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Original Article

Propofol combined with alfentanil for general anesthesia in vocal cord polypectomy under suspension laryngoscopy

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Abstract: Objective: To investigate the clinical effect of propofol combined with alfentanil in vocal cord polypectomy under suspension laryngoscopy. Methods: A total of 308 patients undergoing vocal cord polypectomy under suspension laryngoscopy in the First Affiliated Hospital of Nanchang University were included in this prospective study, and the patients were randomly divided into an observation group and a control group. Patients in the observation group received alfentanil combined with propofol, while those in the control group were anesthetized with sufentanil combined with propofol. The heart rate (HR), mean arterial pressure (MAP), real portfolio project (RPP), and Steward postanesthetic recovery scores were compared between the two groups before anesthesia induction (T0), at intubation (T1), 5 min after intubation (T2), at the time of placing suspension laryngoscopy (T3), 1 min after placing the suspension laryngoscopy (T4), 1 min after extraction of support laryngoscope (T5), and 1 min after extubation (T6). In addition, the propofol dosage and peripheral plasma levels of epinephrine (E) and norepinephrine (NE) were also compared between the groups. Results: The MAP, HR, and RPP of the patients in the observation group were higher than those in the control group at T1-T5 (all $P<0.05$), while there was no statistical difference at T0 and T6 (all $P>0.05$). The Steward postanesthetic recovery scores and the propofol dosage in the observation group were lower than those in the control group. In addition, there was a statistically significant difference in the E and NE levels between the two groups after surgery ($P<0.001$). There was also an interaction effect between the groups and among the time points (both $P<0.001$). Conclusion: Alfentanil can reduce the fluctuation of hemodynamics during vocal cord polypectomy under suspension laryngoscopy, and therefore improve anesthesia effect. Simultaneously, the usage of propofol was reduced, as well as the stress levels. Clinical trial number: ChiCTR2100054186.

Keywords: Alfentanil, microscopic laryngeal surgery, anesthetic effect, sufentanil, adverse reactions

Introduction

Vocal cord polypectomy under suspension laryngoscopy is widely applied in clinical practice due to its unique advantages [1-3], including clear exposure of the larynx structure, high illumination, as well as fine and accurate surgical operation. Because of these advantages, this operation can not only completely remove the diseased tissue, but also retain the normal vocal cord mucosa as much as possible, greatly improving the postoperative efficacy and reducing recurrence [4].

Although vocal cord polypectomy under suspension laryngoscopy offers short operation time and involves minor surgical trauma, it has a strong stimulating effect on the larynx, demands a high surgical field, and involves sharing the same airway for both anesthesia and surgery. As a result, anesthesiologists have limited access to the endotracheal intubation, posing challenge for patient anesthesia. At the same time, reducing stress response associated with intraoperative stimulation is also of great significance for postoperative recovery [5, 6].

Currently, intravenous anesthesia with propofol plus sufentanil is widely used in clinical practice for vocal cord polypectomy under suspension laryngoscopy. However, it has been found that propofol combined with sufentanil has an impact on the blood pressure and heart rate (HR) of patients, and increases the surgical risk. Additionally, propofol can also cause hippocampus-related injury [7]. Recent research has shown that alfentanil works faster and has a longer duration of action than sufentanil, with less inhibitory effect on the respiratory and circulatory systems, can mitigate the propofol-related neurological injury, and has achieved good practical results in other procedures [8]. Furthermore, alfentanil injection can prevent bronchial spasms and reduce respiratory secretions, thereby ensuring a clear surgical field of view and reducing the risk of aspiration [9]. Currently, there are few reports comparing the anesthesia effects of alfentanil with sufentanil plus propofol in vocal cord polypectomy under suspension laryngoscopy. Based on this, this study aims to analyze the application effects of propofol combined with alfentanil on patients with vocal cord polyps, providing more evidence-based medical findings to improve clinical anesthesia effectiveness.

Materials and methods

General data and sample size calculation

This is a 2-group prospective randomized trial (ChiCTR2100054186) conducted at The First Affiliated Hospital of Nanchang University from January 2022 to July 2023. After preoperative assessment of 412 patients undergoing vocal cord polypectomy, 308 patients were included for surgery under suspension laryngoscopy. Using a random number table, the 308 patients were randomly divided into two groups, with 154 patients in each group. The study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Nanchang University, and informed consent form for surgery and for participating in the trail was obtained from all subjects.

