ANALGOSEDATION WITH DEXMEDETOMIDINE IN PEDIATRIC CARDIAC SURGERY

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Abstract. *Relevance. The principles of postoperative multimodal analgesia are reflected in numerous publications; however, this issue remains insufficiently studied in pediatric cardiac surgery.*

Keywords: *congenital heart defects, pediatric cardiac surgery, postoperative sedation-analgesia.*

OBJECTIVE OF THE STUDY: to increase the effectiveness of postoperative analgosedation with the combined intravenous use of dexmedetomidine and paracetamol in children after cardiac surgery.

MATERIALS AND METHODS: The study was a prospective, controlled, non-randomized study (n = 65, from 2 to 4 years). Elective heart surgeries were performed on children with congenital heart defects: ventricular and/or atrial septal defect, Tetralogy of Fallot, under conditions of artificial circulation and general anesthesia. Patients were divided into 2 groups according to the type of postoperative pain relief: Group 1, main (n = 35): 30 minutes after surgery, dexmedetomidine infusion with a loading dose of 1.0 mcg/kg/h for 10 minutes, then infusion of 0.8 mcg /kg/hour during the day against the background of planned analgesia with paracetamol (15 mg/kg, intravenously, bolus) 2 hours after surgery and subsequent every 8 hours during the day. Group 2, comparison (n =30), morphine 0.3 mg/kg, intramuscularly, first dose - 2 hours after surgery. The effectiveness of postoperative analgosedation in children was analyzed using the Richmond scale and FLACC + systemic hemodynamics, acid-base status and blood gases, cortisol, glucose and blood lactate.

RESULTS. Sufficient stabilization of the main parameters of hemodynamics and breathing confirmed the adequacy of postoperative analgosedation in patients of group 1. A decrease in heart rate, specific peripheral resistance and mean arterial pressure of up to 14% was recorded. Respiratory depression was not noted in any case, and the decrease in blood pressure and heart rate was hemodynamically insignificant. Changes in acid-base balance and blood gases in children in the postoperative period were unreliable and within normal limits. Postoperative stability of blood lactate, glucose and cortisol levels recorded the absence of gross metabolic disorders and emotional pain stress in children of the main group.

CONCLUSION. Multimodal analgesia with dexmedetomidine in combination with paracetamol provides an adequate level of sedation, suppresses irritation to extubation, prevents psychomotor agitation and provides effective analgesia. Preservation of the swallowing reflex contributed to the early initiation of enteral feeding. Transfer of 74.3% of patients in group 1 42.3±5.5 hours after surgery to a specialized department reduced costs and burden on ICU medical staff.

RELEVANCE.

Treatment of postoperative pain syndrome (PS) in all areas of surgery remains one of the most pressing problems of clinical anesthesiology. According to a systematic review by Gregory J. et al. (2016), postoperative BP, on average, was observed in 50% of patients with the incidence

of high-intensity pain up to 35% [1]. The severity of postoperative pain in cardiac surgery patients is one of the most intense, which requires adequate treatment [2]. Inadequate pain relief often leads to a complicated course of the postoperative period, contributing to chronic pain. Thus, according to the results of a study by Choinière M. et al. (2014) in 40.1% of patients after cardiac surgery, BS persists for 3 months [3]. The results of other studies revealed the presence of BS in 21% of children in the early postoperative period [4], while the formation of chronic PS was noted in 10% of children after 1 year, in 3% - 5 years after cardiac surgery [5].

No less important is the problem of perioperative cardioprotection, especially in conditions of artificial circulation (CPB) [6]. Today, the understanding of the pathophysiology and prevention of ischemia-reperfusion damage to the myocardium of the operated heart has expanded significantly [7-10]. Issues of additional pharmacological cardioprotection are being discussed [11]. In this regard, the interest of clinicians in the α_2-adrenergic receptor (α_2-AR) agonist dexmedetomidine has increased [12,13], which is widely used both for sedation and as an organoprotector and adjuvant during various operations [14,15]. The mechanism of sedation of α2-AR agonists is similar to the second stage of natural sleep [16]. Postoperative sedation is necessary for pediatric patients to prevent the development of delirium, anxiety and fear [17,18]. To assess its effectiveness, rating scales generally accepted in resuscitation are used [19].

