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Quality and Safety of General Anesthesia with Propofol and Sevoflurane in Children Aged 1-14 Based on Laboratory Parameters

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ABSTRACT

Introduction: Knowledge of anatomic, physiological, biochemical and physical characteristics of children of all age groups, the existing illness and possible pathological response of the organism to the existing situation, require a pediatric anesthesiologist to participate in the preparation of a child for surgical treatment, to choose the best anesthesia technique and medications, and manipulative techniques to enable the scheduled surgical treatment with minimum anesthesia risks. **The aim** of this clinical study was to prove reliability and quality of propofol or sevoflurane general anesthesia in children in the age group of 1-14 years from the ASA I group and in the elective surgical treatments in duration of 60 minutes, based on preoperative and postoperative levels of laboratory findings (transaminases, blood sugar, urea and creatinine). **Materials and methods:** the study included 160 patients randomized in two groups based on different approaches: total intravenous anesthesia was used for the propofol group (n=80) (TIVA) and the inhalation technique was used for the sevoflurane group (n=80). **Results:** statistical evaluation of the obtained results indicates stability of laboratory findings in the immediate postoperative course (after 24 hours) in respect to the preoperative period. Based on the Mann Whitney test (P), preoperative and postoperative blood sugar levels in the sevoflurane vs. propofol group were P=0.152 vs. 0.021; creatinine levels P=0.113 vs. 0.325; urea levels P= 0.016 vs. 0.900; AST levels P=0,031 vs. 0,268 and ALT levels P=0.021 vs. 0.058. Level of significance was P<0.5. **Conclusion**: Analysis of the examined laboratory parameters show that propofol and sevoflurane provide full security and quality of general anesthesia in children age group 1-14 years, from the ASA I group. All analyzed laboratory levels in the postoperative course remained in their referential values in both groups of participants.

Key words: propofol, sevoflurane, pediatric anesthesia, laboratory values.

1. INTRODUCTION

Propofol and sevoflurane are intravenous, inhalator anesthetics of a new generation used in our country in the past two decades. At the very beginning both of these hypnotics were used to induce and maintain general anesthesia in adult patients based on recommendations of pharmaceutical companies in charge of their production. Their use in children, especially in those up to 3 years of age, was not recommended given that there was insufficient data and experience on their side effects and reactions to the medications. Propofol is an intravenous anesthetic agent which for its highly positive pharmacological characteristics, except for total intravenous anesthesia (TIVA), can also be used for sedation of patients in the Intensive Care Unit (ICA). When administered in the recommended dosage for anesthesia it has fast effects, a patient is put into sleep in 20-40 seconds, which based on the effectiveness is almost equal to dosages of thiopentone, with propofol being 1.6-1.8 times stronger (1). Its effect is realized via GABAA receptor (2). Propofol is administered intravenously, metabolized in liver and usually eliminated through urine. For inducing and maintenance of general anesthesia along with opioids (analgetic effect is weak and temporary), relaxants and oxygen can also be used (TIVA) or in combination with inhalation sedation (balanced anesthesia) (1, 2, 3). It is quickly and fully metabolized by conjugation in the liver thanks to enzymes and cytochrome P_{450} in products without any hypnotic or sedated effects, and is eliminated through kidneys.

Based on its chemical composition sevoflurane is completely fluorinated methyl isopropyl ether. It causes sleep via respiratory system, and is subsequently absorbed from alveolus and transferred into the blood stream and by diffusion distributed to all tissues. Anesthesia by sevoflu-

rane starts when adequate partial anesthetic pressure is achieved in the brain tissue, which is in balance with alveolar partial pressure of anesthetic. It is to a large extent eliminated through the respiratory system, and partially through urine in the shape of organic fluoride metabolites (3, 4, 5).

In a study on general intravenous anesthesia by propofol and standard practice in pediatric anesthesia, Strauss JM et al. do not save words of praise for quality, efficiency, hemodynamic stability and minimal side effects during general anesthesia, but they also emphasize and emphasized great caution and experience in work with propofol and total intravenous anesthesia in children (6). A study of Suzuki KS et al. from 2002 and a study of Kamal AH et al, compared the time from inducing anesthesia and waking up from general anesthesia (sevoflurane in comparison with propofol) and reached identical conclusion as in the previously cited study regarding patients treated with sevoflurane, emphasizing minimal incidence in the postoperative complications (laryngospasm, stridor, nausea and vomiting) in the same group of patients (7). A study of Shmit J et al. performed on 120 children in infant and preschool age divided in two groups, propofol and sevoflurane, showed higher hemodynamic stability in patients treated with propofol (8). We did not find any special studies related to analysis of preoperative and postoperative laboratory findings which we could use for the purpose of comparison. The aim of this clinical study was to prove the reliability and quality of general anesthesia by propofol and sevoflurane in children of the age group 1-14 years, ASA I group, and in pre elective 60 minute surgery based on preoperative and postoperative values of laboratory findings (transaminases, blood sugar, urea and creatinine).

