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Retrospective Study

Effects of propofol combined with lidocaine on hemodynamics, serum adrenocorticotropic hormone, interleukin -6, and cortisol in children

Abstract

BACKGROUND

Children are a unique patient population. Anesthesia for pediatric abdominal surgery has long been achieved mainly with intravenous amiodarone and propofol alone or combined with other anesthetics. The incidence of complications and postoperative adverse reactions is relatively high owing to the imperfect development of various protocols for children. Choosing the most appropriate anesthesia program is an important means of reducing adverse reactions.

AIM

To explore the clinical value of propofol combined with lidocaine-assisted anesthesia in pediatric surgery.

METHODS

A total of 120 children who underwent abdominal surgery at our hospital from January 2016 to March 2018 were selected and divided into groups A and B using the random number table method, with 60 patients in each group. Group B received ketamine for anesthesia, while group A received ketamine, propofol, and lidocaine. The pre- and postoperative heart rate (HR); mean arterial pressure (MAP); arterial oxygen saturation (SpO$_2$); serum adrenocorticotropic hormone (ACTH), interleukin-6 (IL-6), and cortisol (Cor) levels; restlessness score during the recovery period [Paediatric Anesthesia

Emergence Delirium Scale (PAED)]; and adverse reactions were compared between the two groups.

RESULTS

The HR, MAP, and SpO_2 Level at five minutes before initiating anesthesia were compared between groups A and B, and the difference was not statistically significant ($P > 0.05$). At 10 and 20 minutes after anesthesia initiation, the HR and MAP were lower in group A compared with group B ($P < 0.05$). The differences in preoperative serum ACTH, IL-6, and Cor levels between groups A and B were not statistically significant ($P > 0.05$); however, the postoperative serum ACTH, IL-6, and Cor levels in group A were lower compared with group B ($P < 0.05$). Furthermore, the visual analog scale scores of group A at 2 h and 8 h postoperative were lower than those in group B, and the differences were statistically significant ($P < 0.05$). The mean PAED score in group A was lower than that in group B ($P < 0.05$), and the incidence of restlessness in group A was 23.33% lower than that in group B (36.67 %) ($P < 0.05$). The incidence of adverse reactions was lower in group A than in group B (6.25% vs 16.25%).

CONCLUSION

The anesthetic effect of propofol combined with lidocaine and ketamine in pediatric surgery was better than that of ketamine alone, and had less influence on hemodynamics and pediatric stress response indices, lower incidence of restlessness in the recovery period, and lower incidence of adverse reactions.

INTRODUCTION

Pediatric abdominal surgery is a common type of pediatric surgery. Due to the poor tolerance of children and their susceptibility to crying and other adverse emotions, general anesthesia is typically used in clinical operations. Therefore, the selection of the most appropriate anesthetic drugs is of great significance for improving pediatric surgery outcomes. The best choice for anesthesia should not only meet the surgical requirements, but also allow children to recover in the shortest amount of time[1]. At present, the compound anesthesia method is commonly used for pediatric general anesthesia, as ketamine is a deep analgesic drug that has little effect on children's respiratory and circulatory systems, and is commonly used in clinical settings. However, when the dosage is too high or the operation time is prolonged, ketamine is associated with increased adverse reactions. In recent years, propofol has been found to be a fast and effective general anesthesia drug with the advantages of rapid onset, short duration, and rapid recovery. However, propofol injections cause obvious pain during the process; therefore, lidocaine is combined with propofol to reduce the injection pain[2]. This study observed the anesthetic effect of propofol combined with lidocaine in pediatric surgery to provide guidance and a basis for clinical practice.

MATERIALS AND METHODS

Clinical data

A total of 120 children who underwent abdominal surgery at our hospital from January 2016 to March 2018 were selected and randomly divided into groups A and B, with 60 patients in each group.

Group A included 39 boys and 21 girls aged 1–12 years (mean 6.3 ± 2.6 years) with an average weight of 22.6 ± 4.5 kg and an average operation time of 48.2 ± 9.0 min. Group B included 42 boys and 18 girls aged 1–12 years (mean 6.1 ± 3.2 years) with a mean weight of 23.0 ± 4.9 kg and an average operation time of 50.0 ± 10.2 min. Age, sex, weight, and operation time were compared between the two groups and the differences were not statistically significant ($P > 0.05$).

The inclusion criteria were as follows: (1) children who underwent elective surgery; (2) children 1-12 years old; (3) children who underwent surgeries performed by the same group of anesthesiologists and surgeons; and (4) provision of written informed consent from the parents or guardians.

The exclusion criteria were as follows: (1) history of liver and kidney function diseases; (2) history of congenital heart diseases; (3) history of immune function and blood system diseases; and (4) history of major diseases associated with other systems.

