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Original Article

Anesthetic effect of propofol combined with remifentanil and propofol combined with ketamine in ophthalmic surgery

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Abstract: Propofol combined with ketamine has been used for anesthesia in the past. Remifentanil presented a good analgesic effect, rapid onset, short half-life, and a high clearance rate. Propofol combined with remifentanil also shows good effects in the clinic. This study compared the effect and safety of propofol combined remifentanil and propofol combined ketamine in pediatric eye surgery. Pediatric patients that received eye surgery in our hospital were selected and randomly divided into two groups, the experimental group (n=30), in which patients received propofol combined with remifentanil anesthesia and control group (n=30), and the group receiving propofol combined with ketamine anesthesia. The curative effect, FCO_2, SPO_2, MAP, HR, anesthesia complications, operation time, recovery time, and leaving PACU time were compared. The rate of good anesthesia was 93.33% in the experimental group, which was significantly higher than control ($P < 0.05$). FCO_2 at 2 and 5 minutes after anesthesia, preoperative, intraoperative, and postoperative elevated, while SPO_2, MAP, and HR decreased ($P < 0.05$). The experimental group showed smaller fluctuation range than the control. The rate of Nausea (6.67%), vomiting (3.33%), and somnolence (10%) in the experimental group was significantly lower than control ($P < 0.05$). Experimental group presented significantly shorter recovery time and leaving PACU time than control ($P < 0.05$). Propofol combined with remifentanil shows good effect in patients' eye surgery including steady hemodynamics and lower adverse reaction, suggesting they might be used in clinic.

Keywords: Propofol, remifentanil, ketamine, ophthalmology

Introduction

Pediatric patients are special in surgery including poor self-control and low pain tolerance. Though eye surgery has advantages of small operation scope, short operation time, and few requirements of muscle relaxation, there is a high requirement on the depth of anesthesia due to the complexity of anatomical position and children's hyperactivity. The depth needs to be appropriate so that body dynamic response or excessive anesthesia may not produce a series of complications [1]. Propofol combined with ketamine is most commonly used in clinic, whereas, ketamine shows poor analgesic effect. Pediatric patients were short of self-control ability and lacked of tolerance for pain, and often appeared to have a stress reaction and dynamic response. Ketamine or propofol often need additional dosage in the surgery to maintain the operation smoothly. For young pediatric patients, high anesthetic concentration may cause MAP and HR unstable, recovery time elongation, and different types of adverse reaction [2, 3]. It has been reported that propofol combined with remifentanil showed rapid onset, strong analgesic effect, fast recovery, and safe airway in the surgery [4]. This study intended to compare the effect of propofol combined remifentanil with propofol combined ketamine in pediatric eye surgery.

Materials and methods

General information

Sixty cases of children patients that received eye surgery in First Affiliated Hospital of

Table 1. General information

Group	Cases	Age (y)	Weight (kg)	Anesthesia time (min)	Extubation time (min)
Experimental group	30	10.7 ± 2.2	21.8 ± 1.5	32.42 ± 7.05	9.13 ± 4.75
Control	30	11.6 ± 1.9	22.1 ± 1.2	31.86 ± 6.59	8.25 ± 4.13

The difference showed no statistical significance, P > 0.05.

Table 2. Anesthetic effect

Group	Cases	Excellent	Fine	Bad	Good rate
Experiment group	30	22 (73.33)	6 (20)	2 (6.67)	28 (93.33)
Control	30	9 (53.33)	3 (33.33)	18 (13.33)	12 (40)
Chi square		11.279	1.176	19.2	19.2
P		< 0.001	0.278	< 0.001	< 0.001

Soochow University between January 2014 and January 2015 were retrospectively enrolled. There were 31 males and 29 females with average age at 11.2 ± 1.2 years old (1-14). Of these, 32 patients received vitreous retinal surgery, while 28 patients received frontal muscle suspension. ASA was at grade I~II. No other body abnormal was observed. Patients' gender, age, and weight showed no significant difference (P > 0.05) (**Table 1**).

