The role of regional anesthesia in the postoperative analgesia in pediatric patients

Dušica Simić1,2, Irena Simić1, Marija Stević1,2, Nevena Jovičić1, Maja Mitrović1, Ivana Budić3,4, Miodrag Milenović5, Vesna Marjanović5,6, Biljana Miličić6
1University Children’s Hospital, Belgrade, Serbia; 2University of Belgrade, Faculty of Medicine, Belgrade, Serbia; 3Niš Clinical Centre, Clinic for Pediatric Surgery and Orthopedics, Niš, Serbia; 4University of Niš, Faculty of Medicine, Niš, Serbia; 5Clinical Centre of Serbia, Emergency Centre, Belgrade, Serbia; 6University of Belgrade, Faculty of Dental Medicine, Belgrade, Serbia

INTRODUCTION

Pain, according to the new definition, is a disturbing experience associated with existing or potential tissue damage, with a sensory, emotional, cognitive, and social component [1]. During childhood, pain has numerous adverse effects – it can prolong hospital stay and even increase incidence of death due to the onset of the systemic inflammatory response [2]. Inadequate treatment of acute pain is one of the important prerequisites for the development of chronic pain. Repetition of painful procedures determines the threshold for pain for the whole life [3].

In pediatric patients, less local anesthetic concentration is more effective than in adults [4]. The effect of the block is faster and shorter. In children under one year of age, nerve fibers are thinner, myelination is scarce, and Ranvier’s knots are closer. The volume of distribution is higher, clearance is smaller, and the free drug fraction is higher, so the doses are almost the same as in adults [5, 6, 7]. Cytochrome CYP1A2 that catalyzes the metabolism of ropi-vacaine matures around the age of 4–7 years, and CYP3A4/7 that catalyzes the metabolism of levobupivacaine matures at the end of the first year [4].

The goal of analgesia in the postoperative period is to reduce or eliminate pain with minimal additional harmful effects. Adequate postoperative analgesia, especially during the first 48 hours, reduces the organism stress response to the surgical procedure, thereby affecting endocrine, metabolic, and inflammatory changes, which improves the outcome of surgical treatment [3, 8–11].

METHODS

We performed retrospective review of pediatric patients (1–14 years), who had been operated on in regional anesthesia techniques, between January 2013 and December 2016. The patients were divided into the following four groups: children younger than three years, those aged 3–7 years, those 7–14 years old, and children...
older than 14 years. All the patients were classified by the American Association of Anesthesiologists classification and all belonged to groups 1–3.

Regional anesthesia techniques were performed during general anesthesia, analgesedation or in the waking state of the patients. We used bupivacaine, lidocaine, and levobupivacaine, as well as combinations that consisted of lidocaine with levobupivacaine and lidocaine with bupivacaine.

Types of applied regional anesthesia techniques were classified into the following six groups: caudal block, epidural, spinal, upper limb blocks, lower limb blocks, and truncal nerve block. The diagnosis of patients involved in the study included injuries, tumors, congenital anomalies, arteriovenous fistula, and appendicitis. Pulse, blood pressure, and oxygen saturation were used as standard anesthesia monitoring.

Postoperatively, the patients were diagnosed with pain based on a scale for age-related pain by nurses who were trained for this follow-up after two, four, six, eight, 10, 12, and 14 hours. The time when analgesia caused by regional anesthesia became insufficient and when it was necessary to apply the analgesic was recorded, and the patients were then classified accordingly into one of the following groups: < 3 hours, 3–6 hours, 6–9 hours, 9–12 hours, > 12 hours.

Also, we analyzed the postoperative occurrence and we measured the intensity of pain by different methods in different ages of children: in children ≤ 12 months old we used the CRIES scale, in children ≤ 3 years old by using FLACC scale, in children 3–5 years old we used Wong scale with facial expressions, and in older children we used linear scales [3, 12, 13].

The exclusion criteria were the following: patients with hypotension, thrombocytopenia, coagulopathy, sepsis, myelodyplasia, and sacral dysgenesis.

The study was approved by the Belgrade University Children’s Hospital Ethics Committee (No. 26/343-017).

Descriptive statistical methods of absolute and relative numbers were used for attribute observation marks, variability measures, central tendencies for numerical labels and methods of inferential statistics. The selection of tests for numerical markings depended on the distribution of data. We used the χ² test for the attributive features of observation marks, and the patients were classified according to the following groups: < 3 hours, 3–6 hours, 6–9 hours, 9–12 hours, > 12 hours.

