Efficacy and safety of propofol in preventing emergence agitation after sevoflurane anesthesia for children

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Abstract. Application of propofol in preventing emergence agitation after sevoflurane anesthesia in children was evaluated. Clinical data of 200 children who received sevoflurane anesthesia in Children's Hospital of Xuzhou Medical University were retrospectively analyzed. Among them, 120 patients who received inhaled sevoflurane for pediatric anesthesia and intravenous infusion of propofol (2 mg/kg) were included in observation group. The remaining 80 cases who were directly anesthetized by sevoflurane alone were the control group. T PAED scores, modified Aldrete scores, extubation time, PACU time and adverse reactions (gastrointestinal tract and respiratory response) were analyzed and compared between the control and observation group. PAED scores, extubation time, PACU time and incidence of adverse reactions were significantly lower in observation than in control group, and the modified Aldrete scores were higher in observation than in control group ($P<0.05$). Spearman 's correlation analysis showed that the PAED scores were negatively correlated with modified Aldrete scores and positively correlated with extubation time. There was positive correlation between the PACU time and incidence of adverse reactions and between the PAED scores and extubation time. There was negative correlation between PACU time and incidence of adverse reactions and between Aldrete scores and extubation time ($P<0.05$). Therefore, we conclude that propofol can be used to prevent agitation after sevoflurane anesthesia in children.

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Introduction

Anatomical and physiological functions of children change rapidly, and is different from adults. Therefore, physiological characteristics of children should be carefully considered for the determination of anaesthesia dosage, methods and equipment. In addition, drug metabolism should also be considered (1,2). Sevoflurane as a volatile colorless halide is commonly used for the induction and maintenance of general anaesthesia through inhalation (3). Sevoflurane is a commonly used drug for pediatric anesthesia. Sevoflurane has the advantages of quick recovery, low distribution coefficient and less damage to respiratory system (4). However, sevoflurane also causes restless reaction and unstable mood (5), leading to the increased difficulties in post-operation care (6). Propofol (7) is a new type of short-acting intravenous anesthetic. It is commonly used in the induction and maintenance of general anesthesia. Propofol has a sedative effect and is often used with other narcotic drugs (8). In this study, the application of propofol in the prevention of agitation after sevoflurane anesthesia in children was evaluated. Our study provided guidance for the use of propofol in the prevention of agitation in children.

Patients and methods

Clinical data of children. Pediatric patients who received treatment in Children's Hospital of Xuzhou Medical University (Xuzhou, China) from December 2016 to March 2018 were included. Clinical data, agitation index, anaesthesia recovery index, extubation time and PACU time were analyzed. Among those patients, 120 patients who received inhaled sevoflurane for pediatric anesthesia and intravenous infusion of propofol (2 mg/kg) were included in observation group. The remaining 80 patients who were directly anesthetized by sevoflurane alone were included in the control group. Pediatric Anesthesia Emergence Delirium (PAED), Aldrete scores, extubation time, PACU time and adverse reaction (gastrointestinal tract reaction) were compared between observation and control group, and PAED scores and Aldrete scores were recorded.

The present study was approved by the Ethics Committee of Children's Hospital of Xuzhou Medical University. Signed

Table I. The standard for modified Aldrete scores.

Items	Standards	Scores
Movement	Moving arms and legs and head spontaneously or by request	2
	Moving arms or legs spontaneously or by request; restrictedly raising head spontaneously or by request	1
	Not able to move limbs or raise head	0
Breathing	Deep breathing and effective coughing, normal respiratory rate and amplitude	2
	Breathing is difficult or restricted, but spontaneous breathing is shallow and slow, and it is possible to breath through oropharyngeal airway	1
	Breathing is paused or weak, it requires respirator therapy or assisted breathing	0
Blood pressure	Within ±20% before anesthesia	2
	±20-49% before anesthesia	1
	Above ±50% before anesthesia	0
Consciousness	Completely awakening, answer questions accurately	2
	Able to wake up, drowsiness	1
	No reaction	0
SpO_2	Air breathing SpO_2 >92%	2
	Oxygen breathing SpO_2 >92%	1
	Oxygen breathing SpO_2 <92%	0

written informed consents were obtained from the parents of the child patients.