When using average therapeutic doses of dexmedetomidine, in addition to sedation, effects on the cardiovascular and central nervous systems are manifested. Dexmedetomidine does not affect the respiratory center and does not depress respiration. Its effect on hemodynamics is dose-dependent and is caused by a decrease in noradrenergic activity [20, 21]. The authors of works testing dexmedetomidine during operations with bypass recorded its significant positive effects: a decrease in the level of norepinephrine in the blood, a decrease in hemodynamic reflex reactions to tracheal intubation, prevention of hypertension, etc. [22, 23]. Most researchers indicate a decrease in heart rate with dexmedetomidine compared to other sedatives [24, 25], without excluding the risk of bradycardia [26].

Despite sufficient experience with the use of dexmedetomidine in adult patients, the number of similar publications in children is limited [27-30]. The principles of non-opioid and multimodal analgesia (MMA) are reflected in numerous publications on postoperative pain relief, but this issue remains insufficiently studied in pediatrics, especially in pediatric cardiac surgery. The advantage of paracetamol over NSAIDs and the rationale for its inclusion in MMA regimens is the minimum of side effects [31].

Purpose of the study: to increase the effectiveness of postoperative analgosedation with the combined intravenous use of dexmedetomidine and paracetamol in children after cardiac surgery.

Materials and methods:

Study design

A prospective controlled non-randomized study was conducted. study.

Table 1. Study design

Sign	1 group (n =35)	2nd group (n =30)
Boys, n /%	16/45.7	9/30.0
Girls, n /%	19/54.2	21/70.0
Age, years	2.43± 1.42	3.17±0.12
Body weight, kg	12.76 ±4.81	15.01 ±3.49
Diagnosis, n /%		
VSD	11/31.4	12/40.0
ASD	19/54.2	11/36.6

Tetralogy of Fallot	5/14.2	7/23.3
General anesthesia with artificial circulation		
Postoperative pain relief	Dexmedetomidine + Paracetamol IV	Morphine, IM
Evaluation of the effectiveness of postoperative pain relief		
Echocardiography		
Acoustic acid and blood gases		
Blood cortisol		
Blood glucose		
Blood lactate		
Behavioral Pain Scale FLACC		
Scale excitement - sedation Richmond		

Eligibility Criteria

Criteria for inclusion of patients in the study:

1. Surgical approach is median sternotomy.
2. The patient's level of consciousness is clear or mild stunned, 14-15 points on the Glasgow Coma Scale.
3. Signing of voluntary informed consent by the child's relatives/legal representatives to participate in the study.

Patient exclusion criteria:

1. Intolerance to drugs used in the study.
2. Hepatic-renal failure.
3. Perioperative brain lesions.
4. Cardiovascular and/or respiratory failure requiring long-term mechanical ventilation (> 2 days).
5. Postoperative bleeding >1.5 ml/kg/hour.
6. Patients meeting anesthesia risk ASA III-IV.
7. Refusal of the child's relatives/legal representatives to sign informed consent to participate in the study.

Study conditions and duration

Conducted during the period 2020-2022 in the pediatric resuscitation and intensive care unit of the Fergana Regional Children's Multidisciplinary Medical Center. The study included 65 children aged 2 to 4 years with congenital heart defects: Ventricular and/or atrial septal defect, Tetralogy of Fallot (see Table 1).

Description of medical intervention

All patients underwent planned radical surgery under artificial circulation (CPB) after standard preoperative preparation and examination.

All patients underwent surgery under general anesthesia. At the intraoperative stage, the patients were under the same conditions. Induction of anesthesia was carried out by intravenous administration of Propofol 3 mg/kg, Fentanyl 5-8 mcg/kg, Ardoin 0.06 mg/kg, followed by tracheal intubation and transfer to artificial ventilation (ALV). Ventilation with an oxygen-air mixture with EtO_2 - 30% (Primus, Drager, Germany). Maintenance of anesthesia - Sevoflurane 1.0-1.2 MAC, boluses of maintenance doses of Propofol, Arduan, Fentanyl. The assessment of the compliance of delivery and consumption of O_2 by tissues was carried out using the level of blood lactate, pulse oximetry data (SpO^2), the acid-base state and gas composition of arterial blood, the level of hemoglobin and hematocrit were assessed. Infusion therapy: 0.9% saline and HES 6%

(Valustim, Republic of Uzbekistan), on average 4-6 ml/kg/h. All patients received transfusion of donor red blood cells and albumin during cardiopulmonary bypass. Before cannulation of the great vessels, artificial hemophilia was carried out by heparinization at a dose of 300 U/kg with control of the activated blood clotting time. Kustadiol (20 ml/kg) was used as a cardioplegic solution. After IR, a modified ultrafiltration rate of 21.7% was performed depending on the current hematocrit.

