:** Проведено проспективное рандомизированное исследование 143 детей, рожденных от матерей, которым проводили конверсию ЭА в анестезию для оперативного родоразрешения методом кесарева сечения. В зависимости от используемого местного анестетика пациенток распределили на три группы, в 1-й группе в эпидуральное пространство вводили 20,0 мл 2 % раствора лидокаина в комбинации с 0,1 мг эpineфрина, во 2-й группе — 20,0 мл 0,5 % раствора бупивакаина, в 3-й — 20,0 мл 0,75 % раствора ропивакаина.



of life and on the NACS scale in the first 15 minutes, 2, 24 and 72 hours after birth. **RESULTS:** The assessment of newborns on the Apgar scale, regardless of the local anesthetic used during epidural anesthesia at the first and fifth minutes, corresponded to 7 or more points ($p > 0.05$). The neuropsychiatric state of newborns when assessed on the NACS scale did not differ statistically significantly in all groups and at all stages of the study. Within each group, between the study stages, the average values of the NACS scores increased statistically significantly compared to the previous one. **CONCLUSIONS:** The conversion of epidural analgesia in childbirth through the natural birth canal into anesthesia during cesarean section is safe for the fetus and newborn when using 20.0 ml of 2 % lidocaine in combination with 0.1 mg of epinephrine or 20.0 ml of 0.5 % bupivacaine, or 0.75 % ropivacaine in a volume of 20.0 ml.

KEYWORDS: epidural anesthesia, epidural analgesia, conversion, caesarean section, local anesthetics, newborns

* *For correspondence:* Oksana V. Ryazanova — Dr. Med. Sci., Leading Researcher of the Department of Obstetrics and Perinatology, D.O. Ott Research Institute of Obstetrics and Gynecology RAMS, head of Department of anesthesiology and intensive care, City Perinatal Center No 1, St. Petersburg, Russia; e-mail: oksanaryazanova@mail.ru

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Оценку состояния новорожденных проводили по шкале Апгар на 1-й и 5-й минутах жизни и по шкале NACS в первые 15 мин, через 2, 24 и 72 ч после рождения. **РЕЗУЛЬТАТЫ:** Оценка новорожденных по шкале Апгар независимо от применяемого местного анестетика при эпидуральной анестезии на 1-й и 5-й минутах соответствовала 7 баллам и более ($p > 0,05$). Психоневрологическое состояние новорожденных при оценке по шкале NACS статистически значимо не различалось во всех группах и на всех этапах исследования. Внутри каждой группы между этапами исследования средние значения оценок по NACS статистически значимо увеличивались по сравнению с предыдущим. **ВЫВОДЫ:** Конверсия ЭА в родах через естественные родовые пути в анестезию при кесаревом сечении безопасна для плода и новорожденного при использовании 20,0 мл 2 % раствора лидокаина в комбинации с 0,1 мг эпинефрина или 20,0 мл 0,5 % раствора бупивакаина либо 0,75 % раствора ропивакаина в объеме 20,0 мл.

КЛЮЧЕВЫЕ СЛОВА: эпидуральная анестезия, эпидуральная анальгезия, конверсия, кесарево сечение, местные анестетики, новорожденные

* *Для корреспонденции:* Рязанова Оксана Владимировна — д-р мед. наук, ведущий научный сотрудник отдела акушерства и перинатологии ФГБНУ «Научно-исследовательский институт акушерства, гинекологии и репродуктологии им. Д.О. Отта», заведующая отделением анестезиологии и реанимации городского Перинатального центра № 1, Санкт-Петербург, Россия; e-mail: oksanaryazanova@mail.ru

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Introduction

One of the key issues of modern obstetric anesthesiology-resuscitation is the problem of anesthesia of childbirth. Intense pain during childbirth can cause a number of side effects in women, including a physiological reaction to stress, uncoordinated uterus contractions, increase of labor duration, and even post-traumatic stress disorder or postpartum depression [1–6]. In addition, pain of child-

birth can have a direct or indirect negative impact on the fetus and newborn, for example, aggravate hypoxia and metabolic acidosis, as well as cause cognitive and emotional child development disorders in the future [6, 7–10].