The children were randomly divided into two groups, including 30 cases in the experimental group that received propofol combined with remifentanil anesthesia and 30 cases in the control group who received propofol combined with ketamine anesthesia.

Inclusion criteria: patient's age ≥ 1 year old; tracheal intubation.

Exclusion criteria: congenital nerve; mental disease history; severe MODS; multiple organ dysfunction; physical changes in cerebral function.

Methods

Detecting depth of anesthesia

Monitoring electrocardiogram, blood pressure, blood oxygen saturation, breathing rate, and PCO_2 routinely.

Anesthesia method

Experimental group: propofol combined with remifentanil. Propofol (Sichuan Guorui Pharmaceutical co., LTD) was intravenous injected at 4 mg/kg/h, while remifentanil (Yichang Renfu Pharmaceutical co., LTD) was intravenous injected at 3 μg/kg /h. The children were monitored after drug injection, and endotracheal intubated after body dynamic response disappeared. Regular mechanical ventilation was applied to guarantee the oxygen flow rate.

Control group: propofol combined with ketamine. Propofol was intravenous injected at 4 mg/kg/h, while ketamine (Zhejiang Jiuxu Pharmaceutical co., LTD) was intramuscular injected at 5 mg/kg. The children were monitored after drug injection, and received mask oxygen-inspiration at 3 L/min. During the surgery, propofol was continuously intravenous administrated at 7 mg/kg/min.

Observation index

FCO_2, SpO_2, MAP, and HR were observed at different time including 2 minutes after anesthesia, 5 minutes after anesthesia, preoperative, intraoperative, and postoperative.

Adverse reaction including nausea, vomit, conscious, and somnolence was observed to calculate the incidence.

Recovery time and leaving PACU time were compared.

Criteria of evaluation

Anesthesia effect in two groups was graded [5]: Excellent, no body dynamic response; fine, appear body dynamic response but not affect operation; bad, severe dynamic response and the operation cannot be performed smoothly.

Modified Aldrete score [6]: respiratory tract: 2 points, crying; 1 point, airway obstructed; 0 point, need keeping airway unobstructed. Vital signs: 2 points, stability; 1 point, lack of stability; 0 point: instability. Limb exercise: 2 points, correct autonomic activity; 1 point, independent activities with mistake and no purpose; 0 point, activity. Awareness: 2 points, awake; 1 point, only after the stimulation; 0 point, no

Table 3. FCO_2, SPO_2, MAP, and HR comparison in different times

Group	Cases	FCO_2 (%)	SPO_2 (%)	MAP (KPa)	HR (beats/min)
Before anesthesia					
Experimental group		4.4 ± 1.9	95.1 ± 11.2	14.9 ± 0.7	82.1 ± 12.1
Control		4.6 ± 2.1	94.3 ± 10.1	15.1 ± 0.8	84.2 ± 13.5
2 min after anesthesia					
Experimental group		5.8 ± 1.6*,#	78.6 ± 9.2*,#	13.9 ± 0.8*,#	69.5 ± 9.8*,#
Control		5.1 ± 1.2	78.2 ± 10.2	13.7 ± 1.3	71.5 ± 11.3
5 min after anesthesia					
Experimental group		5.5 ± 1.1*,#	74.1 ± 9.1*,#	11.2 ± 0.8*,#	76.5 ± 11.1*,#
Control		4.8 ± 1.9	78.1 ± 9.4	13.4 ± 1.2	74.7 ± 11.4
Before surgery					
Experimental group		4.9 ± 1.5	74.5 ± 8.6	11.2 ± 0.5	69.3 ± 9.1
Control		4.7 ± 1.6	75.2 ± 8.4	11.4 ± 0.2	70.1 ± 9.4
During surgery					
Experimental group		5.8 ± 1.6*,#	78.6 ± 9.2*,#	13.9 ± 0.8*,#	70.5 ± 9.8*,#
Control		5.1 ± 1.2	78.2 ± 10.2	13.7 ± 1.3	71.5 ± 11.3
After surgery					
Experimental group		4.7 ± 1.6*,#	79.3 ± 7.8*,#	15.1 ± 0.9*,#	72.3 ± 8.7*,#
Control		4.7 ± 1.3	78.5 ± 7.1	14.7 ± 1.2	73.6 ± 8.9

*P < 0.05, compared with before anesthesia; #P < 0.05, compared with control.