This study was approved by the Medical Ethics Committee, and informed consent was obtained from the parents.

Methods of anesthesia

Phenobarbital and atropine were intramuscularly injected preoperatively, and ketamine (5 mg/kg) was used for the induction of anesthesia.

Participants in group A were administered ketamine, propofol, and lidocaine (ketamine 100 mg, propofol 60 mg, and lidocaine 40 mg mixed with 10 mL liquid) at 0.2–0.4 mL/kg/h *via* a pump, according to the individual intraoperative requirements of each child, and was discontinued 5 min before the end of the operation.

Participants in group B were administered 1% ketamine intravenously for anesthesia.

Observation indicators and detection methods

Heart rate (HR), mean arterial pressure (MAP), and arterial oxygen saturation (SpO_2) at 5 min before anesthesia (T0), 10 min after anesthesia (T1), 20 min after anesthesia (T2), and at the end of surgery (T3) were monitored and compared between the two groups. Serum adrenocorticotropic hormone (ACTH), interleukin-6 (IL-6), cortisol (Cor), emergence agitation score [Paediatric Anesthesia Emergence Delirium Scale (PAED)], and adverse reactions were observed before and after the operation.

The agitation score, which included five indicators (eye contact, purposeful behavior, awareness of the surrounding environment, uneasiness, and consolability), was

recorded upon awakening. The higher the score, the more serious the anesthesia emergence delirium, and a PAED score ≥ 10 indicated restlessness.

Fasting venous blood samples (5 mL) were obtained and centrifuged at 2500 rpm, and the serum was extracted for testing. ACTH, IL-6, and Cor levels were measured using the electrochemiluminescence method. The concentration of IL-6 was measured using an enzyme-linked immunosorbent assay. All reagents were obtained from Nanjing Jiancheng Biological Products Co., Ltd., and strictly used in accordance with the manufacturer's instructions.

The degree of postoperative pain was evaluated using the visual analog scale (10 points indicating the highest level of pain and 0 points indicating the lowest). According to the subjective pain scores of the children, the higher the score, the more serious the pain.

Statistical analysis

The measurement data were expressed as means ± SD, and the comparisons between groups were performed using two independent sample t-tests. The χ^2 test was used for comparison of enumeration data between groups. A $P < 0.05$ indicated a statistically significant difference. All statistical analyses were performed using SPSS software version 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Comparison of hemodynamic indexes of two groups of children

At T0, the HR, MAP and SpO_2 Levels were compared between group A and group B, and the difference was not statistically significant ($P > 0.05$). At T1 and T2, HR and MAP in group A were lower than those in group B ($P < 0.05$) (Table 1).

Comparison of serum ACTH, IL-6 and Cor levels in the two groups of children

Preoperative serum ACTH, IL-6 and Cor levels in group A and group B were compared, and the difference is not statistically significant ($P > 0.05$). The levels of

serum ACTH, IL-6 and Cor in group A were lower than those in group B after operation ($P < 0.05$) (Table 2).

Comparison of the occurrence of restlessness during the wake of the two groups of children

The score of PAED in group A was lower than that in group B ($P < 0.05$). The incidence of dysphoria in group A (23.33%) was lower than that in group B (36.67%) ($P < 0.05$). (Table 3).

Comparison of extubation time, awake time, and out-of-room time between the two groups of children

The extubation time, awake time and leaving room time were compared between group A and group B, and the difference was not statistically significant ($P > 0.05$) (Table 4).

Comparison of postoperative visual analog scale scores between the two groups of children

The visual analog scale scores of group A at 2 h and 8 h after operation were lower than those of group B, and the differences were statistically significant ($P < 0.05$) (Table 5).

Comparison of the incidence of adverse reactions in children between the two groups

The incidence of adverse reactions in group A (6.25%) was lower than that in group B (16.25%) ($P < 0.05$) (Table 6).

DISCUSSION

Abdominal surgery is a common surgical procedure in pediatric patients. Due to their unique anatomical and physiological characteristics and relatively narrow airways, they have an increased risk of airway resistance during surgery. Therefore, pediatric patients consume more oxygen during surgery as they are prone to hypoxia. Moreover, children lack type I muscle fibers in the diaphragm and intercostal muscles; therefore,