Despite the wide arsenal of drugs and techniques previously used for systemic analgesia in obstetrics (opioid and non-opioid analgesics, inhalation anesthetics), at the present stage, neuroaxial methods of childbirth anesthesia are considered the most effective. The most common

is epidural analgesia (EA), which provides high-quality anesthesia in parturient women, relieves anxiety and minimally affects the functions of respiratory and cardiovascular systems of mother and fetus [1, 11, 12].

The advantages of epidural analgesia are high analgesia efficiency, low complication rate, and the possibility of switching to epidural anesthesia if cesarean section surgery is necessary [13].

In case, when during delivery through the natural birth canal with EA appear indications for abdominal delivery, a question of choosing the appropriate method of anesthesia, which depends on various factors, in particular, such as operation urgency, patient's condition and preferences, arises to anesthesiologist. In addition, it is necessary to monitor fetus condition, since anesthesia can worsen uteroplacental and fetal blood flow, which generally determines the outcome of childbirth and affects the newborn development in the future [14].

Thus, despite the fact that epidural analgesia in childbirth and its conversion, if necessary, into anesthesia during operative delivery is widely used and the effectiveness of this technology has been proven from the standpoints of clinical, laboratory and instrumental woman status, studies evaluating the neuropsychiatric condition of a newborn in this category of patients are isolated, which requires further study.

Purpose of the study

To evaluate the condition of newborns during the conversion of EA in childbirth through the natural birth canal into anesthesia during cesarean section, depending on the local anesthetic (LA) used.

Materials and methods

A prospective single-center randomized study, approved by the local Ethics Committee of St.Petersburg State Pediatric Medical University of Ministry of Health of Russian Federation (No. 2/19 of 11.12.2017) was conducted. Randomization was carried out by the envelope method. The study involved 143 children who were born in the city maternity hospital No. 1 in Dushanbe (Republic of Tajikistan) from mothers who received prolonged EA during physiological childbirth for the purpose of anesthesia. In the presence of regular labor activity, after the field was treated twice with antiseptic, in the patient's side position, the epidural space was punctured with a Tuohy 18 G needle at the level of LIII–LIV, LIV–LV. Then B. Braun catheter ("Perifix") with 2 cm antibacterial filter was inserted through Tuohy needle in the cranial direction. Catheter was fixed to the skin with a sterile sticker. A 0.125 % solution of bupivacaine was used as LA. In 5 minutes after test dose (60 mg of 2 % lidocaine solution), 10.0 ml of LA was administered. In case of analgesic component insufficiency 15 minutes after (when pain severity, evaluated using visual analog

scale (VAS), was than 40 mm), another 10.0 ml of the drug was additionally administered. Maintenance of analgesia was carried out by continuous LA infusion at a rate of 10 ml/h in combination with patient-controlled EA.

When obstetric tactics changed and there were indications for emergency operative delivery, puerperants were transferred to the operating room, where EA was converted into anesthesia. Patients were divided into 3 groups, depending on LA used. In order to induce anesthesia patients of group 1 ($n = 49$) were injected with 20 ml of 2 % lidocaine solution in combination with 0.1 mg of epinephrine into the epidural space; patients of group 2 ($n = 48$) received 0.5 % bupivacaine solution (20 ml); patients of group 3 ($n = 46$) — 0.75 % solution of ropivacaine in a volume of 20.0 ml.

Inclusion criteria: 1) age of women in labor more than 18 years; 2) health assessment with ASA (American Society of Anesthesiologists), corresponding to class I–II; 3) absence of mental disorders; 4) absence of allergic reactions to LA.

Exclusion criteria: 1) severe somatic diseases; 2) neuropsychiatric disorders; 3) purulent-septic diseases; 4) allergy to LA; 5) coagulopathy; 6) therapy with systemic anticoagulants.

The condition of newborns at birth was assessed according to the generally accepted Apgar scale at the 1st and 5th minutes of life.

The neuropsychiatric status was studied using the NACS (Neurological and Adaptive Capacity Score) scale, which includes five main blocks: 1) adaptive ability; 2) passive tone; 3) active tone; 4) unconditional reflexes; 5) general neurological status. The maximum integral score on the NACS scale is 40 points, which corresponds to the norm. The assessment was carried out within first 15 minutes after birth and after 2, 24 hours and 3 days after delivery. The examination was implemented at ambient temperature of 24–26 °C after 2–3 minutes of child adaptation.

