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SUBSTANTIATION USE METHOD OF PREEMPTIVE ANALGESIA WITH ACETAMINOPHEN FOR PAIN TREATMENT ON EARLY POSTOPERATIVE PERIOD IN CHILDREN

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The aim of the study was to improve the efficiency of non-narcotic analgesics for treatment of postoperative pain.

Materials and Methods. The study was performed in 37 children ((3.2 ± 0.8) years) after surgery: retroperitoneal space tumors – 27 patients (73 %), renal tumors – 8 children (22 %), ovarian tumors – 2 patients (5 %). The first group – 19 patients used continuous infusion of fentanyl as analgesics in combination with preemptive analgesia with acetaminophen, the second group of 18 children used only continuous infusion of fentanyl as analgesics. Evaluating the effectiveness of anesthesia was performed using the method of visual analogue scale, vital signs and biochemical indices were studied (blood glucose and cortisol in the blood), central hemodynamics: stroke volume, cardiac output.

Results and Discussion. The average amount of points that characterized the intensity of pain in early postoperative period, at all stages of the study, according to visual analogue scale, as well as levels of hemodynamic and respiratory lung function, stress hormones blood level and gas composition of the expiratory air in patients from the first group were significantly lower than the corresponding values of the indices in the second group ($p < 0.05$).

Conclusions. Comprehensive study of the reactions of pain behaviors, physiological indicators of stress, and laboratory tests showed that the use of the scheme on the basis of preemptive analgesia with acetaminophen 30 mg/kg and a continuous infusion of fentanyl – 5 mg/kg/h provide effective analgesia.

Key words: *analgesia, non-opioid analgesics, postoperative period.*

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According to many authoritative investigators, inadequate and ineffective analgesia in early postoperative period occurs in 30 – 50 % of patients moreover, the nearest (early) postanesthetic period is considered as a weak link of anesthetic management.

It is known that narcotic analgesics that act through opiate receptors do not impact on peripheral releaser of postoperative pain associated with stimulation of nociceptors by algogenic substances liberated by the injured tissues [1, 8].

Inadequate analgesia in early postoperative period worsens the course and forecast of this period in children as well as increases mortality due to increased risk of sepsis development and postoperative complications.

The pain experienced by a child changes the development of nociception system and leads to irreversible functional and structural changes in the central nervous system (CNS) and thus, modifies programmed body response to the pain in the future [2, 4, 6, 7, 9, 10].

Prime factors of inadequate analgesia in postoperative period in children are as follows: absence in pediatrics of generally accepted and simple techniques for assessment of pain severity; administration of narcotic analgesics is seldom and in less doses than needed for avoiding side effects; impossibility or limitation of use of effective up-to-date methods for postoperative analgesia and conviction of some physicians in fact that such children are less nociceptive [5].

In postoperative pain relief in children as well as in patients from other age groups, the first place is given to narcotic analgesics with traditional way of administration, i.e. intramuscular [4].

The aim of the study was to improve the efficiency of non-narcotic analgesics for treatment postoperative pain in children.

Materials and Methods

The study was performed in 37 children ((3.2 ± 0.8) years) after surgery: retroperitoneal space tumors – 27 (73 %) patients, renal tumors – 8 (22 %) patients, and ovarian tumors – 2 (5%) children. All patients received multimodal intensive therapy: infusion and transfusion therapy; breathing support via Dragger Carina apparatus – AC/PC mode with the following settings: FiO_2, 40 %, PEEP 3 – 4 sm H_2O, PIP 15 – 20 sm H_2O; antibiotics therapy; and syndromic treatment.

Assessment of pain relief effectiveness in early postoperative period was performed using visual analogue scale (VAS) Observation Scale for Infants and Small Children. The following parameters were studied: respiration rate (RR); heart rate (HR); systolic (BP_{syst}), diastolic (BP_{diast}) and mean barometric pressure; oxygen saturation (SaO_2); concentration of CO_2 in expiratory air; glucose and cortisol blood levels; clinical progress of anaesthesia. Central hemodynamics indices were studied additionally: stroke volume and cardiac output. Recording of readings was performed automatically via Datascope and Novometrix monitors.

