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Comparative Evaluation of Analgesic Effectiveness of Various Anesthelic Drugs in Combination with Dexmedetomidine in Children after Cardiac Surgery

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ABSTRACT: In pediatric practice, for postoperative pain therapy, in addition to analgesia, sedation must also be taken into account in order to prevent the development of delirium and irritation to discomfort. Therefore, the purpose of our work was to evaluate the efficacy and safety of various forms of non–opioid drugs in combination with dexmedetomidine in children with congenital heart defects after cardiac surgery. The study included 60 children aged 2 to 4 years with congenital heart defects operated on for radical corrections of congenital heart defects in conditions of artificial circulation. The patients were divided into 2 groups, identical in anthropometric data. All patients underwent sedation and analgesia with dexmedetomidine, paracetamol and diclofenac. After the conducted examinations and observations, it was concluded that the use of non–opioid analgesics in combination with dexmedetomidine gives good results in the postoperative period, without causing any special complications from organs and systems.

KEYWORDS: Children, Cardiac surgery, Postoperative pain relief, Sedation.

INTRODUCTION

In anesthesiology practice, one of the main problems is pain and the issues of its elimination at the stages of examination and treatment for various pathological conditions in children, especially in newborns, in the early stages. And this problem makes itself felt day after day in connection with the introduction of new technologies and new methods of operations in neonatal surgery, ways of their identification and treatment. It should be noted that the perception of pain sensations, their transmission and ongoing changes appear in the early stages of intrauterine development of the fetus.

The manifestation of generalization of pain sensations is considered a feature of the reaction in children at the neonatal age, and any pain reactions are repeated with renewed vigor, which subsequently can lead to an imbalance of organs and systems, with a violation of the neuropsychic development of the child at the stages of development [1, 2, 3]. It is generally accepted that operations requiring sternotomy and especially thoracotomy are the most debilitating of patients in the postoperative period, both in terms of pain and in terms of respiratory function. In addition, in addition to pain in the area of the skin incision, after cardiothoracic surgery, other sources of discomfort are of great importance [7, 8, 9]. Currently, the question of the role and place of narcotic and non–narcotic analgesics for the relief of postoperative pain in children is being actively discussed [5, 6]. The principles of non–opioid and multimodal analgesia are reflected in numerous recommendations for postoperative analgesia, but this issue remains insufficiently studied in pediatrics. The use of non–steroidal anti–inflammatory drugs is pathogenetically determined [4]. The issue of choosing the type and form of non–opioid analgesics for children in cardiac surgery remains a debatable topic, which requires careful clinical research.

In pediatric practice, for postoperative pain therapy, in addition to analgesia, sedation must also be taken into account in order to prevent the development of delirium and irritation to discomfort. In modern anesthesiology, the term "procedural sedation" is used, which means the administration of hypnotics or their combination with analgesics that cause progressive depression of the central nervous system [10, 11]. For this purpose, many clinics use the drug dexmedetomidine. Dexmedetomidine is an effective sedative for children, including infants, which causes little or no respiratory depression while maintaining airway patency. Despite the rich experience of clinical use, the pharmacokinetic and pharmacodynamic profile of dexmedetomidine in children has not been fully studied [12, 13]. The number of studies investigating the pharmacokinetics of dexmedetomidine in children is limited.

OBJECTIVE

To evaluate the efficacy and safety of various forms of non–opioid drugs in combination with dexmedetomidine in children with congenital heart disease after cardiac surgery.

MATERIAL AND METHODS

The study was conducted in the department of pediatric resuscitation and cardiac surgery of the Fergana Regional Children's Multidisciplinary Medical Center. The study included 60 children aged 2 to 4 years with a diagnosis of "ventricular septal defect", "atrial septal defect", "tetralogy of Fallot", operated on for radical correction of congenital heart defects under cardiopulmonary bypass. The study included patients (normotrophics) without premorbid pathology. Anesthesia risk according to ASA I – II. The operations were planned, standard preoperative preparation and examination were carried out. Criteria for exclusion from the study:

1. Individual intolerance to the drugs used in the study;
2. Patients corresponding to the risk of ASA III–IV anesthesia;
3. Conversion during the operation;
4. Non–consent of the patient or his relatives to participate in the study. Refusal to sign informed consent.