Inclusion criteria: 1. Patients undergoing first-time surgery for vocal cord polyps; 2. Patients with American Society of Anesthesiologists Class I-II; 3. Patients with Mallampati I-II; 4. Patients aged from 20 to 55 years old; 5. Patients weighing 50 to 80 kg.

Exclusion criteria: 1. Patients with severe respiratory and circulatory system diseases; 2. Patients with acute respiratory inflammation within the last two weeks that had not yet been cured; 3. Patients who were predicted to have or have had difficulty in their airways; 4. Patients allergic to opioid drugs in emulsion; 5. Patients failing to cooperate with medical workers or communicate effectively; 6. Patients who were found to have renal dysfunction (serum creatinine >177 μmol/L) or active liver disease in preoperative biochemical examinations; 7. Patients with abnormal function of vital organs, combined with other systemic diseases, such as myocardial infarction, cerebral infarction, history of psychiatric disease, or the use of related drugs; 8. Patients with acute and chronic infection before surgery; 9. Patients whose operation time was over 30 minutes.

The study utilized a parallel design with a 1:1 allocation ratio. The patients were divided into an alfentanil group and a sufentanil group. Referring to the literature with similar design, the average awakening Steward score was estimated to be μ1=4.9 in the sufentanil group, while μ2=4 in the alfentanil group [10]. The standard deviation =1. Considering a dropout rate of 10%, a Type I error probability (α) of 0.05, and a power (1-β) of 80%, we estimated the required sample size for this study. To calculate the sample size for this clinical trial, taking into account the primary efficacy outcome measure, we used the following formula:

$$n1 = n2 = \frac{2\left(Z\alpha/2 + Z\beta\right)2 \times \sigma 2}{\left(\mu 1 - \mu 2\right)2}$$

In the formula, μ1=4.9, μ2=4, σ=1, α=0.05, and β=0.2. By substituting these values into the equation, we obtain n1=n2=20 cases. Therefore, the minimum sample size for this study was 20. To enhance the reliability of the study results, all patients who met the inclusion criteria during the study period were selected, leading to a total of 308 cases.

Anesthesia methods

All patients who participated in this trial were randomized and double-blinded. Patients were

given an intramuscular injection of 0.5 mg atropine before surgery. After patients entered the operation room, an intravenous line was established to ensure airway patency. The electrocardiogram (ECG), blood pressure, pulse oximetry, end-tidal carbon dioxide ($PetCO_2$), and bispectral index (BIS) values were continuously monitored. During the operation, muscle relaxant monitors were used to guide the use of muscle relaxants, and monitoring the depth of anesthesia.

Patients in the observation group were anesthetized with alfentanil combined with propofol for anesthesia induction at a dose of 4 μg/kg, and a maintenance dose of 0.5-1.5 μg/kg/min. While those in the control group received sufentanil combined with propofol for anesthesia. After 0.4 μg/kg of sufentanil was slowly infused intravenously for 2 min, 1-2 mg/kg of propofol and 0.6 mg/kg of rocuronium were slowly injected intravenously for anesthesia induction. All endotracheal intubations were performed by the same surgeon. The anesthesia machine was hooked up and its respiratory parameters were set (tidal volume VT=8-12 mL/h, respiratory rate f=12 times/min) for mechanical ventilation. $PetCO_2$ was monitored and maintained at 35-45 mmHg. The control group received propofol with a plasma concentration target of 2-4 μg/mL and sufentanil at 0.2 μg/kg/min for intraoperative anesthesia maintenance. The observation group were given propofol with a plasma concentration target of 2-4 μg/mL and alfentanil at 0.15 μg/kg/min for intraoperative anesthesia maintenance. Smooth operation of anesthesia machine, correct pipeline connections, and stable vital signs of patients were ensured. Intraoperatively, the propofol dosage was adjusted according to blood pressure, HR, and BIS values, and the fluctuation range of intraoperative blood pressure did not exceed 30% of the baseline value. Sufentanil at 0.2 μg/kg/min and alfentanil at 1.5 μg/kg/min are drug equivalent [11].