The study was carried out on the following stages of anaesthesia: Stage 1 – 1 hour after surgery; stage 2 – 6 hours; stage 3 – 12 hours; stage 4 – 18 hours, and stage 5 – 24 hours after surgery.

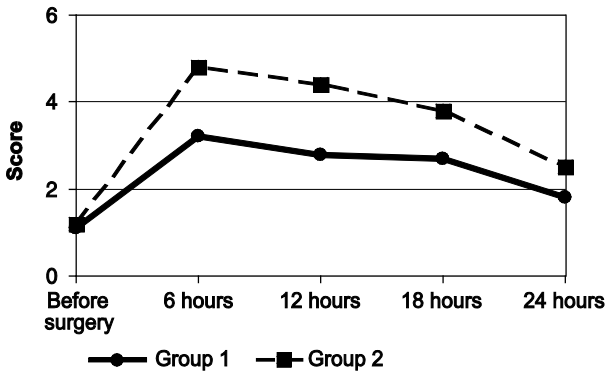
Statistical processing of obtained data was performed using methods of variation statistics and Student's-test. Differences at $p < 0.05$ were considered statistically significant.

Study results

The first group consisted of 19 patients receiving as analgesics continuous infusion of fentanyl (5 mcg/kg/h) in combination with preemptive analgesia with acetaminophen (Infulgan manufactured by Yuria Pharm LLC) administered in a dose of 30 mg/kg 60 minutes before the surgery, the daily dose did not exceed 60 mg/kg [3,5]. In 18 children included in the second group only continuous infusion of fentanyl (5 mcg/kg/h) was used as analgesics [4]. Indications for administration of additional boluses were as follows: motor excitement and hypertonia with certain facial activities, pain behavior, desynchronization with mechanical ventilation and tachycardia.

In the first group, 2 (5 %) children required additional administration of morphine (0.5 mg/kg), and in group 2, additional boluses were administered to 12 (32 %) children. Maximum number of additional boluses in all groups were administered 14 – 24 (18.4 ± 4.4) hours after surgery. Up to this time, the residual action of analgesic products administered in intraoperative period ended and the postoperative pain syndrome was extremely pronounced. That is why it is the very time for particularly close examination.

Average score demonstrating pain severity in early postoperative period at all stages of the study, according to visual analogue scale Observation Scale for Infants and Small Children, in patients from group 1 was significantly lower than the corresponding values of the indices in patients from group 2 ($p < 0.05$) (Fig. 1).



■ **Figure 1**. Average score, according to VAS ($p < 0.05$); by comparison pain relief in groups 1 and 2.

Analysis of HR in children from group 1 showed that mean value of HR in the most of patients (16 (84.2%) children) during infusion of fentanyl in combination with acetaminophen was less than 120 bpm.

Minimum value of mean HR for the whole study period amounted to 100.4 ± 6.4 bpm and the maximum one was 125.0 ± 5.2 bpm. In group 1, mean value of BP_{syst} for all the time of analgesics administration was 72.6 ± 4.2 mm Hg, and mean value of BP_{diast} was 50.3 ± 2.2 mm Hg.

In group 2, in most children (10 (55.5 %) patients), mean value of HR for all the time of fentanyl administration remained less than 130 bpm, at that, this value in 4 (40 %) patients was less than 120 bpm. Minimum mean HR for the whole study period amounted to 112 ± 6.0 bpm and the maximum one was 134.4 ± 4.2 bpm.

Analyzing mean values of BP_{syst} for the whole time of fentanyl infusion in group 2, it was detected that in 8 (44.4 %) children this index was higher than 80 mm Hg, in 2 (11.1 %) patients it was lower than 70 mm Hg, and in 8 (44.5 %) children mean value of BP_{syst} was within 70 – 79 mm Hg.