All children underwent combined endotracheal anesthesia with sevoflurane inhalation, anesthesia machine Primus (Drager). Anesthesia was induced by administering Propofol 3 mg/kg, Fentanyl 1–2 µg/kg, Arduan 0.06–0.08 mg/kg, followed by tracheal intubation and transfer to artificial lung ventilation (ALV). Respiratory support was performed with the Primus anesthesia machine (Drager, Germany), using the forced ventilation mode by volume, with an oxygen–air mixture with EtO2 – 30% in the normoventilation mode (EtCO2 at the level of 34–44 mm Hg). Anesthesia was maintained with Sevoflurane 1.0–1.5 MAC according to the low–flow anesthesia technique (LFA, flow <1 liter). Analgesia was maintained by fractional administration of Fentanyl at a dose of 0.5–1 µg/kg every 30 minutes. During cardiopulmonary bypass, the introduction of fentanyl was carried out through the AIC.

The patients were divided into 2 groups: group 1 – 30 (50%) subjects who underwent postoperative analgesia with paracetamol injectable form (15 mg/kg); 2–group 30 (50%), in which the drug diclofenac was used in the form of a suppository (2 mg/kg). Postoperative observation and therapy was carried out in the intensive care unit with the continuation of artificial lung ventilation and constant monitoring of vital signs of the body. Before extubation, all patients received dexmedetomidine, a highly selective α2–adrenergic agonist with a powerful sedative effect (1.0 µg/kg). Pain relief with non–opioid analgesics was carried out in the early postoperative period and every 8 hours for 3 days. Accordingly, patients were examined in 4 stages: stage 1, early postoperative period (before extubation), stage 2, 8 hours after surgery, stage 3, 12 hours after surgery, stage 4, before the transfer of the child from the intensive care unit. Both groups were identical in anthropometric and age parameters.

Infusion therapy was similar in both groups and was represented by crystalloids and colloids: isotonic NaCl solution and 6% HES solution, on average 4–6 ml/kg/h. All patients underwent transfusion of donor erythrocyte mass and human albumin to maintain hematocrit and blood oncotic pressure during cardiopulmonary bypass. Before cannulation of the great vessels, artificial hemophilia was performed by heparinization at a dose of 300 units/kg. Custadiol (20 ml/kg) was used as a cardioplegic solution. After cardiopulmonary bypass, some patients underwent modified ultrafiltration depending on the current hematocrit. In our study, the use of modified ultrafiltration was in 13 (21.7%) cases.

Hemodynamic parameters were studied by invasive monitoring using a Nihon Kohden heart monitor (BPs, BPd, BPmean, CVP, HR,), pulse oximetry using a BLT device. The gas composition of the blood was studied by the apparatus Nova of the acid–base state. Analyzed the level of glucose and cortisol as a mediator of pain analyzer Cobas 6000.

RESULTS AND ITS DISCUSSION

In all patients at all stages of the study, the heart rate remained stable, within the normal range. The heart rate indicators in children of the 1st group were as follows, in the early postoperative period there was a slight increase in heart rate by 15–20% of the age norm. After the introduction of dexmedetomidine, heart rate decreased by 12.2±2.3%. In other stages, heart rate varied within 88–122/min. Arterial pressure (A/P) in the early postoperative period in children of the 1st group at the second stage compared to the first stage showed a downward trend, for example: A/Ps by 5%, A/Pd by 2%, A/Pavg. by 4.5%. A day later, these data were changed:

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A/Ps decreased by 3.6%, A/Pd increased by 0.8%, A/Pavg. – increased by 1.7%. Before the transfer from the intensive care unit (ICU), the following indicators were observed: A/Ps– decreased by 2.7%, A/Pd – by 2.4%, A/Pavg. – by 7.5%.

The value of central venous pressure (CVP) and oxygen status (Sat02) at all stages of the study fluctuated as follows: CVP at the first stage was within the normal range, on the second day it decreased by 18.25%, at the third stage there was a slight increase in CVP – 2.87%, before transfer patient from the ICU, this indicator decreased by 6.24%.

The oxygenation index ($Sat0_2$) in the initial stages of the study during mechanical ventilation with humidified oxygen was as follows: stage 1 – 98.38% ± 1.23, stage 2 – 98.42% ± 1.18, at the third and fourth stages, i.e. after switching to spontaneous breathing, these values were 97.12% ± 1.61, 96.12% ± 1.08.

Table 1. Indicators of blood pressure, heart rate, $Sat0_2$, CVP in the postoperative period in children of the 1st group (M±m)

Indicators	stage 1	stage 2	stage 3	stage 4
HR (heart rate) (min.)	122±21	118±18	120±20	114±16
A/Ps (mmHg)	98,12±14,44	93,61±15,51	95,63±12,15	95,42±10,06
A/Pd (mmHg)	59,19±12,36	58,12±10,15	60,31±9,49	57,69±9,56
A/Pavg. (mmHg)	66,36±13,64	63,44±12,51	67,14±11,21	61,17±9,54
CVP (mm water column)	5,92±2,31	4,81±2,57	6,09±1,58	5,54±2,44
$Sat0_2$ (%)	98,38±1,23	98,42±1,18	97,12±1,61	96,12±1,08

Note: * – in comparison with the 1st stage of the study – p<0,05

Heart rate indicators in children of the 2nd group were as follows: at the first stage, heart rate was within the age physiological norms; on the second – a slight decrease by 2.6%, on the third – increased by 2.5%, on the fourth – decreased by 9.4%.

