·Clinical Research·

Effects of propofol *versus* urapidil on perioperative hemodynamics and intraocular pressure during anesthesia and extubation in ophthalmic patients

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Abstract

• AIM: To compare the effect of propofol versus urapidil on hemodynamics and intraocular pressure during anesthesia and extubation for ophthalmic patients.

• METHODS: Eighty-two surgical patients (Class: ASA I-Ⅱ) were randomly assigned to propofol (n=41) and urapidil groups (n=41). Their gender, age, body mass, operation time and dosage of anesthetics had no significant difference between the two groups (P>0.05). The patients of propofol and urapidil groups were given propofol (1.5mg/kg) and urapidil (2.5mg/kg) respectively; and two drugs were all diluted with normal saline to 8mL. Then the drugs were given to patients by slow intravenous injection. After treatment, the patients were conducted immediate suction, tracheal extubation, and then patients wore oxygen masks for 10 minutes. By double-blind methods, before the induction medication, at the suction, and 5, 10 minutes after the extubation, we recorded the systolic and diastolic blood pressure (BP), heart rate (HR), pH, PaO_2, $PaCO_2$, SaO_2 and intraocular pressure (IOP) respectively. The complete recovery time of the patients with restlessness (on the command they could open eyes and shaking hands) was also recorded during the extubation. The data were analyzed by using a professional SPSS 15.0 statistical software.

• RESULTS: The incidence of cough, restlessness and glossocoma was significantly lower in the propofol group than that in the urapidil group after extubation (P<0.05). There were no episodes of hypotension, laryngospasm, or severe respiratory depression. There was no statistical difference in recovery time between two groups (P>0.05). In propofol group, the BP and HR during extubation and thereafter had no significant difference compared with those before induction, while they were significantly lower than those before giving propofol (P <0.05), and had significant difference compared with those in urapidil group (P<0.05). Compared to preinduction, the BP of urapidil group showed no obvious increase during aspiration and extubation. The HR of urapidil group had little changes after being given urapidil, and it was obviously increased compared with that before induction. The stimulation of aspiration and extubation caused less cough and agitation in propofol group than that in urapidil group (P<0.05). The IOP of propofol group showed no obvious increase during extubation compared with that in preinduction, while in the urpidil group, extubation caused IOP significantly increased (P<0.05). The changes in these indicators between the two groups had no significant difference (P>0.05).

• CONCLUSION: Compared to urapidil, propofol is superior for preventing the cardiovascular and stress responses and IOP increases during emergence and extubation for the ophthalmic patients. Moreover, it has no effects on patient's recovery.

• KEYWORDS:propofol;urapidil;ophthalmic surgery; extubation; general anesthesia; hemodynamics; intraocular pressure

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INTRODUCTION

The vast majority of ophthalmic surgeries are performed only under local anesthesia. However, its regional anesthesia is also described in association with general anesthesia for pediatric cases and for postoperative analgesia. Eye blocks have long been limited to retrobulbar anesthesia as performed by surgeons [1-3]. Surgical technique changes to improve patients' safety during eye operation have resulted in the development of alternative analgesic techniques, such as anesthesia of cataract surgery and intraocular lens implantation. Some neurophysiologists suggest that an anesthetized state may reverse effects of hemodynamic deprivation. The effect of anesthesia on hemodynamic homeostasis, however, is unknown. Eye tumors and eye trauma requires surgical treatment under general anesthesia [3-5]. Extubation after general anesthesia during the awaked period of agitation does not cause heart rate, blood pressure and other stress response. Tracheal extubation may apply in patients with myocardial ischemia hypertension, heart disorders, and cardio-cerebral vascular accident, *etc*. Eye surgery can also cause increased intraocular pressure, thus affecting the outcome. Cardiovascular drugs commonly used clinically to reduce cycle fluctuations, but without sedation, the patient can not suppress restlessness[6-9].

The extubation may apply during anesthesia in ophthalmic surgery. The general requirements necessary for an eye block were present and then each technique was briefly described, and their respective advantages and inconveniences were also discussed[2,5,8]. In this investigation, the intravenous injection of propofol and urapidil before and after extubation was performed and the influence of two drugs on blood cycle, intraocular pressure, sedation and regained consciousness was evaluated for the prevention of the patients with eye surgery from hemodynamic and intraocular pressure changes during extubation.

