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### **OPTIMIZATION OF CURRENT POSTOPERATIVE PERIOD AFTER CHILDRENS' ADENOTOMY**

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*The article studied the incidence of emergence delirium (ED) in children depending on the method of general anesthesia (GA) and identified predictors of ED. There was established, that after GA using sevoflurane ED occurred significantly more often than after GA using propofol or thiopental sodium (P = 0,014 and P = 0,001 respectively). The authors at first*

*made mathematical models with consideration of ED independent predictors for surgery (heart rate, blood glucose level, average of the cardiac cycle, Baevsky' stress index), which allow to choose optimal method of GA (with using propofol or sevoflurane) to conduct adenotomy and prevention of ED.*

**Key words:** adenotomy, children, intravenous anesthesia, inhalation anesthesia, emergence delirium, mathematical model.

**Introduction.** Nowadays one of the most debatable issues from the standpoint of evaluation of negative influence of anesthetics on the postoperative period in children is the so-called «agitation» or emergence delirium. ED was assumed dissociation of state of mind of the child, which is inconsolable, irritable, stubborn or unwilling to cooperate, crying or moaning and may harm themselves and others [8]. ED is a frequent complication in children undergoing anesthesia, which on average occurs in 18–80 % of cases [1], children aged 2–5 years are a group of particularly high risk and those who carried out procedures of the head and face, such as during otolaryngology operation [9]. The development of this state can lead to injury of the baby or nurse, which consequently requires substantial patient care, postoperative resources and reduces the degree of satisfaction of parents and medical staff [4]. Although the etiology and pathophysiology of ED is still completely unclear results of previous studies confirm, that the incidence of ED in children are greater after carrying out sevoflurane anesthesia as compared to propofol [2, 3]. But at the same time there are works that has not established the difference between the frequency of ED in children during propofol or sevoflurane anesthesia [5–7].

Based on this we consider that by now the ED issues and possible prevention of development in children remain relevant and finally unresolved.

The aim of our study was to improve the postoperative period after adenotomy in children by reducing the incidence of emergence delirium.

**Materials and methods.** Research was conducted at the Department of Anesthesiology and Intensive Therapy of Municipal health care facility “Regional Children Clinical Hospital” (Kharkiv, Ukraine) during 2014. It includes 117 children with mean age ( $7,5 \pm 0,4$ ) years old which was carried out adenotomy and conform to ASA I-II. The average duration of surgery was ( $7,3 \pm 0,3$ ) minutes.

Depending on the method of anesthesia patients were divided into 3 groups. Patients in group I ( $n = 41$ ) was performed induction of anesthesia using 1% solution of propofol ( $2,5 \text{ mg/kg} \pm 0,03 \text{ mg/kg}$ ), maintaining was performed fractional entering of propofol ( $1 \text{ mg/kg}$ ) on average 2,5–3 minutes after previous entering.

Patients in group II ( $n = 40$ ) was performed “bolus” method of mixture of sevoflurane-oxygen without filling breathing circuit 8 % sevoflurane vapor in oxygen flow 4 l/min. Upon reaching a clinic of surgical stage of anesthesia maintaining anesthesia was performed about serving the 2–2.5 % sevoflurane fresh gas flow at 2 l/min.

Patients in group III ( $n = 36$ ) was performed induction of anesthesia using 1% solution of thiopental sodium ( $5–6 \text{ mg/kg}$ ). Considering short duration of the intervention, there was no need for a repeated entering of anesthetic in order to maintain anesthesia

Muscle relaxation to patients of all groups was provided by entering a 2 % solution of suxamethonium iodide in dose ( $2 \text{ mg/kg}$ ). When necessary additional entered fractionally suxamethonium iodide in middle doses ( $1 \text{ mg/kg}$ ). Analgesia performed intraoperatively of 0,005 % solution of fentanyl in dose ( $2 \text{ mg/kg}$ ).

There was carried out perioperative noninvasive monitoring of heart rate (HR), ECG, systolic and diastolic, mean arterial pressure (MAP), heart rate variability (HRV), respiration rate, index of blood oxygen saturation ( $\text{SpO}_2$ ) using the monitor UM-300 (Ukraine).

The aforementioned parameters investigated in the following stages: 1st is before surgery; 2nd is induction of anesthesia; 3rd is tracheal intubation; 4th is traumatic moment of operation; 5th is extubation; 6th is 1st hour after surgery; 7th is 6th hour

after surgery; 8th is 1st postoperative day. Indicators HRV investigated at all stages, except 3rd is stage of tracheal intubation.

BIS-index was investigated using monitors UM-300 (Ukraine) and the BIS VISTA (USA), data were estimated at the 1st, 3rd, 4th, 5th stages. Doses titrated in the range of 40–60 % in order to maintain BIS-index. Watcha scale used to evaluate the frequency of ED [1].