Table 2. Indicators of blood pressure, heart rate, $Sat0_2$, CVP in the postoperative period in children of the 2nd group (M±m)

Indicators	stage 1	stage 2	stage 3	stage 4
HR (min.)	115±14	112±12	118±16	112±14
A/Ps (mmHg)	95,04±13,6	96,11±12,72	92,13±11,77	98,17±10,6
A/Pd (mmHg)	59,16±13,22	58,04±12,14	60,14±11,78	63,21±9,12
A/Pavg. (mmHg)	70,87±9,1	67,02±8,47	65,67±9,5	71,66±8,4
CVP (mm water column)	5,7±1,34	5,8±1,54	4,98±1,79	6,4±1,47
$Sat0_2$ (%)	98,87±1,56	98,64±1,24	97,52±1,96	96,17±1,68

Note: * – in comparison with the 1st stage of the study – p<0,05

CVP and $Sat0_2$ index at all stages of the study: CVP at the first stage was within the average standard values, on the second day the CVP index increased by 1.9% compared with the first stage, at the third stage the same decrease was observed by an average of 14%. At the fourth stage, in the course of a gradual improvement in the state of the hemodynamics of the body, the CVP increased by 12%.

Blood oxygenation ($Sat0_2$) in the initial stages of the study on the background of mechanical ventilation: stage 1 – 98.87% ± 1.56, stage 2 – 98.64% ± 1.24, at the third and fourth stages during the transition to independent breathing, these values were 97.52% ± 1.99, 96.17% ± 1.68.

Clinical and laboratory studies of acid–base balance were carried out and analyzed in accordance with the program of the master's thesis. As a comparative value, the average normative indicators of the COR in children of these groups were taken.

Table 3. Indicators of acid–base balance in children of the 1st group (M±m)

Indicators	stage 1	stage 2	stage 3	stage 4
pH (unit)	7,31±0,02	7,34±0,08	7,35±0,04	7,37±0,01
pCO_2 (mmHg)	40,14±14,56	36,14±8,51	24,85±18,9	28,94±16,1
pO_2 (mmHg)	124,95±30,11	119,44±28,96	126,14±45,1	111,85±36,89

Note: * - in comparison with the 1st stage of the study – p<0,05

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Changes in acid–base balance in children of the 1st group in the postoperative period were as follows: The pH value immediately after surgery was low, compared with the standard values (7.36=100%), that is, it decreased by 0.6%, pCO_2 – by 60% above the norm (25=100%), pO_2 – slightly increased (110=100%) – by 11.5%. At the second stage, these values gradually began to return to normal: the decrease in pH was – 0.36%, pCO_2 increased to 40%, pO_2 was slightly increased – by 10.8%. At the third stage, the pH difference with the norm was 0.1%, pCO_2 decreased to 4%, pO_2 increased by 0.9% of the norm. At the fourth stage, pH increased by 0.1%, pCO_2 by 12%, pO_2 – 1.1% above the norm.

Table 4. Indicators of acid–base balance in children of the 2nd group (M±m)