Statistical analysis

Statistical data processing was carried out [15] using Statistics 12.0 software package. Graphic material was prepared using the libraries of the open software environment R. To compare the average values of the 2 groups, the Student's *t*-test was used. In the case of comparison of more than 2 groups, ANOVA analysis of variance was used, and then the Tukey HSD Test was used for post-hoc analysis — pairwise comparisons. To compare the average values of 2 (two) groups, the Student's *t*-test was used. In case of more than 2 (two) groups comparison, ANOVA analysis of variance was used. For post-hoc analysis — pairwise comparisons the Tukey HSD Test was used.

Results

General characteristics of women included in the study are presented in Table 1.

Table 1. Characteristics of mothers and operations

Parameter	Group		
	1 (n = 49)	2 (n = 48)	3 (n = 46)
Age, years	25.6 ± 5.4	28.0 ± 6.2	25.7 ± 4.1
Body weight, kg	73.3 ± 10.7	71.6 ± 12.7	73.0 ± 10.2
Woman's height, cm	159.3 ± 5.6	157.0 ± 7.1	159.3 ± 5.3
Gestation period, weeks	39.3 ± 1.7	38.9 ± 1.7	39.6 ± 1.5
Duration of the operation, min	48.6 ± 8.1	47.2 ± 7.2	50.7 ± 7.7

As shown in Table 1, there were no statistically significant differences in the age and anthropometric indicators of women in labor in the study groups. The average age of group 1 patients was 25.6 ± 5.4 years, group 2 — 28.0 ± 6.2 years, group 3 — 25.7 ± 4.1 years. Delivery was carried out at a gestation period of 38–40 weeks. The average duration of cesarean section under epidural anesthesia in patients with 2% lidocaine was 48.6 ± 8.1 minutes, with bupivacaine — 47.2 ± 7.2 minutes, with ropivacaine — 50.7 ± 7.7 minutes, which was statistically insignificant ($p > 0.05$).

The main indications for emergency caesarean section are presented in Table 2.

As shown in Table 2, in the absolute majority of cases, indication for emergency cesarean section was clinical discrepancy between mother's pelvis size and fetal head, discoordination of labor, fetal hypoxia.

In order to study features of anesthesia course, depending on the technique used, an analysis of the dynamics of mean blood pressure (BP) was performed. The results obtained are presented in Table 3.

The highest values of mean BP after surgery at all stages of the study were recorded in patients who received ropivacaine as LA, and were statistically significant between the 2nd and 3rd groups 3 and 6 hours after surgery ($p = 0.01$ and $p = 0.03$, respectively). After surgery in ropivacaine group mean BP value was 91 ± 6.1 mmHg compared with 89 ± 4.4 mmHg in bupivacaine group ($p = 0.01$). 3 hours after surgery, mean BP was 92 ± 6.8 and 87 ± 8.7 mmHg, respectively ($p = 0.03$).

When pairwise comparing the average BP values within the group between the study stages, statistically significant differences were obtained between the measurement of BP before induction of anesthesia and 12 hours after surgery in all patients ($p < 0.01$). In the group where bupivacaine was used, a statistically significant difference in mean BP values was achieved between the following stages of the study: before induction of anesthesia — 3 hours after surgery ($p < 0.01$), before induction — 6 hours after surgery ($p < 0.01$).

When analyzing the status of newborns, it was revealed that the physical data of infants did not differ statistically

Table 2. Indications for cesarean section

Pathology	Group					
	1 (n = 49)		2 (n = 48)		3 (n = 46)	
	abs. number	%	abs. number	%	abs. number	%
Fetal hypoxia	4	8.2	2	4.2	4	8.7
Clinical inconsistency	9	18.4	13	27.1	8	17.4
Weakness of labor activity	1	2.0	2	4.2	5	10.9
Discoordination of labor activity	10	22.0	13	29.3	10	22.0
Premature placental abruption	4	8.2	3	6.3	0	0.0
Cervical dystocia	0	0.0	0	0.0	1	2.2

in the study groups ($p > 0.05$). Newborns in group 1 had a body weight of 3468.2 ± 400.7 g, height — 51.2 ± 1.9 cm, in group 2: body weight — 3409.6 ± 462.9 g, height — 50.8 ± 1.9 cm, in group 3: body weight — 3446.3 ± 374.9 g, height — 51.2 ± 1.8 cm, which indicates the identity of the studied groups ($p > 0.05$).