There was a significant difference between the type of patients’ age and the time of administration of analgesics postoperatively. There was no statistically significant difference between the sex and the time of administration of analgesics postoperatively.

There was a significant difference between the time for postoperative analgetic requirements and the preoperative diagnosis. The shortest time to administer analgetics was in patients with injuries and tumors. Arteriovenous fistula was made in only three patients and the first dose of analgetics was given to all 3–6 hours after intervention (Table 3).

There was a significant difference between the type of block and the first dose of analgetics. The longest postoperative analgesia was recorded in the group with the caudal

### RESULTS

The study was conducted over a period of four years, between January 2013 and December 2016. The summarized patient characteristics, sex, age, indications for surgery, type of local anesthetics, and regional anesthesia techniques are shown in Table 1.

There was no statistically significant difference between type of regional anesthesia techniques and pulse, blood pressure, and oxygen saturation during the operation. After administration of the block as well as during the surgical procedure, all vital signs were within the limits of the reference values for the patient’s age in all our patients.

| Table 1. Patient characteristics, indications for surgery, type of local anesthetics, and regional anesthesia techniques |
|---|---|---|---|---|---|---|
| Number (%) | Male | 377 (66.8%) | Female | 187 (33.2%) |
| Age (years) | < 3 | 84 (14.9%) | 3–7 | 139 (24.6%) |
| | 7–14 | 224 (39.7%) | > 14 | 117 (20.7%) |
| Diagnosis | Tumors | 101 (17.9%) | Injury | 201 (35.6%) |
| | Arteriovenous fistula | 3 (0.5%) | Appendicitis | 21 (3.7%) |
| | Congenital anomaly | 237 (42%) |
| Type of regional anesthesia techniques | Caudal block | 168 (29.8%) | Epidural | 20 (3.5%) |
| | Spinal | 12 (2.1%) | The upper limb block | 179 (31.7%) |
| | The lower limb block | 163 (28.9%) | The hull block | 22 (3.9%) |
| | Bupivacaine | 213 (37.8%) | Lidocaine | 13 (2.3%) |
| | Bupivacaine + Lidocaine | 287 (50.9%) | Levobupivacaine | 28 (5%) |
| | Levobupivacaine + Lidocaine | 23 (4.1%) |

There was a significant difference between the age of children and the reduction in the time of postoperative analgesia (Table 2). There was no statistically significant difference between the sex and the time of administration of analgesics postoperatively.

| Table 2. Time to first dose of postoperative analgesic in relation to age |
|---|---|---|---|---|---|---|
| Age (years) | < 3 hours | 3–6 hours | 6–9 hours | 9–12 hours | > 12 hours | Significance |
| < 3 | 6 (7.1%) | 9 (10.7%) | 28 (33.3%) | 33 (39.3%) | 8 (9.5%) | *p = 0.000* |
| 3–7 | 9 (6.05%) | 27 (19.4%) | 50 (36%) | 46 (33.1%) | 7 (5%) |
| 7–14 | 20 (8.9%) | 72 (32.1%) | 73 (32.6%) | 44 (19.6%) | 15 (6.7%) |
| > 14 | 14 (12%) | 42 (35.9%) | 30 (25.6%) | 23 (19.7%) | 8 (6.8%) |

*Statistically significant difference; χ² test
Table 3. Time to first dose of postoperative analgesic in relation to diagnosis

| Diagnosis        | < 3 hours | 3–6 hours | 6–9 hours | 9–12 hours | > 12 hours | Significance |
|------------------|----------|-----------|-----------|------------|------------|--------------|
| Tumors           | 14 (13.9%) | 29 (28.7%) | 27 (26.7%) | 21 (20.8%) | 10 (9.9%)  | *p = 0.000*  |
| Injury           | 19 (9.5%)  | 79 (39.3%) | 61 (30.3%) | 35 (17.4%) | 7 (3.5%)   |              |
| AV fistula       | 0 (0%)     | 3 (100%)   | 0 (0%)     | 0 (0%)     | 0 (0%)     |              |
| Appendix         | 0 (0%)     | 0 (0%)     | 5 (23.8%)  | 14 (66.7%) | 2 (9.5%)   |              |
| Congenital anomalies | 16 (6.8%) | 39 (16.5%) | 88 (37.1%) | 75 (31.6%) | 19 (8.8%)  |              |