MATERIALS AND METHODS

Patients A total of 82 patients (Class:ASA Ⅰ-Ⅱ), aged 24 to 65 years old, male 48 cases, female 34 cases in the Third Hospital of Chinese People's Liberation Army and Xijing Hospital, the Fourth Military Medical University during January 2005 to December 2009 were enrolled, and endotracheal anesthesia was applied in the vitrectomy and open eye surgery of orbital tumor. Before the operation, the routine examination and biochemical tests showed no abnormalities for these patients. At the same time, cardio-cerebrovascular diseases and organ diseases were excluded.

Methods Thirty minutes before surgery, the patients were given subcutaneous injection of scopolamine 0.3mg and intramuscular injection of phenobarbital 0.1g. Fentanyl 4.0μg/kg, vecuronium 0.1mg/kg and propofol 2.0mg/kg were given for induction. After that, the patients were intubated. For all patients, a local nerve block plus isoflurane (20g/L) inhalation, propofol intravenous infusion (5mg/kg) every hour, and intermittent intravenous injection of rocuronium was applied to maintain anesthesia effects. After the conjunctiva sutured, the inhalation of isoflurane was stopped, and the propofol was also discontinued by the end of surgery. At that time, there is no obvious sense in the reaction of the patient. The tidal volume (>6.0mL/kg) of isoflurane (mass concentration, <2g/L) in the end expiratory was given to induce the recovery of spontaneous breathing until the reflex of swallowing and cough appears.

Eighty-two surgical patients were randomly assigned to propofol group (n=41) and urapidil group (n=41). The gender, age, body mass, operation time and dosages of anesthetics in the two groups had no significant differences (P>0.05). In the patients of propofol and urapidil groups, propofol (1.5mg/kg) and urapidil (2.5mg/kg) were used respectively. Both drugs were diluted with normal saline to 8mL, and then intravenously injected slowly. After the treatment in all patients suction, tracheal extubation were conducted immediately, and then oxygen masks were worn for 10 minutes. By double-blind methods, the systolic and diastolic blood pressure (SBP and DBP), heart rate (HR), pH, PaO_2, $PaCO_2$, SaO_2 and intraocular pressure were recorded before the induction medication, at suction, at the extubation, and 5, 10 minutes after the extubation respectively. The complete recovery time (on the command they could open eyes and shaking hands) of the patients with restlessness was also recorded during extubation.

Statistical Analysis The findings were depicted as mean± standard deviation, variances between the two groups, and between pre- and post-treatment with repeated measures were analyzed. For countable data, χ^2 test was applied; Variance analysis and t-test were performed for the non-matched data. Professional SPSS 15.0 Windows statistical software was applied. P<0.05 was considered significant.

RESULTS

General Conditions After extubation, in the patients of propofol group and urapidil group cough occurred in 2 cases (4.9%) and 11 cases (26.8%), agitation in 1 case (0.2%) and 10 cases (24.4%), and tongue fall back in 5 cases (12.2%) and 9 cases (22.0%), respectively. By statistical analysis, in propofol group patients the incidences of cough, restlessness

Table 1 Hemodynamic changes of the ophthalmic patients during propofol or urapidil injection

(n=41, mean±SD)

Group	Preinduction	Pretreament	Aspiration	Extubation	Postextubation (5min)	Postextubation (10min)
Propofol						
SBP(mmHg)	124.1±9.4	142.2±9.8[a]	129.2±9.2[bc]	132.4±9.8[b]	121.4±9.8[c]	124.2±9.5
DSP(mmHg)	72.4±8.6	85.7±8.3[a]	78.1±8.5[bc]	78.2±8.8[c]	72.1±8.7[c]	73.2±8.9[c]
HR	78.6±9.3	89.2±9.8[a]	88.7±7.9[bc]	78.1±9.2[c]	75.3±9.4[c]	75.6±8.7[c]
Urapidil						
SBP(mmHg)	124.7±9.9	140.1±9.8[a]	125.5±9.2[cb]	127.5±9.4[b,c]	121.4±9.8[c]	124.2±9.1
DSP(mmHg)	72.6±8.8	86.2±8.7[a]	75.2±8.5[b]	75.6±8.9[b,c]	71.4±8.3[c]	73.2±8.9[c]
HR	76.2±9.7	86.2±9.3[a]	94.2±9.7[bc]	95.7±9.8[b,c]	84.7±9.6[a]	75.9±9.2[a]

[a]P<0.05, [b]P<0.01 *vs* preinduction, [c]P<0.05 *vs* pretreatment

Table 2 The changes of pH, PaO_2, $PaCO_2$, SaO_2 and IOP of the ophthalmic patients during propofol or urapidil injection

(n=41, mean±SD)