All patients were divided into 2 groups according to the type of postoperative pain relief:

Group 1, main (n = 35), where patients 30 minutes after surgery began intravenous infusion of dexmedetomidine with a loading dose of 1.0 mcg/kg/h for 10 minutes, followed by infusion at a rate of 0.8 mcg/kg/h in during the day against the background of planned postoperative analgesia with paracetamol (Infulgan, 15 mg/kg, intravenously, bolus) 2 hours after surgery and subsequent every 8 hours during the day.

Group 2, control (n = 30), morphine 0.3 mg/kg, intramuscularly, was used for analgesia, the first dose was 2 hours after surgery, then every 6-8 hours as necessary. Both groups were homogeneous in terms of surgical pathology, age, body weight, duration of surgery, cardiopulmonary bypass, and postoperative mechanical ventilation (Table 2). The study in children of group 1 was carried out at the following stages: 30 minutes after surgery, 2 hours from the start of dexmedetomidine infusion, after extubation and anesthesia with paracetamol, 8 hours, 24 hours after surgery. Stages of the study in patients of group 2: 2 hours after surgery - resumption of BS and extubation; After 1 hour; after 3 hours; 6 hours after anesthesia.

Table 2. Distribution of patients according to the method of postoperative analgesia, age, body weight, duration of surgery, CB and ALV (M ± SD)

Options	Group 1, n=3 5	Group 2, n=30	R
Postoperative analgesia	Paracetamol + Dexmedetomidine	Morphine	
Age (years)	2.43± 1.42	3.17±0.12	>0.05
Body weight (kg)	12.76 ±4.81	15.01 ±3.49	>0.05
Operation duration (min)	197.02 ± 37.82	202.3 ± 39.74	>0.05
IR duration (min)	59.44 ± 31.73	64.49 ± 29.18	>0.05
Duration of software ventilation (min)	127.37 ± 35.22	131.77 ± 34.08	>0.05

Main outcome of the study

The results of the study were to evaluate the effectiveness of postoperative analgosedation in pediatric cardiac surgery. The effectiveness of the optimized technique for the combined use of dexmedetomidine with paracetamol was assessed by the shift in hemodynamic parameters (HR, SBP, SBP) within + 15% and -15% from the initial one, according to the state of neuroendocrine status, metabolism, acid-base balance and blood gases.

Methods for recording outcomes

During the first day after the operation, the patient's condition was monitored, blood pressure, heart rate, acid-base balance and blood gases were recorded, parameters of mechanical ventilation or spontaneous respiratory rate, and pulse oximetry; assessment of the level of sedation using the RASS-scale (Richmond Agitation-Sedation Scale), assessment of pain intensity using the FLACC behavioral scale, intended for children under 7 years of age (Tables 3, 4). Central hemodynamics were studied by echocardiography (Chison Edit 60, China). Monitoring and invasive measurements of A/D and CVP (Nihon Cohden, Japan). Acoustic acid and blood gases (BGA Wondfo analyzer, China). Artificial circulation (device Liva Nova S5 Sorin, Italy). On the 2nd day, the results of clinical and biochemical data, the duration of postoperative mechanical

ventilation, the presence of adverse reactions and side effects in children in the studied groups were assessed.

Table 3. FLACC Behavioral Pain Scale [32]

Description	point
Face: _ without any special grimaces or expressions sometimes gloomy, tense, distracted The chin often/constantly trembles, the lower jaws are clenched.	 0 1 2
Legs: _ normally positioned/relaxed restless movements, tense kicked, or raised up.	 0 1 2
Activity: _ lies calmly, in a normal position, moves easily writhing, moving back and forth, tense arched, rigid, or moves abruptly (jerky).	 0 1 2
Cry: _ not crying (awake or asleep) whines or whines; rarely bothers cries often, screams or sobs, often worries.	 0 1 2
Consolability: _ calm, relaxed calms down when touched, from words, hugs, in arms, distracted difficult to calm down.	 0 1 2

Note: 0 points - calm, 1-3 - slight discomfort,
4-6 - slight pain, 7-10 - severe pain.

Statistical analysis of the obtained data was carried out using the application package StatSoft© Statistica ®10 and Microsoft® Office Excel, 2016. To compare groups, non-parametric tests were used: to assess the significance of differences, the Mann-Whitney test (U-test) was used. To compare qualitative characteristics, the Pearson criterion (χ^2) was used. Differences were considered significant at $p<0.05$.

RESULTS

Study participants

The study involved 65 children with congenital heart defects, of which 38.4% were boys and 61.5% were girls.

Main results of the study

Upon admission, in CICU after 30 minutes operation of group 1, on mechanical ventilation, an intravenous infusion of dexmedetomidine was immediately started with a loading dose of 1.0 mcg/kg/h for 10 minutes, followed by an infusion at a rate of 0.8 mcg/kg/h over the course of 24 hours.