The Apgar scores of newborns, regardless of the LA used during epidural anesthesia at the 1st and 5th minutes, corresponded to 7 points or more ($p > 0.05$) (Table 4).

Results of comparison of average values of psycho-neurological status of newborns in accordance with NACS scale between groups and between study stages within

Table 3. Dynamics of mean blood pressure values at the stages of the study

Mean blood pressure, mmHg	Group		
	1 ($n = 49$)	2 ($n = 48$)	3 ($n = 46$)
Before induction	93 ± 6.4	$88 \pm 5.8^*$	95 ± 9.3
After operation	90 ± 5.9	$89 \pm 4.4^*$	91 ± 6.1
After 3 hours	90 ± 6.8	$87 \pm 8.7^{*, **}$	92 ± 6.8
After 6 hours	90 ± 7.6	$87 \pm 6.7^{*, \#}$	92 ± 8.4
After 12 hours	$90 \pm 6.9^{\text{E}}$	$86 \pm 7.8^{\text{E}}$	$92 \pm 8.9^{\text{E}}$

* Differences are significant between 2nd and 3rd group.
 ** Differences are significant within the group at the stages of the study before induction of anesthesia — 3 hours after surgery.
 # Differences are significant within the group at the stages of the study before induction of anesthesia — 6 hours after surgery.
 E Differences are significant within the group at the stages of the study before induction of anesthesia — 12 hours after surgery.

Table 4. Average values of the studied indicators

Indicator	Group		
	1 ($n = 49$)	2 ($n = 48$)	3 ($n = 46$)
Child's weight, g	3468.2 ± 400.7	3409.6 ± 462.9	3446.3 ± 374.9
Child's height, cm	51.2 ± 1.9	50.8 ± 1.9	51.2 ± 1.8
Apgar 1, points	7.3 ± 0.6	7.4 ± 0.6	7.3 ± 0.5
Apgar 5, points	7.8 ± 0.5	7.9 ± 0.4	7.8 ± 0.5

Table 5. Dynamics of average values of ratings on the NACS scale

NACS	Group			p (ANOVA)
	1 ($n = 49$)	2 ($n = 48$)	3 ($n = 46$)	
15 min, points	31.3 ± 4.2	32.5 ± 4.1	32.0 ± 3.8	0.365
2 hours, points	34.7 ± 3.3	35.4 ± 3.2	35.2 ± 2.8	0.585
24 hours, points	36.6 ± 2.3	37.0 ± 2.3	36.4 ± 2.2	0.430
3 days, points	38.4 ± 2.0	38.8 ± 1.8	38.6 ± 1.6	0.589
p	< 0.001	< 0.001	< 0.001	—

each group for 3 days after childbirth are shown in Figure 1 and in Table 5.

As shown in Figure 1 and in Table 5, the psychoneurological status of newborns assessed with NACS scale did not differ significantly at all stages of the study, regardless of LA used when converting EA in childbirth through the natural birth canal into anesthesia during cesarean section ($p > 0.005$). In all three compared groups at birth in first 15 minutes, the integral score on the NACS scale corresponded to 31–32 points, after 2 hours the average score of newborns increased to 34–35 points, and after 72 hours it already reached 38–39 points.

It should be noted that in the study in each group, the scores on the NACS scale increased statistically significantly at the next stage compared to the previous one ($p < 0.001$), which indicates an adequate adaptation of newborns to the conditions of life after birth (see Table 5).

Discussion

Currently, cesarean section is the most common delivery operation, which is facilitated by the development and improvement of modern medicine, especially anesthesiology-resuscitation and neonatology. A distinctive feature of obstetric anesthesiology is the need to monitor the safety not only of the woman in labor, but also of infants, which makes it necessary to search for new simple and accessible tools for assessing newborn condition, exposed to anesthesia drugs during childbirth [6, 16–20].

There are very few works in the available literature devoted to the study of the condition of newborns whose mothers were exposed to various methods of anesthesia. The first anesthesiologist who proved the advantage of regional anesthesia over general anesthesia in terms of its effect on the fetus and newborn was Virginia Apgar [21].