respiratory muscle fatigue can easily occur during breathing. Therefore, abdominal surgery is often performed with controlled mechanical breathing[3]. Due to the incomplete development of various physiological functions, imperfect development of the myocardial structure, poor myocardial systolic function, poor ventricular compliance, and thin abdominal walls in children, a series of complications can occur during the operation. Therefore, selecting the most appropriate anesthesia program is extremely important[4,5]. Historically, general anesthesia has been mainly used in pediatric abdominal surgery. General anesthesia can meet the needs of analgesia and sedation in children, and anesthetic equipment facilitates unobstructed breathing, effectively reducing the risk of reflux aspiration during the operation and ensuring the safety of the operation. However, in the process of general anesthesia, children's bodies show obvious stress responses, and hemodynamic fluctuations usually occur. In order to reduce these adverse reactions, anesthesia is deepened by increasing the anesthetic and analgesic drug doses; however, this can lead to liver and kidney dysfunction. Therefore, adverse reactions such as delayed recovery, recovery, and postoperative respiratory depression are prone to occur[6,7]. In addition, it was also reported that general anesthesia could inhibit the cerebral cortex of children and was unable to block the conduction process of surgical nociceptive stimulation towards the sympathetic nerve, evidenced by an increase in the excitability of the sympathetic and adrenal medulla systems and hemodynamic fluctuation. Therefore, effective regulation of stress responses during anesthesia and achievement of good muscle relaxation and analgesia has been an important research topic in anesthesia for pediatric abdominal surgery[8,9].

In this study, propofol combined with lidocaine was used to assist general anesthesia in pediatric abdominal surgery. The role of propofol is to lower the level of consciousness and reduce body movements, as well as other general anesthetic actions in which the release and transmission of neurotransmitters play an important role. Among them, ligand-gated ion channels play an important role in general anesthesia, including γ-aminobutyric acid receptors, an important central nervous system inhibitory neurotransmitter which has a significant regulatory effect on the release of

other neurotransmitters in the body. Propofol can inhibit the influx of ions in the body and inhibit the increased glutamate release caused by presynaptic membrane depolarization, which enhances the postsynaptic effect of γ-aminobutyric acid. Its role in respiratory smooth muscle function and the cardiovascular system is mediated by calcium channels. The decreased sodium-potassium-ATPase activity in the central nervous systems of children results in decreased electrochemical gradients caused by sodium ions and increased calcium ion concentration, which leads to increased acetylcholine content in the body, resulting in general anesthesia[10,11]. However, the required dose of propofol alone is high, and the analgesic effect is only observed in some children. Adverse reactions, including myocardial inhibition and blood pressure reduction can also occur[12].

Lidocaine, an amide-type local anesthetic, can be dispersed outside the blood vessels after entering human blood. The drug can react with hepatic microsomal mixed functional oxidase, an amide enzyme, and can be metabolized in multiple organs. The study also found that lidocaine used in anesthesia can inhibit human hippocampal neuronal sodium channels, thereby inhibiting central nervous system action potential, blocking nerve conduction, and causing a central inhibitory and anesthetic effect[13]. The combined use of these two anesthetics has an important synergistic effect because propofol acts directly on the blood vessel walls to release pain mediators. Meanwhile lidocaine acts as a kinin inhibitor and stabilizer by blocking and thereby reducing the release of pain mediators[14]. The combined application of lidocaine and ketamine can enhance the sedative and hypnotic effect of propofol. Lidocaine inhibits propofol from binding to protein, which increases the amount of free propofol in the body and enhances the anesthetic effect of propofol. In addition, lidocaine can promote the recovery of sodium-potassium-ATPase activity in the sarcoplasmic reticulum, inhibit the overload of calcium ions, and reduce myocardial ischemia-reperfusion injury in children. When used together, the advantages of these two drugs complement each other, making it ideal for the application of surgical anesthesia[15].

Studies have shown that the levels of adrenocorticotropic hormone and cortisol in the body increase after the activation of the hypothalamic-pituitary-adrenal cortex axis in the perioperative period, which plays a role in promoting gluconeogenesis, proteolysis, and inhibiting inflammatory responses in the body. Cytokines are biologically active peptide compounds released by human immune effector cells, among which IL-6 is an important inflammatory response factor in the human body and has a regulatory effect on systemic inflammatory and immune responses. Cytokines increase significantly and then gradually decrease with decreased stress responses. The incidence of adverse reactions in group A was 6.25% lower than that in group B (16.25%), indicating that the application of propofol combined with lidocaine-assisted ketamine in pediatric abdominal surgery anesthesia can reduce the occurrence of adverse reactions to anesthesia. The advantage of this study is that our findings confirm the anesthesia effect and safety of propofol combined with lidocaine-assisted ketamine in pediatric abdominal surgery anesthesia, and provide a basis for identifying the optimal anesthesia plan for clinical pediatric abdominal surgery. Due to the limited number of children, prospective studies have not been carried out, and the follow-up time was short; therefore, multi-center studies with large sample sizes and randomized controlled trials are needed to validate our results.