Inclusion and exclusion criteria. Inclusion criteria were: Patients who signed informed consent forms; who treated with ligation of inguinal hernia; without other severe diseases and with normal height, and weight. All patients were in American Society of Anesthesiologists (ASA) rate class I-II.

Exclusion criteria were: Patients combined with serious heart disease; with liver and kidney dysfunction; with dementia or mental disorders; allergic to propofol or sevoflurane and other drugs used in this study.

Materials and drugs. Atropine (national medicine permission no. H50020044, Southwest Pharmaceutical Co., Ltd., Chongqing, China); sevoflurane (national medicine permission no. H20080681, Nonan Bate Pharmaceuticals Co., Ltd., Linyi, China); dexamethasone 0.3 mg/kg (national medicine permission no. H41020056, Zhengzhou Zhuo Feng Pharmaceutical Co., Ltd., Zhengzhou, China); sodium chloride 0.9% (national medicine permission no. H37021756, Shandong Lu Chen Xin Pharmaceutical Co., Ltd., Shandong, China); propofol (national medicine permission no. H20051842, Guangdong Gabor Pharmaceutical Co., Ltd.); anesthesia monitor (General Electric Company, Boston, MA, USA).

Anaesthesia for different groups. Both groups of patients were not allowed to drink water 6 h before operation, and were not allowed to eat 4 h before operation. Intramuscular injection of atropine (0.01 mg/kg) was performed 30 min before operation. By setting a venous trocar, 4 ml dexamethasone (0.3 mg/kg) sodium chloride (0.9%) solution were injected through the indwelling needle. An anaesthesia monitor was used to monitor the vital signs of the children.

Intraoperative anesthesia: General anesthesia was performed with mask inhalation. Sevoflurane (8%) was first used to induce anaesthesia and the reactions of children's eyelashes and spontaneous breathing were observed. When there was no reaction of eyelashes but spontaneous breathing was maintained, the concentration of sevoflurane was reduced to 3-4% (adjusted according to the depth of the anaesthesia). Oxygen inhalation was kept at a speed of 2 l/min, and anesthesia was maintained until 5 min before the end of operation.

Post-operative treatment: Oxygen inhalation speed was raised to 6 l/min. Patients in observation group were intravenously injected with 2 mg/kg propofol, while patients in control group received intravenous drip of 0.1 ml/kg of normal saline. Monitoring blood pressure and other indexes of children was performed. After vital signs returned to normal, children were sent back to the ward.

PAED scores. PAED (9) mainly evaluates the conditions through 3 aspects: i) Whether they have eye contact with other people, ii) whether they can perceive changes in surrounding environment, and iii) whether they can dominate their own activities. The 3 items are reversely rated according to the severity, 4 points for none, 3 points for poor activity, 2 points for fair activity, 1 point for good activity and 0 point for excellent activity. The total scores is 20 points, the higher the scores is, the more serious the restlessness is; 11-15 points are evaluated as restlessness, and more than 15 points are evaluated as severe agitation.

Modified Aldrete scores. Modified Aldrete scoring (10) were performed according to the standard shown in Table I. The total score is 10. Higher scores indicate better awakening situation. Patients with scores >9 points were extubated. Patients

Table II. General information on patients.

Clinical features	Observation group (n=120)	Control group (n=80)	χ^2/t	P-value
Age (years)	5.86±1.87	5.78±1.72	0.31	0.76
Operation time (h)	1.76±0.46	1.82±0.51	0.85	0.40
Weight (kg)	15.52±1.65	15.78±1.74	1.06	0.29
Sex (n, %)			0.65	0.42
Male	64 (53.33)	38 (47.50)		
Female	56 (46.67)	42 (52.50)		
ASA classification			0.16	0.69
I	62 (51.67)	39 (48.75)		
II	58 (48.33)	41 (51.25)		
HR (times/min)	107.14±7.25	105.21±8.93	1.61	0.11
SBP (mmHg)	98.24±6.24	96.88±7.45	1.35	0.18
DBP (mmHg)	76.24±6.68	77.42±5.67	1.34	0.18

were monitored in recovery room for 15 min and were sent back to ICU if no abnormal conditions were observed.