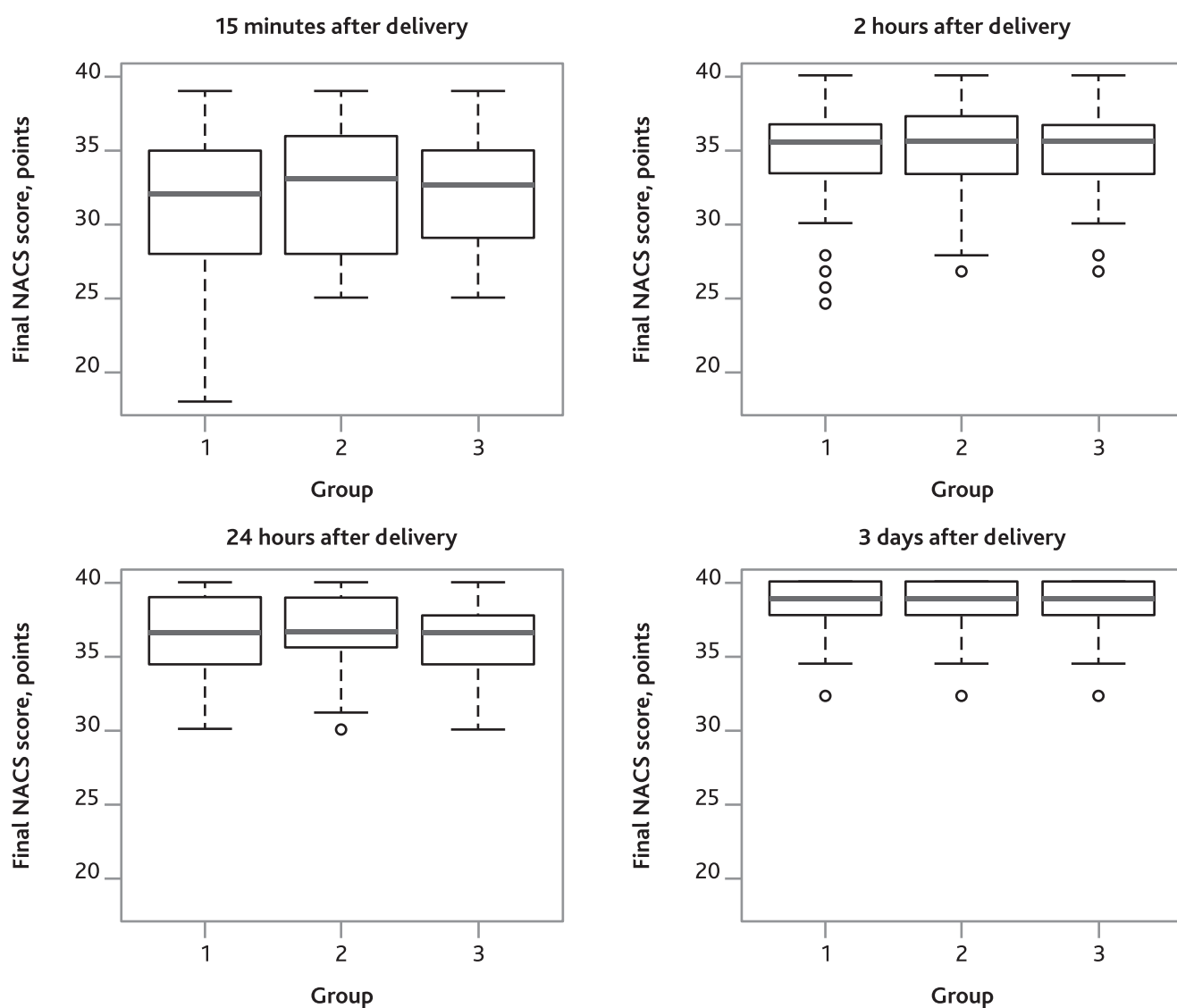


Fig. 1. Comparison of distributions of newborn status assessments on the NACS scale

The scale proposed by her became the first tool for assessing the clinical condition of a newborn after childbirth [14, 21, 22].