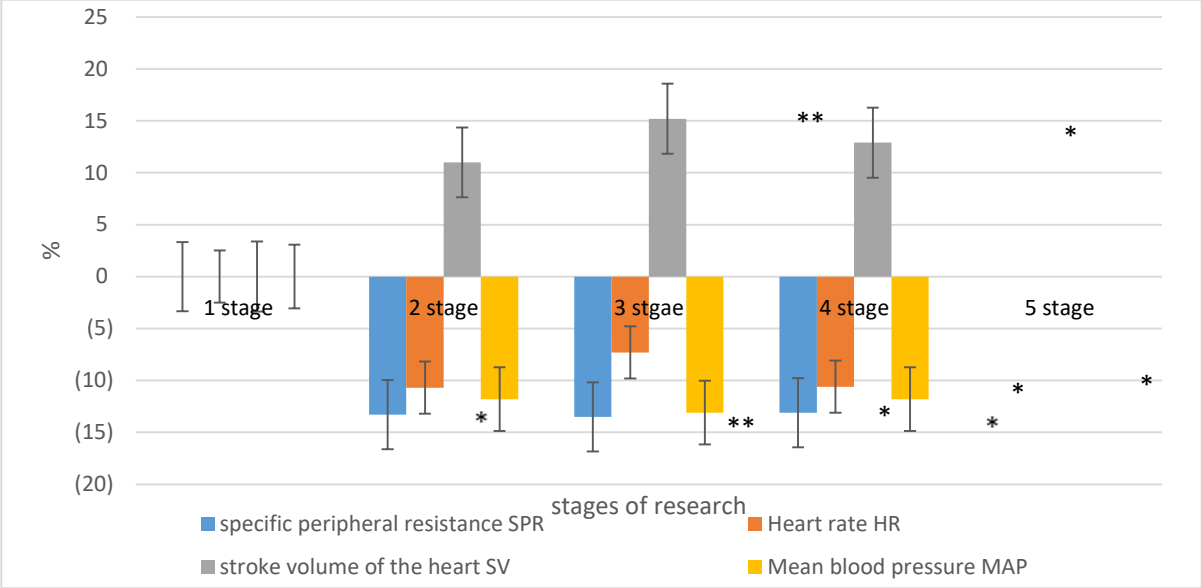
Table 4. Richmond Agitation - Sedation Scale, RASS

Score	Term	Description	Awakening
+4	Agressive	Aggressive state with potential threat to personal	
+3	Extremely agitated	The patient is restless negative towards treatment (removes catheters, probes, drains)	
+2	Agitated	Frequent non-purposeful movements and/or desynchronization with ventilation	
+1	Restless	Excited, but movements are not vigorous or abrasive	
0		Awake, calm, alert	
-1	Drowsy	Loss of attention, but does not close eyes for more than 10 seconds during verbal contact	Verbal stimulation
-2	Light sedation	Quick awaking, opens eyed when called, ability to make eye contact in less then 10 second	Verbal stimulation
-3	Moderate sedation	Any movement (but not eye contact) in response to voice	Verbal stimulation
-4	Deep sedation	Response (motor) to physical stimulus	Physical stimulation

In all patients at the 1st stage of the study (1st postoperative hours), the heart rate remained stable, within the age norm, which could be explained by the preservation of the residual effects of anesthesia, analgesia and myoplegia. Against the background of infusion administration of dexmedetomidine after 28 and 24 hours of the study, heart rate, SBP and SBP decreased within the range of 7.3% -13.5% ($p<0,05$), with a simultaneous significant increase in SV up to +15.2% ($p<0,01$), with stage 1gr. As can be seen from Diagram 1, a long-term and sufficient stabilization of the studied parameters of systemic hemodynamics was recorded against the background of dexmedetomidine infusion and planned analgesia with paracetamol, which confirmed the adequacy of sedation-analgesia in patients in group 1f. About reliable suppression of postoperative BS after cardiac surgery in children, evidenced by practically unchanged indicators of SI and FI at the stages of the study.

Blood oxygenation (Sat 0_2) at all stages of the study corresponded to standard indicators and fluctuated within the range, both against the background of mechanical ventilation (stages 1-2) and against the background of adequate spontaneous breathing (stages 3-4). Changes in acid-base balance and blood gases in children of group 1 in the postoperative period were unreliable, did not exceed age-related norms, and were characterized by relative stability (Table 5).