Other observation indexes. Extubation time, time period from the end of the operation to the extubation; PACU time, from the time of the operation to the time of stay in the recovery room. Incidence of adverse reactions: Adverse reactions include mental stress, nausea and vomiting, gastrointestinal reactions, hypotension and arrhythmia.

Statistic analysis. The scoring results, extubation time, PACU time and other measurement data were recorded as mean ± standard deviation and compared by t-test. Incidence of adverse reactions was tested by χ^2. Correlation between PAED scores/modified Aldrete scores and extubation time/PACU time/incidence of adverse reactions was analyzed by Spearman 's correlation coefficient. The significant level of the test was α=0.05.

Results

Comparison of general data between two groups. There was no significant difference in age, weight, sex, operation time and classification of ASA between observation and control group (P>0.05) (Table II).

Comparison of PAED scores between observation and control group. Mean PAED score of the control group was 9.87±3.15, and mean PAED score of the observation group was 5.66±1.74. PAED score of the observation group were significantly lower in observation group than those in control group (P<0.01; Fig. 1).

Comparison of modified Aldrete scores between observation group and control group. Mean modified Aldrete scores of the observation group was 7.91±2.14, which was significantly higher than that in control group (5.41±1.22) (P<0.01; Fig. 2).

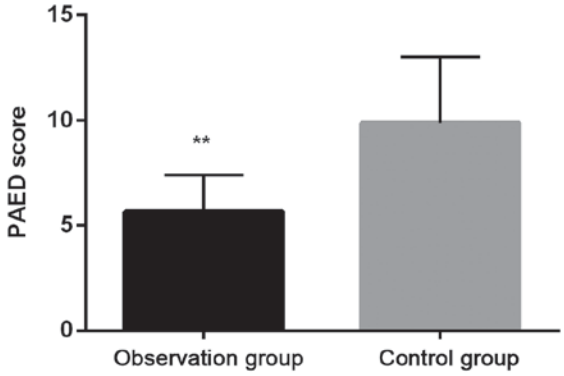

Figure 1. Comparison of PAED scores between observation group and control group. Mean PAED score of observation group in the recovery room was 5.66+1.74, and mean PAED score of control group was 9.87+3.15. Mean PAED score of observation group was significantly lower than that in control group (P<0.01). **P<0.01. PAED, Pediatric Anesthesia Emergence Delirium.

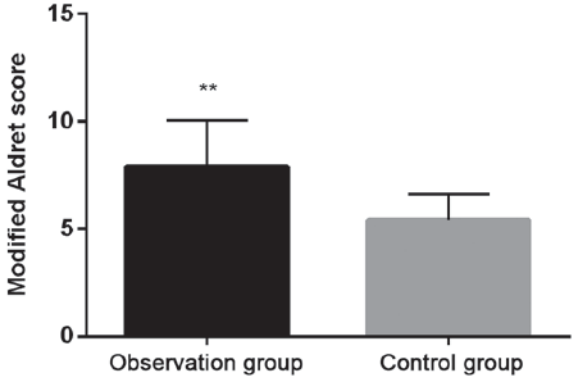

Figure 2. Comparison of the modified Aldret scores between the observation group and the control group. Mean modified Aldret score of observation group was 7.91+2.14, which was significantly higher than that in control group (5.41+1.22; P<0.01). **P<0.01.

Table III. Comparison of extubation time, PACU time and incidence of adverse reactions among patients.

Items	Observation group (n=120)	Control group (n=80)	χ^2/t	P-value
Extubation time (min)	11.35±3.17	21.41±4.62	16.99	<0.001
PACU time (min)	46.57±7.43	49.23±8.22	2.33	0.02
The incidence of adverse reactions (n, %)	6 (5.00)	11 (13.75)	6.52	0.03

Comparison of extubation time, PACU time and incidence of adverse reactions in each group. Mean extubation time of observation group was 11.35±3.17 min, which was significantly lower than that of control group (21.41±4.62 min). PACU time of observation group was 46.57±7.43 min, which was significantly lower than that in control group (49.23±8.22 min). Incidence of adverse reactions in observation group was 5.00%, which was also significantly lower than that in control group (13.75%; P<05) (Table III).