Table 4. Complications

Group	Cases	Nausea	Vomit	Sober	Somnolence	Incidence
Experimental group	30	2 (6.67)	1 (3.33)	1 (3.33)	3 (10)	7 (23.33)
Control	30	8 (26.67)	7 (23.33)	3 (10)	7 (20)	25 (83.33)
Chi square		4.32	5.192	1.071	1.92	21.696
P		0.037	0.022	0.301	0.165	0

response after intense stimulation. SpO_2: 2 points, $SpO_2 > 95\%$; 1 point, $90\% < SpO_2 < 94\%$; 0 point, $SpO_2 < 90$.

Data analysis

All statistical analyses were performed using SPSS17.0 software (Chicago, IL). Numerical data are presented as means ± standard deviation (SD). Differences between two groups were analyzed by student t-test and Comparison of difference among two groups at different time points were assessed by two-way ANOVA. Enumeration data were compared by Chi-square test. P < 0.05 was considered as significant difference.

Results

Higher anesthetic effect of propofol combined with remifentanil

Comparing the anesthetic effect in two groups, it was found that the rate of good anesthesia was 93.33% in experimental group, which was significantly higher than that in the control group (P < 0.001) (**Table 2**).

Increased FCO_2 and decreased SPO_2, MAP, and HR after anesthesia

No significant differences were found in FCO_2, SPO_2, MAP, and HR before anesthesia (P > 0.05). However, FCO_2 at 2 minutes and 5 minutes after anesthesia increased significantly, while SPO_2, MAP, and HR decreased markedly (P < 0.05). The experimental group showed a smaller fluctuation range than the control group (P < 0.05).

FCO_2, SPO_2, MAP, and HR showed no statistical differences before surgery between the experimental group and control (P > 0.05). They elevated gradually during surgery and recovered after surgery in both of two groups (P < 0.05) (**Table 3**).

Complications

The rate of Nausea rate (6.67%), vomiting (3.33%) and somnolence (10%) in the experi-

Table 5. Recovery time and leaving PACU time

Group	Cases	Recovery time (min)	Leaving PACU time (min)
Experimental group	30	12.42 ± 5.33*	20.73 ± 5.84*
Control	30	17.63 ± 6.67	26.97 ± 5.98
t		3.342	4.089
P		0.0015	0.0001

mental group was significantly lower than those in the control group ($P < 0.05$) (**Table 4**).

Shorter surgery time, recovery time, and leaving PACU time of propofol combined with remifentanil

Recovery time and leaving PACU time in the experimental group were 12.42 ± 5.33 and 20.73 ± 5.84 min, respectively. Whereas they were 17.63 ± 6.67 and 26.97 ± 5.98 min in the control group. The experimental group presented a shorter time than the control group ($P < 0.01$) (**Table 5**).

Discussion

Pediatric eye surgery has its own characteristic that is different from other pediatric surgeries. Pediatric eye surgery presents limited operation range, but the eye anatomy is very complicated. Therefore, it needs precision manipulation. Although the operation time is shorter than others, children's poor self-control and hyperactivity often affects the surgical process. Pediatric ophthalmology preoperative anesthesia has to ensure the child under sedation and analgesia state with no dynamic response during the surgery. In addition, muscle looseness should be controlled to guarantee the eyeball is fixed well and is easy to operate [7, 8].