The level of cortisol (C) in serum was determined by ELISA using a set of reagents of production (XEMA-MEDICA, Russia). Insulin levels (I) was determined by a set of reagents of production (DRG, Germany). Glucose was determined by glucose oxidase method using a set of reagents of production (Filisit-Diagnostics, Ukraine).

We investigated the ratio C/I which was calculated using formula:

$$\frac{C}{I} = \frac{(\text{level of } C \text{ at the research stage}) \cdot 100\% / (\text{level of } C \text{ before surgery})}{(\text{level of } I \text{ at the research stage}) \cdot 100\% / (\text{level of } I \text{ before surgery})}$$

Investigation was carried out on the 1st, 4th, 5th and 8th stages. Statistical analysis of the data was performed using SPSS 19 for Windows. Results of descriptive statistics are presented as  $M \pm m$  (mean  $\pm$  standard error of mean). Check for normal distribution was carried out by the Kolmogorov-Smirnov criterion. We used *t*-Student test to compare quantitative indicators and determine the differences between them for dependent and independent samples with Bonferroni correction. Correlation analysis was carried out using the criterion of Pearson (*r*) and the Cheddok scale to evaluate the relationships between indicators. ANOVA was performed with the calculation Fisher criterion to estimate the impact factors studied in ED. Logistic regression has been used to determine the likelihood of the ED.

**Research results.** Patients of all groups were comparable by gender, age, anthropometric data and duration of surgery. Indicators of hemodynamics in patients of all groups did not differ for surgery and were stable during it.

BIS-index had the same tendency to change in patients of all groups, but the study stages between groups been identified some differences. Preoperative data indicated that the children are in a state of wakefulness. However, significant differences were recorded between patient in groups I and III and in groups II and III ( $P = 0,002$  and  $P = 0,014$  respectively), that were not clinically significant (Table).

**Dynamics of indicators of hypnotic component of general anesthesia (BIS-index) in patients of all groups in the perioperative period ( $M \pm m$ )**

Groups	Stages of studies			
	1st	3rd	4th	5th
Group I	95,8 $\pm$ 0,5 <sup>***I-III</sup>	52,2 $\pm$ 1,7	51,5 $\pm$ 1,6 <sup>*I-III</sup>	76,5 $\pm$ 0,9
Group II	96,6 $\pm$ 0,3 <sup>**II-III</sup>	42,1 $\pm$ 1,1 <sup>***II-III; ***II-I</sup>	46,4 $\pm$ 2,6 <sup>***II-III</sup>	78,5 $\pm$ 0,6
Group III	97,5 $\pm$ 0,2	54,8 $\pm$ 1,0	56,0 $\pm$ 1,2	78,3 $\pm$ 0,6

Note. Significant differences between the groups at appropriate stages: \* $P < 0,05$ ; \*\* $P < 0,01$ ; \*\*\* $P < 0,001$ .

Subsequent analysis of carried BIS-monitoring demonstrated that during a surgery in patients of all groups was adequate level of hypnotic component of the GA (40 % < BIS-index < 60 %), which allowed to avoid excessively deep or too superficial level of hypnotic component of the GA.

ED (on a Watcha Scale) was registered in 6 children of group I (14 %  $\pm$  5 %). 1 of them (2 %  $\pm$  2 %) was excited and calm it was impossible and 5 children (12 %  $\pm$  5 %) were crying, but they calmed down as soon as they returned to the ward to parents. ED in group II was registered in 14 children (35 %  $\pm$  6 %), 3 of them (8 %  $\pm$  4 %) on a Watcha scale were excited and to calm them was impossible and the remaining 11 children (28 %  $\pm$  7 %) were crying, but they calmed down as soon as they returned

to the ward to parents. ED in Group III was reported in 2 children (6 % ± 4 %) and both the child calmed down as soon as they returned to the ward to parents.

Therefore, ED occurred significantly more often in patients of group II than children of I and III groups ( $P = 0,014$  and  $P = 0,001$  respectively).

The results of ANOVA and correlation analysis of hemodynamic parameters (MAP, HR), level of stress markers and their differences ( $\Delta$ ) between stages of research, BIS-index value and its difference ( $\Delta$ ) between stages of research did not find any impacts or relationships with the ED after adenotomy.

To identify predictors of ED when applying intravenous GA using propofol binary logistic regression have been used. As potential predictors were used the following parameters: gender, age group of autonomous regulation, MAP, HR, C and I levels, glucose, ratio C/I, BIS-index, HRV indices at all stages of the study (190 indicators in total).