AV – arteriovenous fistula; *statistically significant difference; χ²-test

Table 4. Time to first dose of postoperative analgesic in relation to type of regional anesthesia

| Block            | < 3 hours | 3–6 hours | 6–9 hours | 9–12 hours | > 12 hours | Significance |
|------------------|----------|-----------|-----------|------------|------------|--------------|
| Caudal           | 8 (4.8%) | 19 (11.3%)| 71 (42.3%)| 59 (35.1%) | 11 (6.5%)  | *p = 0.000*  |
| Epidural         | 6 (30%)  | 6 (30%)   | 5 (25%)   | 3 (15%)    | 0 (0%)     |              |
| Spinal           | 1 (8.3%) | 3 (25%)   | 5 (41.7%) | 3 (25%)    | 0 (0%)     |              |
| Upper limb       | 20 (11.2%)| 75 (41.9%)| 51 (28.5%)| 28 (15.6%) | 5 (2.8%)   |              |
| Lower limb       | 14 (8.6%)| 47 (28.8%)| 44 (27%)  | 38 (23.3%) | 20 (12.3%) |              |
| Truncal          | 0 (0%)   | 0 (0%)    | 5 (22.7%) | 15 (68.2%) | 2 (9.1%)   |              |

*Statistically significant difference; χ² test

and truncal nerve blockade. Spinal anesthesia and blocks of the lower extremities were the following successive blocks in terms of postoperative analgesia. The shortest analgesic time was observed in patients with epidural and upper limb blocks (Table 4).

There was a significant difference between the type of local anesthetic and the first dose of analgesics that was given postoperatively. Longer postoperative analgesia was seen in children in whom the levobupivacaine, bupivacaine or levobupivacaine combined with lidocaine was used to perform the block.

There were significant differences between the blocks under sedation and blocks under general anesthesia and the first time of giving postoperative analgesia. The shortest time of giving the first analgesic postoperatively was in patients who were awake during surgery.

DISCUSSION

Only a few decades ago it was considered that pain was the normal “price” to be paid for successfully performed surgery. It was also thought that the newborn did not feel pain, and surgical interventions during the first few days of life were mostly performed without any anesthesia [14]. Today, we consider that surgical pain not only hurts but can have effects that compromise recovery. Since it is generally accepted that even small children feel pain, analgesia must be ensured for all and after all painful procedures. It has been proven that adequate perioperative analgesia reduces the metabolic response to the trauma, the possibility of chronic pain, and morbidity and mortality [15]. It has been clearly demonstrated that poor postoperative pain control in children leads to emotional disorders [16]. It can also lead to more immediate complications – hypoventilation after thoracotomy, an increase in arterial and intracranial pressure.

Regional anesthesia can provide good perioperative pain control. The pre-surgery block contributes to intraoperative analgesia and reduces the need for other analgetics. There has long been evidence that postoperative pain is lower if general anesthesia is given in combination with the regional one, although regional anesthesia has not yet found full application in pediatric patients [17].

The concept that regional and general anesthesia are complementary rather than competitive is fundamental to comprehensively comprehending the role of regional anesthesia in children and dates back to the early 1990s [18].

In our study, regional anesthesia was performed in pediatric patients, in analgosedation or in general anesthesia. We herein show that postoperative analgesia was needed earlier in patients who were conscious.

All of our patients were completely hemodynamic and respiratory stable during and after the operation, which contributed to a faster release from the hospital. It has been explained long time ago why even very small children maintain hemodynamic stability even after central blocks – it has been explained by the immaturity of the sympathetic nervous system, relatively lower volume of lower extremities, and compensatory vasoconstriction in unblocked blood vessels [19, 20].

In our study, we show that the earliest use of postoperative analgetics was needed in children who were operated on due to injuries or tumors. This demonstrates how much the psychological component of pain in children, i.e. suffering due to the realization of the severity of the disease or potential disfiguration, is important in the feeling of pain.

In this study, the effect of the dose and volume of local anesthetics on postoperative analgesia were not studied, because doses and volume were applied on the basis of consensus adopted [9]. However, statistically significant longer analgesia was achieved when long-acting local anesthetics (levobupivacaine, bupivacaine or levobupivacaine in combination with lidocaine) were used. It is understand-
able that the duration of the block will depend on the pharmacodynamics of the drug used.