CONCLUSION

In summary, the anesthetic effect of propofol combined with lidocaine-assisted ketamine for pediatric anesthesia was better than that of ketamine alone, with less influence on hemodynamics and pediatric stress response indices, lower incidence of restlessness during the recovery period, and lower incidence of adverse reactions.

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Table 1 Comparison of hemodynamic indexes of two groups of children (mean ± SD)

Groups	T0	T1	T2	T3
HR (times/min)				
A group	113.6 ± 8.2	120.5 ± 8.0	118.9 ± 7.5	115.5 ± 8.4
B group	115.0 ± 9.0	126.1 ± 7.4	125.0 ± 8.3	116.8 ± 8.0
F value	*F1* = 13.025, *F2* = 15.776, *F3* = 8.169			

P value	*P*1 = 0.000, *P*2 = 0.000, *P*3 = 0.000			
MAP (mmHg)				
A group	85.2 ± 6.9	92.7 ± 5.5	92.0 ± 5.9	87.0 ± 5.3
B group	84.8 ± 6.5	96.0 ± 6.2	95.1 ± 6.8	89.1 ± 6.5
F value	*F*1 = 9.881, *F*2 = 13.764, *F*3 = 6.990			
P value	*P*1 = 0.000, *P*2 = 0.000, *P*3 = 0.000			
SpO$_2$ (%)				
A group	98.2 ± 0.6	97.7 ± 0.7	97.8 ± 0.6	98.0 ± 0.5
B group	98.3 ± 0.7	97.6 ± 0.6	97.9 ± 0.8	97.8 ± 0.7
F value	*F*1 = 2.514, *F*2 = 6.395, *F*3 = 1.552			
P value	*P*1 = 0.168, *P*2 = 0.000, *P*3 = 0.351			

*F*1 and *P*1 are between groups, *F*2 and *P*2 are time effect, *F*3 and *P*3 are interaction. HR: Heart rate; MAP: mean arterial pressure; SpO$_2$: Arterial oxygen saturation.

Table 2 Comparison of serum adrenocorticotropic hormone, interleukin-6, and cortisol levels in two groups of children (mean ± SD)

Groups	ACTH (ng/L)		IL-6 (ng/L)		Cor (nmol/L)	
	Preoperative	12 h after operation	Preoperative	12 h after operation	Preoperative	12 h after operation
A group (*n* = 60)	116.3 ± 15.7	130.2 ± 18.2	5.77 ± 2.01	12.41 ± 4.29	24.18 ± 4.26	36.80 ± 6.90
B group (*n* = 60)	114.7 ± 13.5	145.0 ± 22.1	6.03 ± 2.28	18.15 ± 5.88	25.04 ± 5.51	53.36 ± 8.15
t value	0.599	-4.004	-0.663	-6.109	-0.956	-12.012
P value	0.551	0.000	0.509	0.000	0.341	0.000

ACTH: Adrenocorticotropic hormone; IL-6: Interleukin-6; Cor: Cortisol.

Table 3 Comparison of the occurrence of restlessness in the two groups of children during the waking period

Groups	PAED score (points)	Incidence of restlessness, n (%)
A group (n = 60)	6.2 ± 2.5	14 (23.33)
B group (n = 60)	8.1 ± 2.9	22 (36.67)
t/χ^2 value	-3.844	4.104
P value	0.000	0.043

PAED: Paediatric Anesthesia Emergence Delirium Scale.

Table 4 Comparison of extubation time, awake time, and out-of-room time between the two groups (mean ± SD)

Groups	Pull-out time (min)	Wake time (min)	Off room time (min)
A group (n = 60)	7.66 ± 1.84	10.59 ± 2.30	22.63 ± 3.81
B group (n = 60)	8.01 ± 1.92	11.36 ± 2.45	23.70 ± 3.54
t value	-1.019	-1.775	-1.594
P value	0.310	0.078	0.114

Table 5 Comparison of postoperative visual analog scale scores between two groups of children (mean ± SD)

Groups	2 h after operation	8 h after operation	12 h after operation	24 h after operation
A group (n = 60)	2.77 ± 0.64	3.38 ± 0.61	3.41 ± 0.74	2.18 ± 0.50
B group (n = 60)	3.10 ± 0.61	3.76 ± 0.74	3.60 ± 0.82	2.34 ± 0.58
t value	-2.891	-3.069	-1.332	-1.618
P value	0.005	0.003	0.185	0.108

Table 6 Comparison of the incidence of adverse reactions between the two groups, n (%)

Group	Feel sick and vomit	Tongue drop	Lethargy	Adverse reactions
A group (n = 60)	3	1	1	5 (6.25)
B group (n = 60)	7	3	3	13 (16.25)
χ^2 value				4.183
P value				0.041

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