Informative predictors of ED were identified: blood glucose levels and mean value of cardiac cycle before surgery. The sensitivity of the test was 0.89, specificity was 1.00. The value of the area under ROC-curve allows estimating the diagnostic value of the constructed model amounted 0.91 and indicating excellent quality of the model. By using the logistic regression equation:

$$\hat{P} = \frac{1}{1 + e^{7,078 \cdot X_1 + 0,008 \cdot X_2 - 30,556}},$$

where,  $X_1$  is blood glucose level before surgery;  $X_2$  is mean value of cardiac cycle before surgery, it is possible to calculate the individual risk of occurrence of ED when used intravenous propofol GA. Overall rating consent between the influence of the identified risk predictors and actually recorded the onset of adverse outcome was conducted using a Hosmer – Lemeshov test  $\chi^2$ . It was established that these predictors influencing the development of the ED in a patient using propofol ( $\chi^2 = 0,95$ ;  $P > 0,05$ ).

Informative predictors of ED in a patient using sevoflurane inhalation anesthesia were HR before surgery, Baevsky' stress index before surgery and blood glucose level before surgery. The sensitivity of the test was 1.00, specificity was 0.89. The value of the area under ROC-curve allows estimating the diagnostic value of the constructed model amounted 0.94 and indicating excellent quality of the model.

By using the logistic regression equation:

$$\hat{P} = \frac{1}{1 + e^{-11,920 \cdot X_1 + 0,927 \cdot X_2 + 187,234 \cdot X_3 + 125,386}},$$

where  $X_1$  is HR before surgery;  $X_2$  is Baevsky' stress index before surgery;  $X_3$  is blood glucose level before surgery, it is possible to calculate the individual risk of occurrence of ED when sevoflurane inhalation anesthesia is used. Overall rating consent between the influence of the identified risk predictors and actually recorded onset of adverse outcome using the Hosmer – Lemeshov test showed acceptable quality of the resulting model ( $\chi^2 = 4,45$ ;  $P > 0,05$ ). The resulting figure by the equation will indicate how likely ED can occur in children.

**Conclusions.** We got similar results with the works, which investigated the risk of ED depending on the method of the GA (sevoflurane or propofol), and namely that anesthesiological support using propofol reduces the risk of ED. Owing to the preoperative data (HR, blood glucose level, mean value of cardiac cycle and Baevsky' stress index) mathematical models have been developed which will allow anesthesiologists to choose the optimal method of GA for adenotomy and prevent growth of ED.

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#### ОПТИМІЗАЦІЯ ПЕРЕБІГУ ПІСЛЯОПЕРАЦІЙНОГО ПЕРІОДУ ПІСЛЯ АДЕНОТОМІЇ У ДІТЕЙ

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Досліджено частоту виникнення синдрому постнаркозного збудження (СПЗ) у дітей залежно від способу загальної анестезії (ЗА) та визначено предиктори розвитку СПЗ. Встановлено, що після ЗА севофлюраном СПЗ виникав достовірно частіше, ніж після ЗА з використанням пропофолу або тіопенталу натрію ( $P = 0,014$  та  $P = 0,001$  відповідно). Вперше авторами синтезовано математичні моделі з урахуванням отриманих до операції незалежних предикторів СПЗ (частота скорочень серця, рівень глікемії, середній кардіоцикл та індекс напруги Баєвського), які дозволяють анестезіологу обрати оптимальний спосіб ЗА (з використанням пропофолу або севофлюрану) з метою проведення аденотомії та запобігання розвитку СПЗ.

**Ключові слова:** аденотомія, діти, внутрішньовенна анестезія, інгаляційна анестезія, синдром постнаркозного збудження, математична модель.

#### ОПТИМІЗАЦІЯ ТЕЧЕННЯ ПОСЛЕОПЕРАЦИОННОГО ПЕРИОДА ПОСЛЕ АДЕНОТОМИИ У ДЕТЕЙ

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Исследована частота возникновения синдрома постнаркозного возбуждения (СПВ) у детей в зависимости от способа общей анестезии и определены предикторы развития СПВ. Установлено, что после общей анестезии севофлюраном СПВ возникал достоверно чаще, чем после общей анестезии с использованием пропофола или тиопентала натрия ( $P = 0,014$  и  $P = 0,001$  соответственно). Впервые авторами синтезированы математические модели с учётом полученных до операции независимых предикторов СПВ (частота сокращений сердца, уровень гликемии, средний кардиоцикл и индекс напряжения Баевского), которые позволяют анестезиологу выбрать оптимальный способ общей анестезии (с использованием пропофола или севофлюрана) с целью проведения аденотомии и предупреждения развития СПВ.

**Ключевые слова:** аденотомия, дети, внутривенная анестезия, ингаляционная анестезия, синдром постнаркозного возбуждения, математическая модель.