Group	pH	PaO_2(mmHg)	$PaCO_2$(mmHg)	SaO_2 (%)	IOP(mmHg)
Propofol					
Preinduction	7.389±0.121	93.8±3.2	39.5±6.3	95.9±3.3	17.1±3.5
Extubation	7.390±0.133	94.2±2.3	40.6±5.6	96.1±1.9	18.4±3.4
10 min postextubation	7.389±0.135	95.1±1.7	38.8±5.1	94.9±2.6	16.5±3.7
Urapidil					
Preinduction	7.391±0.101	95.2±1.5	39.9±6.4	94.9±3.3	16.8±3.6
Extubation	7.387±0.122	96.1±1.8	38.2±4.8	96.8±1.8	29.4±3.9[a]
10 min postextubation	7.391±0.132	95.4±1.7	39.8±2.9	95.1±2.9	17.3±3.8

[a]P<0.01 *vs* preinduetion in propofol and urapidil

and glossocoma were significantly lower than that in the urapidil group after extubation (P<0.05). The patient's recovery time (minutes) of the propofol group and urapidil group had no significant difference (13.8±4.7 *vs* 14.1±4.4, P>0.05). No laryngospasm occurred in two groups.

Hemodynamics and Blood Gas Analysis Data on the changes of SBP, DBP and heart rate for the patients of urapidil and propofol groups before induction, before treatment, at suction, at extubation, and 5 and 10 minutes after the extubation were summarized (Table 1). In propofol group, the BP and HR between extubation and thereafter, no significant difference was found compared with those before induction, while they were significantly lower than those before giving propofol (P<0.05), and had a significant difference compared with urapidil group (P <0.05). Compared to preinduction, the BP of urapidil group showed no obvious increase during aspiration and extubation. The HR of urapidil group had few changes after urapidil was given to patients, and the HR was obviously increased compared with that before induction. The cough and agitation caused by the stimulation of aspiration and extubation were less in propofol group than that in urapidil group (P<0.05). There were no episodes of hypotension, laryngospasm, or severe respiratory depression. There was no statistical difference in recovery time between two groups (P>0.05). The IOP of propofol group showed no obvious increase during extubation compared with that before the induction, while in the urpidil group, the extubation caused IOP to increase significantly (P<0.05). The changes in these indicators between the two groups had no significant difference (P>0.05).

The changes of pH, PaO_2, $PaCO_2$ and SaO_2 in patients of propofol and urapidil groups had no significant differences (P>0.05). The IOP of the patients in propofol group had no significant change (P>0.05), and in urapidil group it was significantly higher during the extubation(P<0.01, Table 2).

DISCUSSION

Anesthesiology is originated from the search for elimination of pain in surgery and anaesthesia implies loss of consciousness and of protective reflexes [2,6,7]. The biological mechanism of effect of general anesthetics has not been well understood. Anesthesia means to use drugs or non-drugs to make completely or partly temporary loss of consciousness and to achieve the purpose of pain-free surgery. Anesthesiology is a science that aims to eliminate the pain of surgery, to ensure patients' safety, and to create favorable conditions for the operation.

Ophthalmic surgical procedures have little systemic impact and are associated with a very low rate of general morbidity or mortality. As a result, in some countries, standard safety measures, such as fasting, are sometimes circumvented for eye blocks [6,7]. However, when taking into account potential complications, as described in complications of injection blocks, we believe that standard safety measures (preoperative evaluation, hemodynamics and monitoring) should be applied. Our study shows that compared to urapidil, propofol is superior for the prevention of the cardiovascular and stress responses and intraocular pressure increase during emergence and extubation for the ophthalmic patient, and has no effects on patient recovery.

When patients regained consciousness during the period of general anesthesia, effects of the anesthetics weakened and respiration was resumed. Since the airway reflex was gradually activated, it was difficult for patients to tolerate the endotracheal tube stimulation. The suction, removal of the tracheal tube and the throat stimulation can cause vagus nerve reflex, such as adrenal system excitation, as well as the surgical local uncomfort for the patient, which often causes high blood pressure, tachycardia and other cardiovascular reactions. In severely ill patients the myocardial oxygen consumption may increase, and cardiac output decrease, leading to the increased incidence of postoperative complications. Before extubation, application of local surface anesthesia, cardiovascular active drugs, and adrenergic blockers, these reactions may be blocked, and the cardiovascular response may be inhibited. Application of sedation and analgesia is also effective means of deepening anesthesia, but respiratory suppression and delayed recovery and so on may occur before extubation[7-9].