Diagram 1. Changes in systemic hemodynamics at the stages of the study in patients of group 1



*Note: * p<0.05, ** p<0.01 compared with stage 1 of the study*

Table 5. The dynamics of the some studied indicators at the stages of the study in children of the 1 st group (M±m)

Indicators	1-stage	2-stage	3-stage	4-stage
$Sat0_2$, %	96,8±1,75	96,91±1,69	95,27±1,30	94,73±1,43
pH	7,37±0,07	7,39±0,04	7,38±0,05	7,39±0,03
pO_2, mmHg	119,05±12,76	105,2±9,13	93,81±7,61	91,67±6,89
pCO_2, mmHg	38,78±5,91	36,61±4,34	37,54±4,25	37,90±3,11
BE, mmol/l	-2,87±1,62	-2 ,79±1,13	-2,54±1,57	-2,37±1,70

*Note: * p<0.05, ** p<0.01 compared with stage 1 of the study*

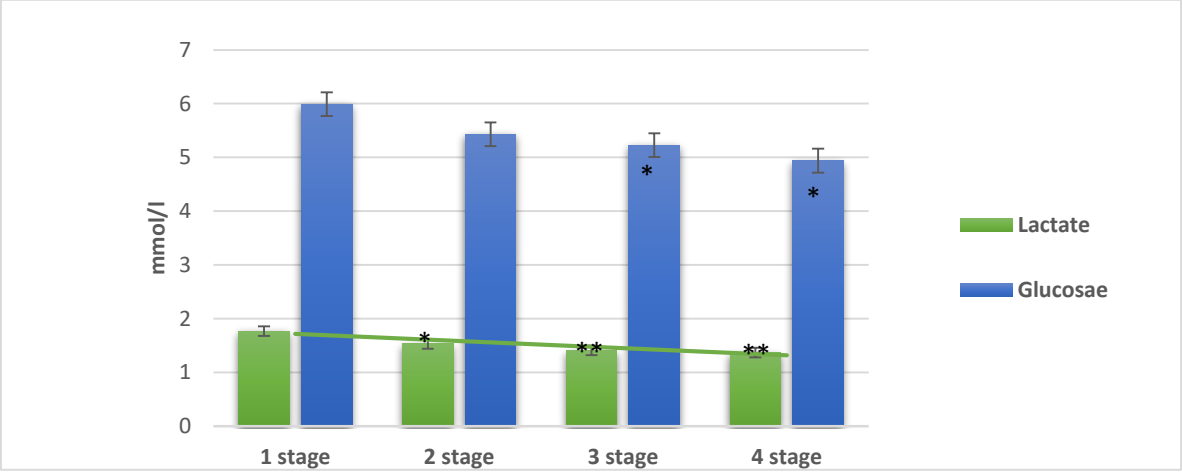
The study of some biochemical parameters, such as blood lactate - a marker of gross metabolic disorders, blood glucose at the stages of the study showed the following results: after surgery at stage 1 recorded, the lactate level 7was 1.7 ± 0.52 mmol/l, which confirmed the absence of intraoperative hypoperfusion and hypoxia.

The glucose level at this stage was 5. 99±0.93 mmol/l. At stages 2-4 of the early postoperative period, there was a significant decrease in lactate levels by 1 3.6%, 20.4% and 2 2.6%, but its values did not go beyond the acceptable limits. Glucose levels were stable and decreased by 9.4%, 12.7% and 17.6% at stages 2-4 compared to stage 1. Infusion therapy on the first postoperative day did not include glucose solutions.

Blood cortisol levels in children of group 1 decreased within the range of 26.1-51.3% (p <0.05) during the study stages (Diagram 3). A gradual decrease in the level of cortisol in the blood serum indicated the absence of emotional and pain stress in children.