Maximum value of BP_{syst} for the whole study period amounted to 82.4 ± 4.4 mm Hg and the minimum one was 54.4 ± 3.3 mm Hg. Mean value of BP_{diast} for the whole time of fentanyl infusion in 3 (16.7 %) children was higher than 50 mm Hg, in 1 (5.5 %) patient it was lower than 40 mm Hg, and in most of patients of group 2 (14 (77.8 %) children) it was within 40 – 49 mm Hg.

Maximum values of mean BP_{syst} for the whole time of fentanyl infusion amounted to 65.6 ± 8.2 mm Hg and the minimum one was 44.4 ± 2.9 mm Hg.

SaO_2 values for the whole study period in all children of groups 1 and 2 remained stable in 98 – 99 % cases (table).

■ T A B L E

Variations of indices of hemodynamics, pulse oximetry and carbonometry at the study's stages (M ± m)

Indices	Study's stage				
	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Group 1(infusion of fentanyl + acetaminophen 30 mg/kg)					
HR	118.4 ± 6.4*	121.3 ± 6.3*	119.4 ± 7.2*	131.3 ± 4.3*	130.4 ± 3.2*
BP_{syst}	70.1 ± 1.3	70.2 ± 1.2	70.1 ± 1.4	70.3 ± 1.2	69.3 ± 1.2
BP_{diast}	41.2 ± 1.4	39.3 ± 1.3	39.4 ± 1.4	40.2 ± 1.4	40.3 ± 1.3
SaO_2	90.1 ± 0.4*	92.4 ± 0.2*	95.2 ± 1.4	92.4 ± 0.2*	95.2 ± 1.4
SV, ml	10.1 ± 1.1	10.6 ± 1.2	10.7 ± 1.3	10.4 ± 1.1	10.4 ± 1.2
MCO, ml	1.7 ± 0.2*	1.6 ± 0.1*	1.3 ± 0.1	1.3 ± 0.2	1.4 ± 0.4
CO_2 et.	38.1 ± 1.1	37.0 ± 1.2	38.0 ± 1.1	36.1 ± 1.1	38.2 ± 0.9
Group 2 (infusion of fentanyl 5 mg/kg/h)					
HR	154.4 ± 7.3	142.3 ± 6.2	138.2 ± 7.1	144.4 ± 7.3	142.3 ± 6.2
BP_{syst}	70.4 ± 1.4	76.2 ± 1.1*	74.2 ± 1.3*	77.2 ± 1.1*	74.2 ± 1.3*
BP_{diast}	41.3 ± 1.3	40.3 ± 1.3*	44.6 ± 1.3	42.3 ± 1.3*	41.6 ± 1.3
SaO_2	96.1 ± 0.1	96.2 ± 0.1	95.4 ± 0.2	97.9 ± 0.1	98.2 ± 0.1
SV, ml	10.3 ± 2.1	10.1 ± 1.9	10.3 ± 2.0	10.2 ± 1.2	10.2 ± 1.1
MCO, ml	1.4± 0.2	1.2 ± 0.1	1.2 ± 0.1	1.4 ± 0.2	1.3 ± 0.3
CO_2 et.	37.4 ± 0.8	36.8 ± 1.1	38.2 ± 1.3	35.9 ± 1.3	38.6 ± 0.9

Note. * $p < 0.05$ by comparison pain relief in groups 1 and 2.