Outcome measures

In both groups, the HR, mean arterial pressure (MAP) and real portfolio project (RPP) were observed before anesthesia induction (T0), at intubation (T1), 5 min after intubation (T2), at the time of placing suspension laryngoscopy (T3), 1 min after placing the suspension laryngoscopy (T4), 1 min after extraction of support laryngoscope (T5), and 1 min after extubation (T6).

Venous blood (4 mL) was drawn into heparinized test tubes 5 min after intubation, 5 min after extubation, as well as 12 h and 24 h after surgery, and centrifuged to obtain plasma. The plasma was pretreated according to the King's modified fluorescence method (XG-E988350, Shanghai Sig Biotechnology Co., Ltd., China), and the levels of norepinephrine (NE) and epinephrine (E) were determined by enzyme-linked immunosorbent assay (E-EL-0047c, Elabscience Biotechnology Co., Ltd.).

The Steward postanesthetic recovery scores were recorded 30 minutes after the patients were transferred to the recovery room and compared between the two groups. The Steward scores include 5 items: activity, respiration, circulation, consciousness, and blood oxygen saturation, each with a full score of 3 points. The total score of the scale is 15 points, and 9 is required for extubation. In addition, the intraoperative propofol dosage in the two groups was statistically analyzed.

In addition to the main outcome measures mentioned above, the following secondary indicators were also observed and analyzed.

Intraoperative sinus bradyarrhythmia (HR<60 beats/min, treated with atropine), hypotension (systolic blood pressure <80 mmHg, corrected with ephedrine), choking during extubation, and postoperative nausea and vomiting (treated with symptomatic management) were identified as adverse reactions.

Statistical analysis

All data were analyzed using the SPSS 22.0 statistical software. The normally distributed measurement data were expressed as mean ± standard deviation ($\bar{x} \pm sd$).

The independent-sample t-test was used for comparisons between the groups. Repeated measures ANOVA followed by post hoc Bonferroni test were used for post-hoc comparisons. Counting data were analyzed with chi-

Table 1. Comparison of general data

Group	Observation group (n=154)	Control group (n=154)	χ^2/t	P
Gender			0.474	0.491
Male	83	89		
Female	71	65		
Age (years)	37.4±5.7	38.3±5.5	1.41	0.16
Duration of disease (years)	1.9±0.5	1.8±0.4	1.938	0.054
Types of polyps			0.833	0.361
Broad-based	69	77		
Bilateral polyps	85	77		
BMI (kg/m^2)	21.3±2.3	22.2±2.4	1.12	0.264
Comorbidities				
Diabetes	10	13	0.423	0.516
Hypertension	10	11	0.051	0.821

Note: χ^2: data from Chi-square test; t: data from t test; BMI: body mass index.

Table 2. Comparison of surgical parameters

Group	Operation time (min)	Hospital stays (day)	Amount of intraoperative bleeding (mL)
Observation group (n=154)	46.7±5.6	9.3±1.3	54.9±7.4
Control group (n=154)	46.9±5.9	9.2±1.5	54.0±6.8
t	0.305	0.625	1.111
P	0.76	0.532	0.267

Note: t: data from t test.

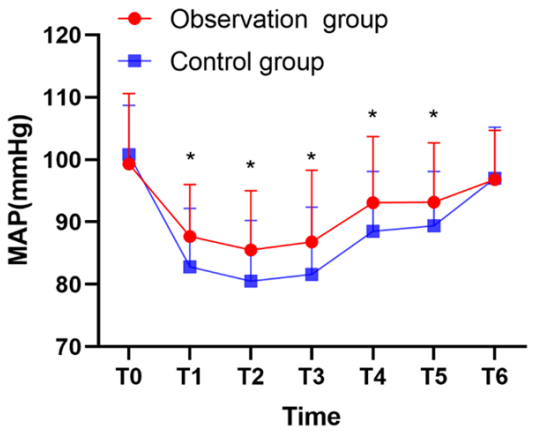

Figure 1. Comparison of intraoperative MAP levels. Comparison between two groups at different time points, *P<0.05. MAP: arterial pressure.

square test. A difference was considered statistically significant when P<0.05.