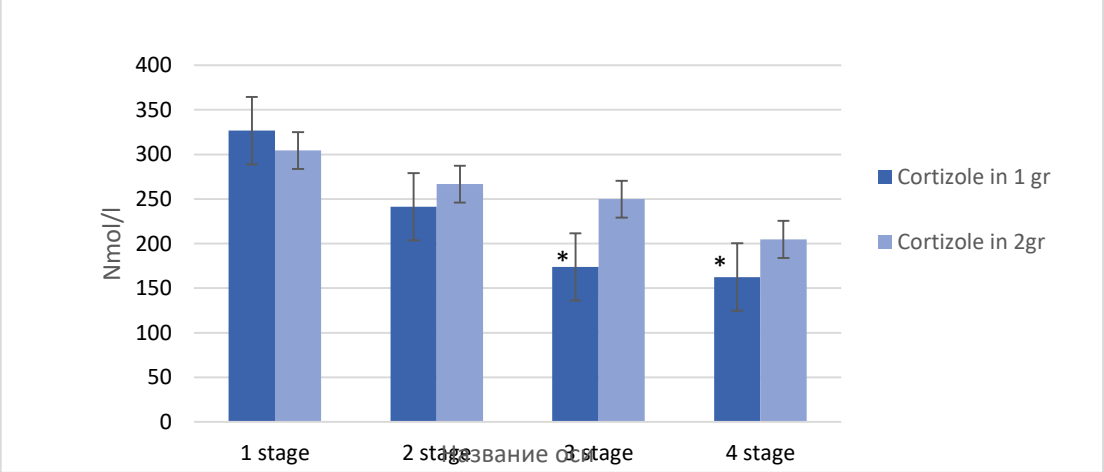
In general, the revealed stability of the indicators confirmed the absence of gross and complex disorders of metabolism and endocrine status in patients of group 1 in the early postoperative period.

Diagram 2. The level of lactate and glucose in the blood in patients of group 1 at the stages of the study



*Note: * p<0.05, ** p<0.01 compared with stage 1 of the study*

Diagram 3. Cortisol levels in selected groups for study stages



Note: Study stages in group 1: 30 min, 2 h, 8 h, 24 h p/surgery
Stages of the study in group 2: 2 hours of surgery, 1 hour, 3 hours and 6 hours of pain relief

When analyzing the postoperative intensity of pain and assessing the level of sedation using the above scales [33], the results were obtained significantly different in the studied groups of patients.

Table 6. Dynamics of changes in the level of sedation - analgesia according to the FLACC and RASS scales in group 1 at the stages of the study

Scale	1 stage	2 stage	3 stage	4 stage
FLACC, score	0,51±0,08	3,83±1,13	3,05±1,27*	2,63±1,14**
RASS, score	-5,0±0,03	-1,8±0,01	-2,4±0,01	-2,1±0,02

*Note: * p<0.05, ** p<0.01 compared with stage 1 of the study*

As can be seen from Table. 6, in children of group 1, immediately after surgery at stage 1 in the ICU, that is, 30 minutes after the administration of dexmedetomidine, drug-induced sleep

remained due to the residual effect of drugs and anesthesia. The children were calm, most of them were asleep and did not respond to speech or touch from medical personnel, and the level of sedation was 0.51 ± 0.08. The pain level at the next stage was 3.83±1.13, at this stage paracetamol (Infulgan was administered) for the purpose of planned treatment Pof BS in patients after tracheal extubation (100%). The patients experienced slight discomfort, with a tense grimace on their face, but lay calmly in a normal position. At subsequent stages 3-4, the pain intensity decreased by 20.4% and 31.4% ($p < 0.05$) in relation to stage 2 - the beginning of postoperative BS therapy. The patients were calm, relaxed, most of them were in a drowsy state. No one complained of pain. As for the assessment of sedation on the RASS scale, in patients of group 1 at stage 1 it was -5.0 ± 0.03, the children did not respond to verbal and/or physical stimulation, they experienced drug-induced sleep. Further, in the following stages, a level of sedation between mild and moderate was observed, which was consistently maintained over the next 24 hours. The children were sleepy during this time and could perform movements in response to voice/verbal stimulation. Their early postoperative period proceeded favorably with relatively stable indicators of hemodynamics, respiration, acid-base balance and blood gases, and the studied metabolic indicators. Overall, Dexmedetomidine in the postoperative MMA regimen with paracetamol (Infulgan) in the above indicated dosages contributed to adequate sedation, prolonged the analgesic effect of Infulgan and ensured a favorable course of the postoperative period in cardiac surgery patients.

In patients of the comparison group, as can be seen from Table 7 at stage 1, i.e., 2 hours after surgery, in extubated patients (100%), the intensity level of postoperative pain was, on average, 6.21±1.02, which corresponded to pain of moderate intensity. The children were restless, wary; their movements in bed were somewhat limited and constrained. The majority of them (75%) reported crying, whining and a reluctance to interact/communicate with medical personnel. Then, 1 and 3 hours after anesthesia with morphine, the children calmed down, most of them (65%) fell asleep/dozed off and the level of pain intensity decreased and amounted to 2.74±0.97 and 3.29±0.98 points, which corresponded to mild discomfort. The intensity of BS at stages 2 and 3 of the study significantly decreased by 55.9% and 47.1% compared to stage 1. At stage 4, 6 hours after anesthesia with morphine, 90% of children noted the resumption of postoperative pain, its intensity was 7.15±1.32 points, which was 138.3% higher than the indicators of the previous 3 stage. This was an indication for re-prescribing morphine in children of this group.