2. MATERIALS AND METHODS

Our country has not conducted any investigation aimed towards the comparison of preoperative and immediate postoperative laboratory parameters in propofol and sevoflurane anesthesia in children age group 1-14 years and ASA I group. This is a prospective, descriptive, randomized clinical study. The study was public and conducted with strict adherence to the requirements of ethics and humanity in accordance with the Helsinki declaration.

The inclusive criteria were as follows: patients from 1 to 14 years of age (n=160) hospitalized at the Pediatric Surgery of the University Clinical Center Sarajevo (UCCS) for the purpose of elective surgery; patients who based on the local report of a pediatric surgeon were indicated for surgery; patients with pediatric report and a surgery consent of a pediatrician; patients from ASA I group; patients with clinical diagnosis whose parents provided full data in the anamnesis questionnaire; patients with all laboratory parameters required for this study; patients whose parents gave consent for surgery; patients pre-medicated according to the established plan. Patient's data and values measured during the study were recorded in a specially designed form.

In the propofol group of patients, opioid fentanyl was administer at a dose of 0.005 mg/kg, followed by a muscle relaxant vecuronium-bromide 10 minutes later at a dose of 0.1 mg/kg. After administration of the muscle relaxant an intravenous propofol bolus doze of 3 mg/kg was immediately administered. During the administration of opioid, muscle relaxant and propofol, all patients from the propofol group received oxygen via anesthetic oxygen mask in the amount of 5 l/h. After achieving the state of sleep and muscle relaxation the patients were intubated with an appropriate size endotracheal tube. Continuous ventilation was achieved mechanically via anesthetic apparatus IPPV (Intermittent positive pressure ventilation). Tidal volume (breathing volume) and the respiration rate were adjusted to the age and weight of a child. The rate of inhaled gases during anesthesia was adjusted as follows: oxygen/ nitrogen oxide 50:50. After bolus intravenous doze and in the further course of the anesthetic and surgery propofol was administered via „BRAUN" perfusor, in the amount of 0.1-0.3 mg/kg/min.

In the sevoflurane group of patients, opioid fentanyl was administered at a dose of 0.005 mg/kg, followed by a muscle relaxant vecuronium-bromide 10 minutes later at a dose of 0.1 mg/kg. During the administration of the opioid and muscle relaxant all sevoflurane group of patients received oxygen via anesthetic oxygen mask in the amount of 5 l/h. Immediately after administration of the muscle relaxant sevoflurane was administered from the appropriate dispenser on the anesthetic apparatus via anesthetic mask. The initial concentration of sevoflurane was 6 vol ‰, and after each three respiratory cycles the value was reduced for one vol ‰ up to the value of 1 vol‰, which was maintained during the entire course of general endotracheal anesthesia. After achieving the state of sleep and muscle relaxation the patients were intubated with an appropriate size endotracheal tube. Continuous ventilation was achieved mechanically via anesthetic apparatus IPPV (Intermittent positive pressure ventilation). Tidal volume (breathing volume) and the respiration rate were adjusted to the age and weight of a child. The rate of inhaled gases during anesthesia was adjusted as follows: oxygen/ nitrogen oxide 50:50 with already stated sevoflurane value of 1 vol ‰.

Immediately after the surgery, sevoflurane and nitrogen oxide were cut off in all patients from the sevoflurane group, and the oxygen ventilation was continued in the amount of 5 l/min. After the surgery and achievement of spontaneous ventilation, decurarization with neostigmine at a dose of 0.05 mg/kg and atropine at a dose of 0.02mg/kg was performed in both groups of patients. Extubation was done after all criteria for safe extubation were met, specifically, after meeting all criteria of good revision of neuromuscular blockade and criteria of the sleep-wake cycle.