The extent of hydroxylation in propofol metabolism was higher after administration of anesthetic doses of propofol. Moreover, the ratio of hydroxylation to glucuronidation of propofol is subject to an inter-patient variability but this does not correlate with the dose of propofol. However, the variation of the metabolite profile observed in the present report does not seem to indicate an extended role of metabolism in pharmacokinetic variability. Propofol is highly protein-bound *in vivo* and is metabolized by conjugation in the liver [10]. The drug potentiates hypoxic pulmonary vasoconstriction, an effect caused by inhibition of K^+/ATP-mediated pulmonary vasodilatation. Most of the pharmacological actions of propofol result from interaction with the γ-aminobutyric acid receptor or with calcium channels. Propofol prolongs inhibitory postsynaptic currents mediated by γ-aminobutyric acid receptors, indicating that its effects are associated with enhanced inhibitory synaptic transmission, but propofol also influences presynaptic mechanisms of GABAergic transmission. Propofol modulates various aspects of the host's inflammatory response. Its rate of clearance exceeds hepatic blood flow, suggesting an extrahepatic site of elimination as well. It has several mechanisms of action [1,10], both through potentiation of gamma-aminobutyric acid receptor activity, thereby slowing the channel-closing time, and also acting as a sodium channel blocker [11]. Recent research has also suggested that the endocannabinoid system may contribute significantly to propofol's anesthetic action and to its unique properties. The half life of elimination of propofol has been estimated at between 2 and 24 hours. However, its duration of clinical effect is much shorter, because propofol is rapidly distributed into peripheral tissues. When used for IV sedation, a single dose of propofol typically wears off within minutes. Propofol is versatile; the drug can be given for short or prolonged sedation as well as for general anesthesia. Its use is not associated with nausea as is often seen with opioid medications. These characteristics of rapid onset and recovery along with its amnestic effects have led to its widespread use for sedation and anesthesia. In this study, the dose of propofol was 1.5mg/kg when tracheal extubation was performed. The patients had no obvious cough and anxiety and cardiovascular response was also effectively controlled. Because the action time of propofol is short, so patients wake up quickly.

Urapidil is a sympatholytic antihypertensive drug. It acts as a α_1-adrenoceptor antagonist and as a 5-HT_{1A} receptor agonist. Although an initial report suggested that urapidil was also a α_2-adrenoceptor agonist, this was not substantiated in later studies in which it was devoid of agonist actions in the dog saphenous vein and the guinea-pig ileum. Unlike some other α_1-adrenoceptor antagonists, urapidil does not elicit reflex tachycardia, and this may be related to its weak β_1-adrenoceptor antagonist activity, as well as its effect on cardiac vagal drive [10,12]. Urapidil itself did not inhibit the stress response in patients. In our study, in the cardiovascular responses it had a certain degree of inhibition when urapidil was used during extubation. Compared with the use of propofol, the patients in urapidil group with extubation had significantly higher stimulation and complications such as IOP pressure, cough and anxiety (P<0.05). Therefore, in patients with suspected glaucoma urapidil may induce serious complications such as acute glaucoma.

The surgeon may also require that other general conditions be prevented. Acute peak arterial hypertension, for instance, may cause catastrophic choroidal expulsive hemorrhage. Tremor and/or restlessness due to anxiety may impair the procedure for obvious reasons. Coughing must be prevented because it results in head movement that increases IOP to very acute and high peak, which can impair surgery. Sedation may help to obtain optimal "akinesia of the head" but should be used cautiously because of the potential risk of ventilatory depression in a context with no airway accessibility. Moreover, the operating time using this procedure is short, and manipulations of ocular tissues are limited. In order to ensure the effects of eye surgery, it is important to maintain the stability of IOP which must remain close to normal, in the range of 10-21mmHg[13-15]. To prevent the content of the eye from effusing from the incision, the patient should avoid coughing, restlessness, nausea and vomiting during anesthesia. Propofol can reduce IOP. Most studies show that propofol can reduce IOP caused by

intubation and extubation during general anesthesia. The role of propofol in eye surgery has a unique advantage[15-17]. Results of this study show that when propofol is used in anesthesia, the IOP can be maintained before the induction during extubation, so that the operation will be safe and the patient is stable throughout the tracheal extubation period in the requests from the surgeon varying with the procedure. During an open eye surgery, the request from the surgeon is analgesia, akinesia, and hypotonia of the eyeball. Because the eyeball is open, the concept of IOP cannot exist. What degree of anaesthesia is necessary for intraocular surgery? It depends on whether surgery is "open" or "closed" [18,19]. We believe that, sedatives used during tracheal extubation, can inhibit adverse reactions in extubation and maintain stability of IOP for ophthalmic surgery. Compared with the use of urapidil, the use of propofol is safe and effective, and there are no significant adverse reactions during anesthesia and extubation.

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