Table 7. Dynamics of changes in the level of sedation - analgesia according to the FLACC and RASS scales in group 2 at the stages of the study

Scale	1 stage	2 stage	3 stage	4 stage
FLACC, score	6,21±1,02	2,74±0,97 **	3,29±0,98**	7,15±1,32
RASS, score	+1,0±0,01	-2,01±0,02	-1,06±0.01	+2,04±0,03

*Note: * $p<0.05$, ** $p<0.01$ compared with stage 1 of the study*

RASS scale, the level of sedation at stage 1 averaged +1.0±0.01, children woke up from narcotic sleep (residual effect general of anesthesia), at this stage 100% of children were extubated. Behavioral characteristics included restlessness, agitation, low-energy, non-aggressive movements, tearfulness, and groaning, which was an indication for starting postoperative pain relief with morphine. At stages 2 and 3, after anesthesia with morphine, the level of sedation was -2.01 ± 0.02 and -1.06 ± 0.01 , which corresponded to mild sedation or drowsiness; during verbal contact, the patient closed his eyes in less than 10 seconds. The children did not complain of pain and/or other unpleasant sensations. Already 6 hours after anesthesia (4 step), the level of sedation increased and amounted to +2.04 ± 0.03 on the RASS scale, by this time the patients became restless, agitated and made frequent non-purposeful movements. An increase in hemodynamic and

respiratory parameters was noted, which required repeated administration of morphine for treatment purposes after operation pain.

The duration of treatment of children in the ICU depended on the severity of congenital heart disease and the condition of the operated child. On average, the stay in the ICU for children in group 1 was 42.3±5.5 hours, for children in group 2 - 68.1±6.2 hours.

Adverse events

In group 1, bradycardia was observed in 8.5% of cases with rapid administration of a loading dose of dexmedetomidine, without a drop in blood pressure and maintaining normal sinus rhythm. After stopping the drug administration, the heart rate returned to normal within 20-30 minutes. In patients of group 1, against the background of a more favorable course of the early postoperative period, enteral feeding began 24 hours after surgery. In group 2, patients had a high incidence of undesirable effects and complications: nausea-vomiting (16.6%), itching (13.3%), intestinal paresis (6.7%), urinary retention (6.7%). In group 2, 7 (23.3%) children with VSD complicated by pulmonary hypertension and postoperative blockade using cardiac pacing spent 4-7 days in the ICU.

DISCUSSION

Summary of the main finding of the study

The development and implementation of postoperative multimodal analgesia and anesthesia based on the combined use of dexmedetomidine with paracetamol promotes optimal control of pain and sedation, reduces the consumption of drugs for symptomatic therapy and postoperative analgesia, helps reduce complications, early activation of patients and rapid postoperative rehabilitation. In general, the multimodal approach provided an opportunity for the introduction of Fast Track Surgery technology - a strategy of active surgical treatment aimed at accelerating various stages of treatment and early postoperative recovery of children with the above-mentioned cardiac surgical pathology.

Discussion of the main result of the study

Multimodal analgesia has almost become the standard of choice for postoperative analgesia in various areas of surgery in adult patients. MMA is aimed at improving the quality of pain relief through the use of a combination of various non-opioid analgesics, reducing opioid doses and the incidence of complications [34].

Sedation in children undergoing cardiac surgery remains an unsolved problem due to the complexity of operations to correct congenital heart defects and the wide range of patient ages. The current approach to sedation and analgesia in children in the postoperative period has been relatively limited and consists of high doses of opioids in combination with additional sedatives. Long-term use of opioids, especially in young children, depresses breathing, which may require prolonged respiratory support and the development of withdrawal symptoms [35]. The primary goal of sedation in children undergoing cardiac surgery should be to achieve adequate analgesia and sedation without compromising hemodynamic status. A combination of opioids and non-opioids may be helpful in this regard. Several nonopioid agents, including dexmedetomidine, acetaminophen, and benzodiazepines, may be used for sedation and postoperative pain management to reduce opioid adverse reactions. Today, the $\alpha_{2\text{-AR}}$ agonist dexmedetomidine is widely used for sedation, synchronization with long-term mechanical ventilation, in multimodal pain relief regimens, etc. The use of dexmedetomidine in young children after surgical correction of a congenital heart anomaly was described for the first time in 2006 [36]. The results of its testing demonstrated a minimum of cardiovascular and respiratory effects while achieving adequate sedation - analgesia after operations. The absence of a negative effect on respiratory drive promotes earlier extubation and allows its safe use in non-intubated patients. Thus, in a systematic

review (2018) studying the effectiveness of dexmedetomidine in various schemes of postoperative analgesia after cardiothoracic operations by thoracotomy/sternotomy, it was shown that in patients receiving dexmedetomidine, the intensity of PBS was significantly lower than in the comparison group [37]. This meta-analysis of 12 medical centers (n = 804) documented a significant reduction in the need for additional postoperative pain management and a reduction in opioid use in patients treated with dexmedetomidine.