HR value less than 130 bpm in the most children in all groups is indicative of opioid effect produced on this index, probably, due to potent sedative effect. Prolonged tachycardia was recorded in 4 (22.2 %) patients from group 2; however, only in 2 of them it was associated with the pain syndrome. In the most of children, tachycardia was recorded at the moment of admission to the surgical unit and was associated with hypovolemia, intoxication and, probably, with insufficient intraoperative analgesia which disappeared after infusion therapy. It is worth notifying that approximately 30 % of children (group 2) in postoperative period had BP at upper normal level or higher. Increase in arterial blood pressure after surgery may be associated with volemic disorders and is often accompanied with HR increase. Disease nature and type of surgery (mediastinal, urogenital system) also matter. In some case, pain syndrome effect cannot be disregarded. Significant decrease of mean values of HR and BP at the last stages of the study in patients from group 2 may be indicative of elimination of haemodynamic changes associated with underlying disease and surgery conducted as well as obtaining sufficient analgesia and sedation. Isolated haemodynamic changes indicative of pain syndrome occur rather seldom. In the most of cases, they are short-

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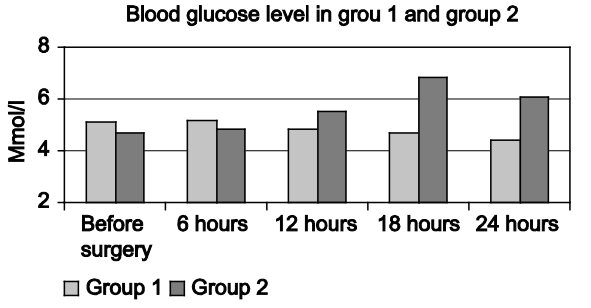
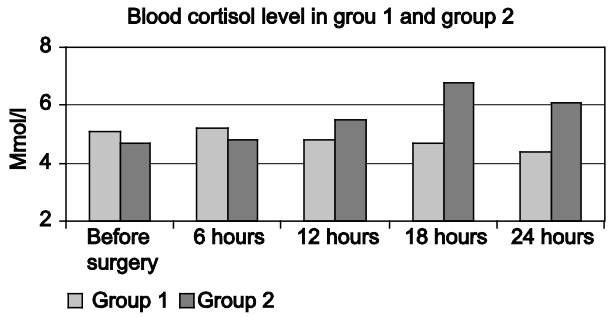
term and arise as a response to increased physical load at pain behavior reaction.

It is known that hyperglycemia is one of the indices of stress reactions, in particular pain reaction. Dynamics of blood glucose level in postoperative period is demonstrated on Fig. 2.



■ Figure 2. Dynamics of blood glucose level (mmol/l), $p < 0.05$ by comparison pain relief in groups 1 and 2



■ Figure 3. Dynamics of blood cortisol levels (nmol/l), $p < 0.05$ by comparison pain relief in groups 1 and 2

Dynamics of blood glucose and cortisol levels in group 1 (Fig. 3) is indicative of elimination of severe stress in the most of children during first 12 – 24 hours after surgery. This stress emergence was associated with the underlying disease or surgery conducted with the following sufficient analgesia.

Thus, effectiveness of the described scheme of analgesia is based on ability of these analgesics to effect on various mechanisms of pain formation. Owing to the data of the recent studies, it was found out that there are three isoforms of cyclooxygenase enzyme in our organism: COX-1, COX-2 and COX-3. As to COX-3, this isoform of cyclooxygenase is localized mostly in nerve cells of the CNS. Acetaminophen products (paracetamol) are selective relating to COX-3 and when blocking it produce their analgesic action [8].

Prescription of acetaminophen in preoperative period allows to reduce significantly the demand for opioids and combination of such products may restore analgesic potential of the latter. Different mechanisms of action of such medicines allow to prescribe them in combination with other products and in small doses in order to reach sufficient analgesic effect.

Conclusions

Comprehensive study of the reactions of pain behaviors and laboratory stress tests made it possible to make sure that the use of the scheme on the basis of preemptive analgesia with acetaminophen 30 mg/kg and a continuous infusion of fentanyl (in a dose of 5 mg/kg/h) for postoperative pain relief provide effective analgesia after traumatic surgery.

Applied methods of continuous intravenous infusions of opioids result in more or less sufficient sedative effect and respiratory depression that gives an opportunity to adapt children to the artificial lung ventilation apparatus after different surgeries.

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