In our study, we did not receive any differences in the newborns' condition assessed on the Apgar scale at the 1st and 5th minutes of life, regardless of the LA used during the conversion of EA in childbirth to anesthesia during cesarean section. All newborns had an average score of more than 7 points. We associate such Apgar scores, among other things, with the refusal to use narcotic analgesics both during EA and during the conversion of analgesia into anesthesia during cesarean section. Despite the small doses of anesthetics used during EA, these drugs can enter the systemic bloodstream and penetrate through the placenta to the fetus. Back in 1995, Loftus J.R. et al. [23] found LA in the venous blood plasma of mother and in the umbilical cord blood after EA in childbirth. Moore A. et al. (2016) described a case of EA in childbirth in woman with gestation period of 39 weeks using combination of 0.06 % bupivacaine and 2 mcg/ml of fentanyl for 11 hours (280 mcg of fentanyl). 24 hours after delivery, fentanyl was still detected in the urine of both the mother (2.0 ng/ml) and the newborn (2.4 ng/ml) [24]. Thus, the authors of this study demonstrated that both LA and opioids injected into the epidural space circulate for a long time in the body not only of mother, but also of newborn, which can cause adverse effects. Herrera-Gomez A. et al. (2015) reported adverse effects of EA on newborns. Retrospective cohort study of 2,399 children was conducted; from this number of investigated, 1,848 were born of mothers who did not receive EA, and 551 were born of women who received it. The results showed that newborns whose mothers were anesthetized by EA method had a small but significant decrease in Apgar scores both after 1 minute and 5 minutes after birth. In addition, among them there was a higher proportion of those, who needed intensive care and hospitalization in the neonatal intensive care unit and a lower proportion of early breastfeeding [25].

It is believed that neonatal depression after EA is mainly caused by opioids. In a cohort study by Poma S. et al. (2019), within which 400 women received 0.1 % levobupivacaine EA in combination with 0.5 mcg/ml of sufentanil or combined spinal-epidural analgesia (with intrathecal administration of 3–5 mcg of sufentanil), newborn Apgar scores did not differ between groups [26]. In an earlier study, when comparing newborns whose mothers underwent EA with sufentanil or a combination of sufentanil + bupivacaine or bupivacaine alone, higher Apgar scores were obtained in children in the bupivacaine-only group [27].

It should be noted that Apgar score subsequently did not confirm specificity for assessing newborns whose mothers received medication during delivery [28, 29]. In 1982, Amiel-Tison C. et al. proposed NACS scale (Neurologic and Adaptive Capacity Score), developed on the basis of neurobehavioral tests that more sensitively identify the degree of depression caused by perinatal asphyxia,

diseases of the newborn, influence of medications taken by the mother, etc. [30, 31].

In addition to narcotic analgesics, epinephrine is added as an adjuvant to increase the duration of action of LA [32]. Permit systems vary from country to country. If in Tajikistan, according to clinical recommendations, epinephrine is allowed during pregnancy, then in the Russian Federation there are contraindications for its use during pregnancy, which limits the possibility of using this drug in obstetrics in our country.

Conclusion

According to the results of our study, neuropsychiatric condition of newborns as assessed by the NACS scale did not differ statistically significantly at all stages of the study, regardless of the LA used during the conversion of EA to anesthesia ($p > 0.005$). 15 minutes after birth, the average score of newborns on NACS scale was in the range of 31–32 points, after 2 hours — 34–35 points and after 72 hours — 38–39 points in all study groups. Within each group, between the study stages, the average values of the NACS scores increased statistically significantly compared to the previous one ($p < 0.001$).

Based on the foregoing, it can be concluded that the conversion of EA in childbirth through the natural birth canal into anesthesia during cesarean section is safe for fetus and newborn, under the condition that the manipulation technique is followed correctly. However, in the available literature we have not found any studies investigating the condition of fetus and newborn during the conversion of EA in childbirth through the natural birth canal into anesthesia during cesarean section, which requires further study in this direction. From the point of view of safety for fetus and newborn, all three studied anesthetics can be used equally: 20.0 ml of 2 % lidocaine solution in combination with 0.1 mg of epinephrine, 20.0 ml of 0.5 % bupivacaine solution and 0.75 % ropivacaine solution in a volume of 20.0 ml.

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Author contribution. All authors according to the ICMJE criteria participated in the development of the concept of the article, obtaining and analyzing factual data, writing and editing the text of the article, checking and approving the text of the article.

Ethics approval. This study was approved by the local Ethical Committee of Saint Petersburg State Pediatric Medical University (reference number: 2/19-11.12.2017).

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Author's ORCID:

Alexandrovich Yu.S. — 0000-0002-2131-4813

Ryazanova O.V. — 0000-0003-2354-8565

Karabaev D.I. — 0000-0001-5205-8616

Nezabudkin S.N. — 0000-0002-4341-4380

Ioslovich A.M. — 0000-0001-6449-0254

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