In pediatric cardiac surgery, where pain is significant, multimodal analgesia regimens have not been sufficiently studied. Optimal postoperative pain relief after cardiac surgery should provide more stable hemodynamics, psycho-emotional peace and reduce the risk of developing ischemic complications in children. This is especially true for young children, when they need adequate protection from stress, pain, negative emotions, fear, depression, etc. Therefore, the state of stress caused by the stay of a small patient in the intensive care unit, first of all, dictates the need for adequate analgosedation. Proper sedative therapy reduces metabolic and neuroendocrine changes, eliminates discomfort, and allows medical procedures to be performed without negatively affecting the cardiovascular system [38]. The results of our study did not record significant hemodynamic disturbances in the early postoperative period; the limit of reduction in heart rate, SBP and SBP was noted to be -14%, which once again emphasizes the dose-dependent hemodynamic effect of dexmedetomidine. In addition, according to the results of studies and our own data, respiratory depression was not detected in patients treated with dexmedetomidine, which is due to the lack of its effect on the respiratory center [37]. And this was a positive side in the favorable course of the early postoperative period in young children against the background of desmedetomidine.

In many studies testing dexmedetomidine, the most common adverse events were bradycardia and hypotension [7,37,38]. Thus, according to some authors, in children with congenital heart defects admitted to the ICU immediately after surgery, the administration of dexmedetomidine at an initial loading dose of 1 mcg/kg intravenously over 10 minutes, followed by an infusion of 1 mcg/kg/h, led to a decrease in heart rate by 18%. However, despite the low heart rate, normal sinus rhythm and blood pressure were maintained [38]. One study reported bradycardia and 10 seconds of asystole during sedation with an opioid and dexmedetomidine in an 18-year-old double-lung transplant patient. After discontinuation of dexmedetomidine, normal sinus rhythm was restored [39].

In addition, the authors [40] revealed the fact that in preschool children (1-6 years old), intravenous administration of dexmedetomidine at a loading dose of 0.5 mcg/kg followed by an infusion of 0.5 mcg/kg/h in cardiac surgery, weakened intraoperative hemodynamic and neuroendocrine reactions (decrease in plasma adrenaline, norepinephrine, glucose and cortisol). These results are consistent with our data on neuroendocrine status in the postoperative period.

The findings were consistent with international meta-analyses where mechanically ventilated intensive care patients receiving dexmedetomidine demonstrated mild, manageable levels of sedation. In our studies, when using dexmedetomidine in moderate therapeutic doses, all patients had a mild to moderate level of sedation (Table 5). The deep level of sedation in the first postoperative hours may be due to the residual effect of general anesthesia. Dexmedetomidine provides a dose-dependent level of sedation while maintaining verbal contact with the patient, facilitating care and medical procedures.

Paracetamol (intravenous acetaminophen) has been used for more than 10 years in the pediatric population, benefiting from its rapid onset of action and relative safety profile. [41]. Some studies have shown that the use of paracetamol reduced the need for opioids and the duration of mechanical ventilation after non-cardiac surgery [42]. In contrast to non-steroidal anti-

inflammatory drugs with a high risk of bleeding and renal dysfunction, paracetamol provides relative safety in the perioperative period, and its combined use may improve pain control and sedation in pediatric cardiac intensive care units. [35,43].

Limitations of the study. There were no significant limitations that influenced the results of the study.

CONCLUSION

Postoperative multimodal analgesia with dexmedetomidine in combination with paracetamol provides an adequate level of sedation, suppresses irritation to extubation, prevents psychomotor agitation and provides effective analgesia. Respiratory depression was not noted in any case, and the decrease in blood pressure and heart rate was hemodynamically insignificant. Preservation of the swallowing reflex contributed to the early initiation of natural feeding. Transfer of 74.3% of patients in group 1 42.3±5.5 hours after surgery to a specialized cardiac surgery department reduced costs and burden on ICU medical staff. An optimized technique of MMA with dexmedetomidine in combination with paracetamol may provide an alternative to traditional opioid-based postoperative analgesia methods in pediatric cardiac intensive care units.

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