Postoperative pain in both groups of patients was treated with analgesics (paracetamol, ibuprofen, metamizole, tramadol) as a suppository or intravenously according to the age and weight of the child. After waking up in the operating theatre patients from both groups were transferred to Pediatric Surgery of the University Clinical Center Sarajevo (UCCS) for further treatment.

3. RESULTS

In our study we obtained the following results:

Table 1 monitors movement of the serum glucose mean level in the preoperative and postoperative period in both groups of patients. In the preoperative period of the sevoflurane group of patients that level was 4.7 mmol/L, and 4.84 mmol/L in the propofol group of patients. In the postoperative period the serum glucose mean level in the sevoflurane group was 4.5 mmol/L, and 4.2 mmol/L in the propofol group. There was a statistically significant difference in the preoperative serum glucose mean level in the sevoflurane group in respect to the propofol group of patients (p=0.15)(Table 1).

	Preoperatively (n=80)		Postoperatively (n=80)	
	Sevoflurane	Propofol	Sevoflurane	Propofol
Level	2.6-6.1	3.1-6.7	4.2-7.1	2.3-5.4
X	4.704	4.839	4.490	4.223
S	0.557	0.627	0.870	0.494
S_X	0.0623	0.0701	0.0972	0.0552
Median	4.7	4.8	4.4	4.2
Mann - Whitney Test	P = 0.152	P = 0.021		

Table 1. Blood sugar in patients treated with sevoflurane vs. propofol (n=80)

Table 2 shows the creatinine mean level in preoperative and postoperative period in both groups of patients. In the preoperative period of the sevoflurane group of patients that level was 51.1 mmol/L, and 53.71 mmol/L in the propofol group of patients. In the postoperative period the creatinine mean level in the sevoflurane group of patients was 48.86 mmol/L, and 50.84 mmol/L in the propofol group of patients. Somewhat lower levels in the postoperative period in respect to the preoperative period (after 24h) were in their referential levels in both groups of patients and did not require any corrections. There was no statistically significant difference in creatinine mean levels between the propofol and sevoflurane group of patients either preopratively or postoperatively (Table 2).

	Preoperatively (n=80)		Postoperatively (n=80)	
	Sevoflurane	Propofol	Sevoflurane	Propofol
Level	42-72	52-74	45-69	46-70
X	51.063	53.712	48.862	50.837
S	9.650	11.333	10.481	10.356
S_X	1.079	1.267	1.172	1.158
Median	51	54	50	50
Mann - Whitney Test	P = 0.113	P = 0.325		

Table 2. Creatinine level in the sevoflurane group vs. propofol group (n=80)

Table 3 shows the urea mean level in preoperative and postoperative period in both groups of patients. In the preoperative period of the sevoflurane group of patients that level was 4.1 mmol/L, and 4.5 mmol/L in the propofol group of patients. The difference was statistically significant (p=0.016). In the postoperative period the urea mean level in the sevoflurane group of patients was 4.34 mmol/L, and 44 mmol/L in the propofol group of patients. The difference was not statistically significant (p=0.9).

	Preoperatively (n=80)		Postoperatively (n=80)	
	Sevoflurane	Propofol	Sevoflurane	Propofol
Level	4.6-6.9	4.9-7.4	3.5-6.1	4.6-7.2
X	4.131	4.558	4.365	4.415
S	1.073	1.151	0.934	1.030
S_X	0.120	0.129	0.104	0.115
Median	4.2	4.4	4.4	4.3
Mann-Whitney Test	P = 0.016	P = 0.900		

Table 3. Urea in the sevoflurane group vs. propofol group (n=80)

Table 4 shows the AST mean levels in the preoperative and postoperative period in both groups of patients. In the preoperative period of the sevoflurane group of patients that level was 28.2 U/L, and 26.00 U/L in the propofol group of patients. The difference in the sevoflurane group was statistically significantly higher than in the propofol group (28.2 U/L vs.26.0; p=0.03). In the postoperative period the AST mean level in the sevoflurane group was 25.40 U/L, and 24.56U/L in the propofol group. The difference was not statistically significant (p=0.268).