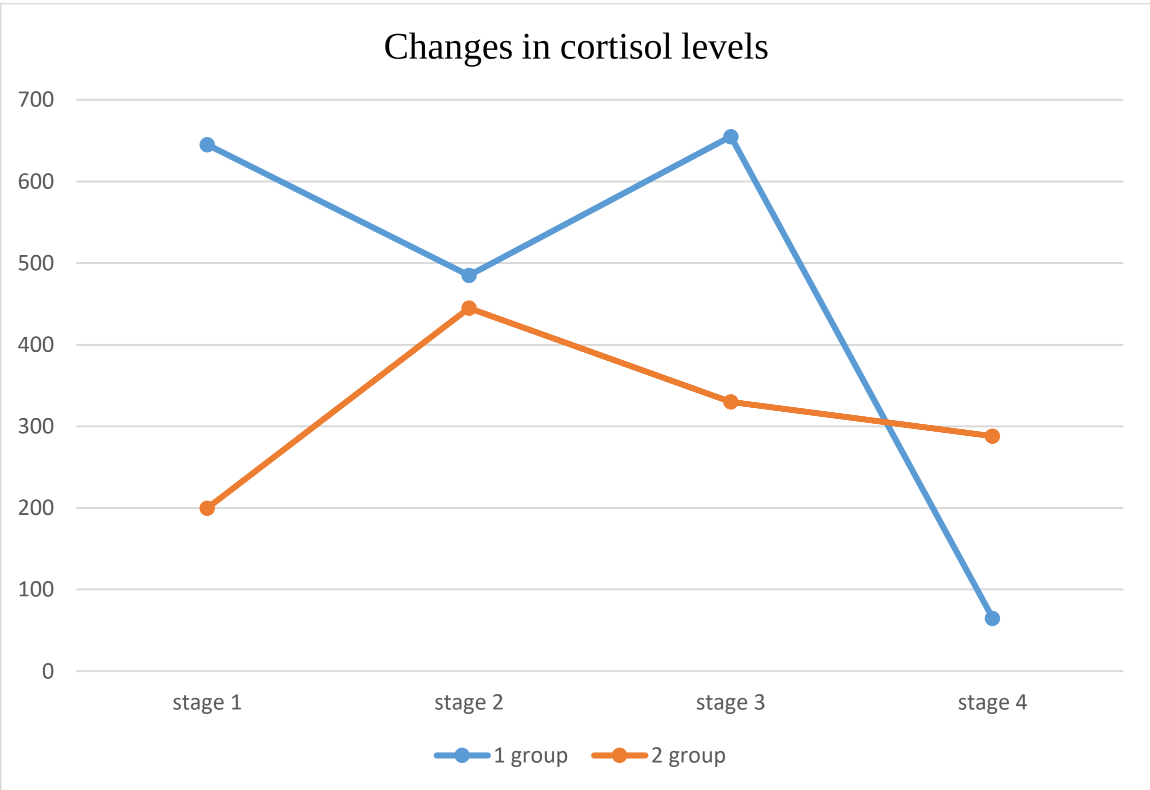
Indicators	stage 1	stage 2	stage 3	stage 4
pH (unit)	7,29±0,05	7,32±0,04	7,35±0,09	7,36±0,01
pCO_2 (mmHg)	40,23±21,85	36,28±18,54	24,5±22,16	28,98±28,21
pO_2 (mmHg)	104,57±30,12	124,74±33,21	118,65±30,45	98,61±24,14

Note: * – in comparison with the 1st stage of the study – $p<0,05$

At the second stage, against the background of antiacidotic therapy, these values gradually began to normalize, so pH was lower by 0.3%, pCO_2 increased by 58%, pO_2 increased by 10%. Based on the results of acid–base balance in the remaining stages, one can judge the improvement in the acid–base state of the child's body. These indicators were reflected in the following: 3–stage; pH is within the normal range, pCO_2 decreased by 3.5%, pO_2 slightly by 3.8%, increased by 114.65±60.45; in the 4th stage, against the background of the patient's transition to spontaneous breathing, pH remained within the normal range, pCO_2 increased by 12%, pO_2 was 11% below normal.

Clinical changes at the time of dexmedetomidine therapy in children in the study groups were recorded according to the stage of the study.

The change in cortisol levels varied within different limits in both groups, and therefore it was decided to make an illustration based on general statistical processing.



The terms of treatment of children in the ICU were different. For example: in children with uncomplicated congenital heart defects 1–2 days, in children with ventricular septal defect (VSD) (11 children) complicated by pulmonary hypertension, postoperative blockade with the use of a pacemaker (9 children), this period ranged from 4 to 8 days, depending on the child's condition.

CONCLUSIONS

1. Postoperative analgesia is the main part of intensive care in pediatric cardiac surgery, and non–opioid analgesics and anxiolytics play an important role. The effectiveness of postoperative analgesia depends both on the method of anesthesia, the choice of a combination of drugs, the genetic characteristics of the patient, and on the regularity of assessing the intensity of pain.

2. With both of the above options for non–opioid analgesia, pain relief occurs quickly, lasts a long time and does not cause complications from the cardiovascular and respiratory systems, which makes them the most unique means of choice in pediatric anesthesiology. The disadvantages of intravenous injection of paracetamol is the parenteral route, and with rectal administration of diclofenac, slight discomfort and a late onset of effect.

3. Sedation with dexmedetomidine in children after cardiac surgery prevents the development of delirium, provides more controlled sedation, inhibits irritation during extubation and prevents psychomotor agitation in the post–anesthesia period. The disadvantages are mild bradycardia and hypotension.

4. The use of non–opioid analgesics in combination with dexmedetomidine showed its high efficiency in the postoperative period, without causing any special complications from organs and systems. This method can significantly reduce the use of narcotic drugs. However, a small range of examined patients does not give us a conclusion about the uniqueness of this combination, which requires further thorough and extensive research.

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