Results

Comparison of general data

The baseline data of two groups were comparable in terms of gender, age, type of polyp, duration of disease and comorbidities, with no statistically significant differences observed (all P>0.05). See **Table 1**.

Comparison of surgical outcomes

There were no significant differences between the two groups in operation time, amount of intraoperative bleeding, and hospital stay (all P>0.05). See **Table 2**.

Comparison of MAP, HR, and RPP levels at different time points

There were significant differences in main effects among MAP, HR and RPP at different times (P<0.001). Without reference to the monitoring time, the main effect difference between the groups was statistically significant (P<0.001), and there were interactions between groups and time points (P<0.001). Besides, the MAP, HR, and RPP of the patients in the observation group were higher than those in the control group at T1-T5 (all P<0.05), while there was no statistical difference at T0 and T6 (all P>0.05). See **Figures 1-3**.

Comparison of E and NE levels at different time points

The E and NE levels in both groups showed a gradual decreasing trend 5 min after intubation, 5 min after extubation, 12 h after surgery and 24 h after surgery (all P<0.05). Moreover, the observation group had lower E and NE levels than the control group at the above four time points (all P<0.05). See **Table 3**.

Comparison of propofol dosage and Steward postanesthetic recovery scores

The Steward postanesthetic recovery scores and propofol dosage in the observation group

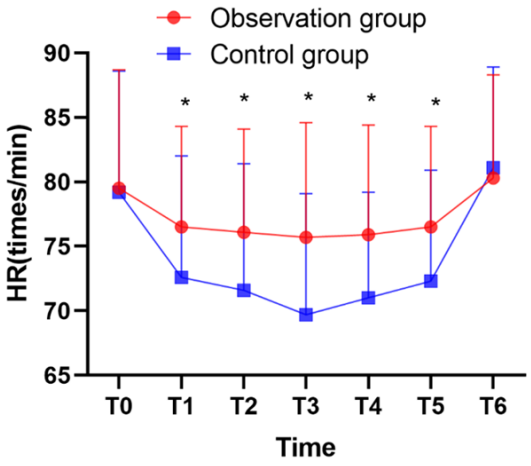

Figure 2. Comparison of intraoperative HR levels. Comparison between two groups at different time points, *P<0.05. HR: heart rate.

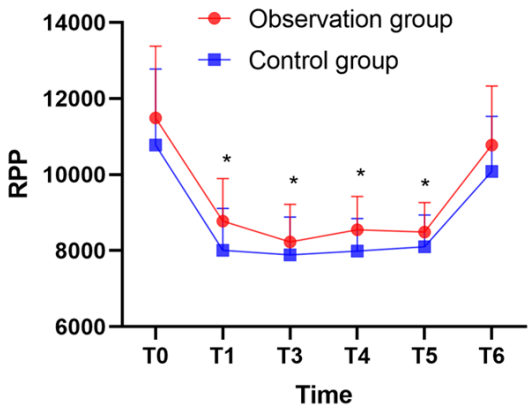

Figure 3. Comparison of intraoperative RPP levels. Comparison between two groups at different time points, *P<0.05. RPP: real portfolio project.

were lower than those in the control group (all P<0.05). See **Table 4**.

Comparison of adverse reactions

There was no significant difference in the incidence of adverse reactions, such as sinus bradycardia, hypotension, choking and postoperative nausea and vomiting, between the groups (16/150 *vs.* 15/150; χ^2=0.036, P=0.850). See **Table 5**.

Discussion

Vocal cord polyps, presenting as small protrusions on the vocal cords and are benign lesions [12]. Vocal cord polypectomy is a common type of surgery in otolaryngology. The surgery can be also managed with outpatient surgery during the day. Stabilizing hemodynamics, reducing anesthetic medications, and mitigating intraoperative stress responses are the major present focuses in perioperative anesthesia for laryngoscopy [13]. Hence, the rational use of anesthesia to enhance analgesic effects and reduce anesthesia-related adverse reactions is of significant importance for the stabilization of the circulatory system [14-16].