Table IV. Value r for analysis of each correlation.

Items	PAED scores	Modified Aldrete scores
Extubation time	0.774	-0.821
PACU time	0.689	-0.769
Incidence of adverse reactions	0.433	-0.524

Spearman correlation analysis results. PAED scores were positively correlated with extubation time, PACU time and incidence of adverse reactions (r=0.774, 0.689, 0.433). Modified Aldret scores were negatively correlated with PACU time and incidence of adverse reactions (r= - 0.821, - 0.769, - 0.524) (all P<0.05) (Table IV).

Discussion

The physiological conditions and premature immune system should be taken into consideration in the selection of narcotic drugs, dosages and methods for pediatric anesthesia (10,11). Dosage of sevoflurane used for pediatric anesthesia is low, the damage to respiratory system is small and the recovery is rapid. However, the use of sevoflurane also causes restless reaction. Restless reaction will affect surgical operations and threaten children's life (12,13). Propofol has a sedative effect and can potentially alleviate the restlessness of children after sevoflurane anesthesia (1,14). In this study, the application of propofol in the prevention of agitation after sevoflurane anesthesia in children was evaluated to provide guidance for the use of propofol for the prevention of agitation.

PAED scores, extubation time, PACU time and incidence of adverse reactions in observation group were significantly lower than those in control group, and modified Aldrete scores of observation group were higher than those in control group. PAED scores was positively correlated with extubation time, PACU time and incidence of adverse reactions. Aldrete scores were negatively correlated with extubation time, PACU time and incidence of adverse reactions (P<0.05). It indicates that propofol can reduce the agitation reaction of children after sevoflurane anesthesia, shorten the extubation time, PACU time and reduce the incidence of adverse reactions. Liang *et al* (12) reported that propofol combined with general anesthesia reduced the intubation time and incidence of adverse reactions, which was consistent with the findings in our study. Meta analysis by Kanaya *et al* (15) revealed that propofol can indeed reduce the incidence of restlessness after general anesthesia in children. Picard *et al* (16) showed that the use of propofol in sevoflurane anaesthesia decreased the PAED scores and reduced the reaction of agitation. Rosen *et al* (17) studied the prophylactic effect of propofol on children's restlessness after sevoflurane anesthesia. It was found that PAED scores were significantly reduced after using propofol. Propofol at 1 mg/kg delayed recovery and prolonged extubation time, which was different from the findings in our study. In the case of propofol administration, intravenous inhalation of propofol can be performed after sevoflurane or intravenous infusion of propofol can be performed during sevoflurane inhalation anesthesia (12,16). Similar to our study, intravenous infusion of propofol was given after sevoflurane inhalation anesthesia in other studies (18). Costi *et al* (19) believe that intravenous infusion of propofol at the end of sevoflurane anesthesia is not as effective in reducing the rate of inflammatory response as propofol is infused throughout the anesthesia maintenance process, but administration is more complicated. Therefore, the administration time of propofol and sevoflurane, and the mode of administration (whether the two are administered simultaneously or continuously) may affect the anesthetic effect and recovery. Our future studies will explore the potential effects. PAED score and the Aldrete score are dynamic. The PAED score and the Aldrete score may change over time. Therefore, it is recommended to perform the scoring at different time-points. In conclusion, propofol can present agitation reaction of children after sevoflurane anesthesia.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

XW drafted the manuscript. XW and JunhuaC were mainly devoted to collecting and interpreting the general data of patients. CS and BP recorded and analyzed PAED scores. RZ, JunliC and FZ were responsible for observation index analysis. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Children's Hospital of Xuzhou Medical University (Xuzhou, China). Signed written informed consents were obtained from the parents of the child patients.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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