Analgesia was the longest after the caudal and truncal nerve blockade, which is in accordance with the literature data [4]. Shorter analgesia was after spinal anesthesia and blocks of the lower extremities. One of the described defects in spinal anesthesia during childhood is just shorter time [4]. It is not entirely clear why the shortest analgesia was after epidural anesthesia. The only explanation is that this type of block was applied in the eldest age group, where additional analgesia was needed at the earliest, most likely because of the psychological, social, and cognitive component of the pain affected [21].

However, if we analyze the literature data on the isolated influence of age on pain, they are extremely contradictory – from the statement that the feeling of pain is the greatest in the youngest population, to the assertion that age is not significant [21, 22].

There are many controversies in the literature concerning the correlation between pain and the sex [21, 23, 24]. In our study, we did not find statistically significant differences between the sex and pain. One of the reasons may be that we had significantly more boys than girls, or that the influence of the sex on pain occurs much later.

Good postoperative analgesia reduces the risk of postoperative anxiety and delirium, which fall into the group of significant complications of anesthesia, especially in the pediatric population [25]. The costs were significantly reduced due to the reduced need for intraoperative use of expensive inhalation anesthetics, and postoperatively due to the reduced need for the addition of analgesics. This decreased the potential side effects of systemic analgesics that could also prolong hospitalization.

**CONCLUSION**

Good analgesia reduces the need for postoperative analgesics and secures better comfort in the postoperative period. Postoperative analgesia is needed the most by older children and by patients who had been awake during surgery, probably due to the most developed cognitive, psychological and social component of the pain. Children with injuries and tumors need postoperative analgesia the earliest. The longest postoperative analgesia was recorded in patients who received caudal block. The longest postoperative analgesia can be seen in patients who received levobupivacaine, bupivacaine or levobupivacaine combined with lidocaine to perform the block.

The goal of a physician should always be to minimize the psychological and physical trauma to the patient, regardless of how young and immature he is. From the ethical point of view, it is not justifiable to allow a child to suffer pain, when simple and safe techniques of regional anesthesia can easily complement or replace conventional general anesthesia.

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Улога регионалне анестезије у постоперативној аналгезији педијатријских болесника

Душица Симић1,2, Иrena Симић1, Марија Стевић1,2, Невена Јовичић1, Мaja Митровић1, Ивана Будић1,4, Миодраг Милановић2,3, Весна Маријановић1,4, Биљана Миличић6

1Универзитетска дечја клиника, Београд, Србија; 2Универзитет у Београду, Медицински факултет, Београд, Србија; 3Клинички центар Ниш, Клиника за дечју хирургију и ортопедију, Ниш, Србија; 4Универзитет у Нишу, Медицински факултет, Ниш, Србија; 5Клинички центар Србије, Ургентни центар, Београд, Србија; 6Универзитет у Београду, Стоматолошки факултет, Београд, Србија

Увод/Циљ
Бол представља узнемирујуће искуство које је повезано са постојећим или могућим оштећењем ткива, са сензорном, емоционалном, когнитивном и социјалном компонентом. Циљ ове студије је приказ ефикасности техника регионалне анестезије на постоперативни бол код деце.

Методе
Ретроспективна кохортна студија је спроведена на групи од 564 педијатријских болесника у периоду од 2013. до 2016. године. Врсте регионалне анестезије су класификоване у шест група: каудална, епидурална, спинална, блокови горњих екстремитета, доњих екстремитета и блок трупа. Од статистичких метода користили смо дескриптивне статистичке методе апсолутних и релативних бројева за атрибутивна обележја посматрања, мере варијабилитета, централне тенденције за нумеричка обележја и методе инференцијалне статистике. Избор тестова за нумеричка обележја посматрања зависиће од расподеле података. За атрибутивна обележја посматрања користили смо χ² тест.

Резултати
У односу на постоперативно време када је био потребан аналгетик, статистички значајна разлика уочена је у узрасту деце (p = 0,000), дијагнози болести (p = 0,000), врсти блока (p = 0,000), врсти коришћеног локалног анестетика (p = 0,000), као и врсти периоперативне анестезије или седације (p = 0,005).

Закључак
Постоперативна аналгезија је најпотребнија старијој деци и деци која су била будна током хируршке интервенције. Најранја постоперативна аналгезија је забележена код болесника који су добили каудален блок, као и болесника који су примили левобупивакаин, бупивакаин или левобупивакаин у комбинацији са бупивакаином за извођење блока.

Кључне речи: регионална анестезија; дете; педијатријски болесник; постоперативна аналгезија