Sufentanil or alfentanil combined with propofol are commonly used in otolaryngology surgeries in current clinical practice [17-19]. However, due to the short market time of alfentanil in China, there is less evidence-based medical findings available. Thus, we conducted a randomized trial to explore the effect of both combinations in vocal cord polypectomy. It was found that the use of alfentanil was superior to sufentanil in terms of MAP, HR, and RPP. This may be related to the following mechanisms: Alfentanil itself is a derivative of fentanyl with low lipophilicity and high plasma protein binding rate, resulting in a quick onset and rapid decrease in blood concentration. This reduces fluctuations in the body's circulatory system. Similar studies have been reported in the past [20-22].

In addition, our results also exhibited that the N and NE levels in the observation group were lower than those in the control group. The possible mechanism is as follows: Alfentanil is an anesthetic analgesic with high analgesic intensity and low addiction. It mainly acts on the μ opioid receptor and has a quick onset and a long duration. Therefore, it can reduce the stimulation on the hypothalamus-pituitary-adrenal cortex system from surgical operations and anesthesia, and reduces the N and NE levels. The above reconfirms that alfentanil is milder than sufentanil and leads to less of a stress response [23].

In this study, we also compared the amount of propofol used during surgery and the Steward score. Our results showed that alfentanil reduced the propofol dosage and promoted patient recovery. This is mainly due to its fast-acting analgesic effect, which reduces the propofol dosage and shortens the anesthetic duration. At the same time, researchers have con-

Table 3. Comparison of epinephrine and norepinephrine levels at different time points

Group	5 min after intubation	5 min after extubation	12 h after surgery	24 h after surgery
Epinephrine (pmol/L)				
Observation group (n=154)	265.6±36.7[b]	224.3±31.0[a,b]	162.9±33.7[a,b]	142.3±34.3[a,b]
Control group (n=154)	268.7±36.3	241.9±32.5[a]	187.7±41.2[a]	166.7±40.8[a]
Norepinephrine (pmol/L)				
Observation group (n=154)	334.3±61.6[b]	289.0±54.2[a,b]	267.4±43.0[a,b]	252.6±43.6[a,b]
Control group (n=154)	336.4±72.5	312.5±55.2[a]	293.5±60.4[a]	274.8±56.7[a]

Note: Compared with 5 min after extubation, [a]P<0.05; Compared with the control group, [b]P<0.05.

Table 4. Comparison of propofol dosage and Steward post-anesthetic recovery scores

Group	Propofol dosage (mg)	Steward postanesthetic recovery scores
Observation group (n=154)	175.9±28.0	4.20±0.92
Control group (n=154)	190.2±30.2	4.92±0.83
t	4.309	7.423
P	0.001	0.001

Note: t: data from t test.

Table 5. Comparison of adverse reactions

Group	Observation group (n=154)	Control group (n=154)	χ^2	P
Complications			0.036	0.85
Choking	6	7		
Nausea	4	3		
Vomiting	3	2		
Sinus bradycardia	1	2		
Hypotension	2	1		
Total	16/154	15/154		

Note: χ^2: data from chi-square.

firmed that the duration of alfentanil anesthesia is only half that of sufentanil, so patients recover quickly after discontinuation of the drug, aligning with the conclusions of previous studies [24, 25].

Finally, we analyzed the safety of alfentanil and sufentanil, and there was no statistical difference in the incidence of adverse reactions between the two groups, which was different from previous findings that the rate of adverse reactions from sufentanil was higher than that from alfentanil (possibly related to a smaller sample size) [26]. However, it also confirmed the safety of alfentanil in laryngeal surgeries, which is consistent with our research [27].

In summary, alfentanil can reduce the fluctuation of hemodynamics during vocal cord polypectomy under suspension laryngoscopy, improve anesthesia effect, reduce propofol dosage and stress levels, and accelerate postoperative recovery without increasing the incidence of adverse reactions. So, this combination is worth recommending for clinical use. However, this is a single-center study with a small number of subjects. It is necessary to confirm the clinical effect of alfentanil combined with propofol in vocal cord polypectomy under suspension laryngoscopy through large sample multi-center studies. Besides, the alfentanil dosage during surgery also needs to be further studied.

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Disclosure of conflict of interest

None.

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