Currently, many kinds of anesthetic drugs are used in pediatric small surgery, such as propofol, ketamine, and remifentanil, etc. Of which propofol belongs to short-acting intravenous anesthesia drug that is characterized as rapid onset, short effect time, strong sedative and analgesic effect, not easy waking up during anesthesia, and recover fast after surgery. At the same time, propofol can inhibit the cough reflex and the dopamine receptor to stop vomiting. The largest drawback of propofol is-dosage-dependent cardiopulmonary inhibition, and its inhibition degree is positively correlated with the injection rate. Propofol-induced arterial pressure and peripheral resistance decline is more apparent compared with thiopental. Furthermore, local pain may appear during the propofol induction period that may cause limb movement in children [9, 10]. As one of the common pediatric anesthetic drugs, ketamine not only has sedative and analgesic effect, but also plays a role in anesthesia. It impacts on the respiratory cycle slightly, but may cause excessive sympathetic nerve excitement, leading to blood pressure elevation, heart rate acceleration, intraoperative agitation, and involuntary dynamic response that affect operation safety [11]. Repeat additional ketamine in the surgery is easy to increase the adverse reactions and extend postoperative recovery time [12]. Remifentanil is a new type of narcotic analgesics belonging to μ receptor agonist. It is featured as fast onset, short action time, short half-life, and high clearance. In addition, its half-life is not related to dosage and input time. It is mainly metabolized by plasma and tissue non-specific esterase, and the clearance rate does not rely on liver and kidney function, age, gender, or weight [13, 14].

In this study, eye surgery patients in our hospital and applied two different anesthesia metods to compare their good rate, FCO_2, SPO_2, MAP, and HR value changes before anesthesia, aftane thesia, before surgery, during surgery, and after surgery, perioperative adverse reation, operation time, recovery time, and leaving PACU time. It was found that the rate of good anesthesia was 93.33% in the experimental group. FCO_2 at 2 and 5 minutes after anesthesia increased significantly, while SPO_2, MAP, and HR decreased markedly. The experimental group showed smaller fluctuation range than the control group, suggesting that propofol combined with remifentanil showed good anesthetic effect and high stability. Research revealed that remifentanil combined with propofol had good effect in pediatric surgery by inhibiting endotracheal intubation stress, maintaining appropriate depth of anesthesia, and reducing the incidence of complications caused by different kind of narcotic drugs [15, 16].

Anesthetic complications comparison showed that nausea rate was 6.67%, vomiting rate was 3.33%, and somnolence rate was 10% in the experimental group that was significantly lower than the control group. It indicated that propofol combined with remifentanil has high safety and few adverse reactions. The experimental group presented significantly shorter operation time, recovery time, and leaving PACU time than the control group. Studies discovered that ketamine will increase oral secretion amount in the operation process, which is easy to cause choking cough and infection. At this time, endotracheal intubation is needed to avoid choking cough and reduce the possibility of postoperative pulmonary infection. Unreasonable anesthetic choice or unsuitable dose used is easy to cause postoperative nausea and vomiting, and even emergence of agitation. Pediatric eye surgery not only needs to maintain stable intraocular pressure, but also narcotic drugs choice and dose control [17]. Propofol combined with remifentanil showed less vomit, nausea, and emergence of agitation incidence in pediatric eye surgery. Propofol intravenous injection not only can stop vomiting, but also can prohibit intraocular pressure elevation caused by anesthesia intubation. Remifentanil plays a role in both anesthesia and analgesia, which can reduce the fluctuation of hemodynamic parameters and even emergence agitation to a certain extent [18]. Literature and clinical practice showed that ketamine and remifentanil sequencing combined with propofol can give full play to their respective advantages characterized by smooth induction, no injection pain, good analgesia, less respiratory depression, stable hemodynamics, fewer stress response, and fast recovery [19, 20].

In conclusion, propofol combined with remifentanil is worth to be widely applied in pediatric eye surgery due to simple manipulation, safe and effective, small stimulation to airway, less oral secretion, stable hemodynamics, fewer adverse reactions, and fast recovery.

Disclosure of conflict of interest

None.

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