	Preoperatively (n=80)		Postoperatively (n=80)	
	Sevoflurane	Propofol	Sevoflurane	Propofol
Level	23-39	30-42	22-37	26-40
X	28.150	26.000	25.400	24.563
S	5.924	6.436	4.983	5.003
S_X	0.662	0.720	0.557	0.559
Median	29	26	24	24
Mann-Whitney Test	P = 0.031	P = 0.268		

Table 4. AST levels in the sevoflurane group vs. propofol group (n=80)

Table 5 monitors movement of the ALT mean level preopratively and postoperatively in both groups of patients. In the preoperative period of the sevoflurane group of patients that level was 21.26 U/L, and 24.16 U/L in the propofol group of patients. In the postoperative

	Preoperatively (n=80)		Postoperatively (n=80)	
	Sevoflurane	Propofol	Sevoflurane	Propofol
Level	38-43	46-57	30-37	45-55
X	21.262	24.163	21.262	23.450
S	7.353	8.789	5.507	8.033
S_X	0.822	0.983	0.616	0.898
Median	20	23	20	22
Mann-Whitney Test	P = 0.021	P = 0.058		

Table 5. ALT levels in the sevoflurane group vs. propofol group (n=80)

period the ALT mean level in the sevoflurane group was 21.26U/L, and 23.45 U/L in the propofol group. The stated levels show that there was no statistically significant difference between the groups.

4. DISCUSSION

The study included 160 respondents divided in two groups according to the anesthetic used (total intravenous anesthesia (TIVA) was used for a group with propofol – and inhalation anesthesia was used for a group with sevoflurane), additionally divided according to the age and gender structure. Out of the total of 160 respondents there were 92 boys and 62 girls. In the sevoflurane group there were 46 boys and 34 girls and the propofol group included 52 boys and 28 girls. The age structure was taken as a parameter given that both propofol and sevoflurane were for a long time used for adults and gradually introduced for children, but their application to the youngest population, specifically to children under 3 years started only a few years ago (9, 10).

Analysis of the preoperative and postoperative values of blood sugar did not show any statistically significant differences between the respondent groups (Table 1). In the preoperative period of the sevoflurane group of patients that level was 4.7 mmol/L, and 4.84 mmol/L in the propofol group of patients. In the postoperative period the serum glucose mean level in the sevoflurane group was 4.5 mmol/L, and 4.2 mmol/L in the propofol group. Somewhat lower levels in the postoperative period in respect to the preoperative period (after 24h) were in their referential levels in both groups of patients and did not require any corrections (?). A study conducted by Mujagic Z et al. in 2007 monitored the serum glucose concentration in patients surgically treated in propofol/fentanyl total intravenous anesthesia (TIVA) vs. balanced isoflurane/fentanyl anesthesia. The blood sugar levels were measured in 5 periods: 30 minutes before the surgery (T0), during the surgery (T1), after the surgery and anesthesia (T2), and after 2 and 24 hours respectively (T3 and T4) in the postoperative period. The serum glucose concentrations measured in the stated periods were significantly lower especially in T1, T2 and T3 than in the preoperative period (T0) in propofol/fentanyl total intravenous anesthesia then in patients treated with balanced isoflurane/fentanyl technique. The results of the study show that the metabolic response to surgical treatment and anesthesia was probably allayed, specifically improved in patients treated in the propofol/fentanyl total intravenous anesthesia in respect to those treated in balanced isoflurane/fentanyl technique (11).

Comparison of the preoperative and postoperative urea and creatinine levels did not show any statistically significant differences as well as the comparison of transaminases between the groups (Table 2, 3, 4, 5). A study conducted by Mazze R et al. in 2000, which included 3,436 patients, monitored preoperative and postoperative urea and creatinine levels in use of different hypnotics and anesthesia techniques. The TIVA technique – propofol, inhalation technique – sevoflurane, isoflurane, enflurane. The obtained results imply stable values of the monitoring parameters both preopratively and postoperatively, which lead to a conclusion that the stated values may have significant changes only in case those surgical treatments are performed on patients with already existing renal diseases (12), and not due to the hypnotics used.

Results of the blood transaminases analysis could not be compared given that we could not find any similar studies.

5. CONCLUSION

The values of laboratory parameters monitored during the study did not show statistically significant differences. Analysis of the examined laboratory parameters, in respect to others used anesthetic agents in everyday clinical practice, shows that propofol and sevoflurane provide full security and quality of general anesthesia in children age group 1-14 years, from ASA I group. Based on the obtained results and taking into account minimal technical preparations for TIVA and inhalation anesthesia, easy handling and control of the anesthetics, simplicity of keeping and storage as well as efficiency of sevoflurane and propofol give them priority above other anesthetics recently used in pediatric anesthesia.

CONFLICT OF INTEREST: NONE DECLARED.

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