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Effects of remimazolam combined with mivacurium on recovery quality of patients after vocal cord polypectomy

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Abstract: Objective To evaluate the effects of remimazolam versus propofol on the quality of postoperative recovery in patients undergoing vocal cord polypectomy with supportive laryngoscopy by the 15-item quality of recovery scale (QoR-15). **Methods** A total of 90 patients who underwent vocal cord polypectomy with supported laryngoscopy from the Fourth Clinical College of Xinxiang Medical University from December 2022 to October 2023 were divided into remimazolam combined with mivacurium group (group R) and propofol combined with mivacurium group (group P) by random block design method, with 45 cases in each group. By intravenous administration, patients in group R and group P were given remimazolam 0.2 to 0.3 mg/kg and propofol 1.5 to 2.0 mg/kg, respectively. After the disappearance of eyelash reflex, sufentanil 0.3 g/kg and mivacurium 0.25 mg/kg were given to all patients. The quality of postoperative recovery was evaluated by the QoR-15 scale 1 day before, 1 day and 2 days after surgery. Mean arterial pressure (MAP), heart rate (HR), saturated pulse oxygen (SpO_2), and Modified Observer's Assessment of Alertness/Sedation Scale （MOAA/S) scores of the two groups were recorded at different time points. The time required including surgery, recovery of spontaneous breathing, endotracheal tube removal, and post-anesthesia monitoring unit (PACU) stay after surgery, and the occurrence of intra- and post-operative adverse reactions were recorded. **Results** The QoR-15 scale score of group R was lower than that of group P (P<0.05) on the first day after surgery, and it was not clinically significant because the minimum clinically significant change value of QoR-15 scale score was 6 points. The recovery time of spontaneous breathing and extubation time in group R were longer than those in group P(P<0.05), but there was no significant difference in PACU stay time between the two groups (P > 0.05). The incidence of hypotension and injection site pain in group R were lower than those in group P (24.4% *vs* 64.4%, χ^2=14.580, P<0.01; 6.7% *vs* 84.4%, χ^2=54.878, P<0.01), and no significant difference was found in the incidence of other adverse reactions (P>0.05). **Conclusion** In the anesthesia of vocal cord polypectomy under supported laryngoscopy, the quality of recovery of patients using remimazolam is comparable to that of propofol. While meeting perioperative needs, it can maintain more stable hemodynamics, without significant injection site pain, and can improve patient's comfort during the perioperative period.

Keywords: Vocal cord polypectomy; Postoperative recovery quality; Remimazolam; Mivacurium; Propofol; The 15-item quality of recovery scale

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Endoscopic vocal cord polypectomy under suspension laryngoscopy is one of the most common procedures in otolaryngology, characterized by its short duration and intense stimulation to the patient's throat. Anesthesiologists typically opt for deep anesthesia induction regimens to alleviate the stimulation caused by inserting the suspension laryngoscope and the stress response induced by local adrenaline use during surgery. However, this approach can result in prolonged postoperative recovery time, poor quality of awakening, incomplete metabolism of muscle relaxants, agitation, and prolonged stay in the post-anesthesia care unit (PACU). With the promotion of enhanced recovery after surgery (ERAS) principles in recent years, which emphasize patient-centered care and optimize clinical pathways involving perioperative management, efforts have been made to alleviate various stress responses during the perioperative period to reduce postoperative complications, shorten hospital stay, and promote recovery [1]. Therefore, in recent years, it has been advocated to select anesthetic drugs with rapid onset and metabolism for vocal cord polypectomy or perform ultrasound-guided superior laryngeal nerve block to mitigate the stress response induced by support laryngoscopy [2]. The dosage of anesthetic drugs should be reduced to shorten patients' recovery time, ensure

high-quality recovery, and enhance perioperative satisfaction.

Currently, the commonly used general anesthetic propofol exhibits significant respiratory depression in patients and has drawbacks such as injection pain and significant hemodynamic effects. The commonly used muscle relaxants, cisatracurium and rocuronium, have half-lives longer than the duration of vocal cord polypectomy. While mivacurium is a short-acting non-depolarizing muscle relaxant with rapid onset and short elimination half-life, which meets the requirements for deep muscle relaxation, provides satisfactory conditions for tracheal intubation and surgery, and is compatible with the short duration of otolaryngological procedures [3]. Remimazolam is a novel benzodiazepine sedative with minimal adverse reactions and rapid metabolism. Its safety and effectiveness in anesthesia induction have been confirmed, making it suitable for sedation and anesthesia induction in short otolaryngological procedures[4]. This study aims to observe the effects of remimazolam combined with mivacurium on vocal cord polypectomy and its impact on postoperative recovery quality in patients, providing reference for clinical anesthesia induction protocols.

1 Materials and Methods

1.1 Study design

This study has been approved by the Ethics Committee of the Xinxiang Central Hospital (Ethics Number: 2022-276-01), registered with the Chinese Clinical Trial Registry (Registration Number: ChiCTR2300068097), and informed consent has been obtained from patients and their families.

The main outcome measure of this study is the postoperative 15-item Quality of Recovery Scale (QoR-15) score. Based on pre-experimental results and reference to previous studies, the difference in QoR-15 scores on the first day after surgery is clinically significant (according to the latest article by the QoR-15 scale authors, the minimum clinically significant difference is 6 points [5]). The sample size was estimated based on the QoR-15 scores on the first day after surgery, with the remimazolam group estimated to have a QoR-15 score 10 points lower than the propofol group, with a standard deviation of 13, a test power (1-β) of 90%, and a significance level of 0.05. Using PASS 15.0 software, it was determined that each group should consist of a minimum of 37 patients. Considering a dropout rate of 20%, the final requirement was determined to be 45 patients per group.

1.2 Study subjects

According to the sample size calculation, inclusion and exclusion criteria, after excluding the patients with abnormal physiological and anatomical structure, difficult to expose the glottis under the support laryngoscope, the operation time being too long, or the patients with poor cooperation during postoperative follow-up, a total of 90 patients scheduled to undergo vocal cord polypectomy under suspension laryngoscopy were included in the study at the Fourth Clinical College of Xinxiang Medical College from December 2022 to October 2023.

A researcher who was not involved in anesthesia induction and follow-up recruited the subjects. Using a randomized block design, the patients were randomly divided into two groups (n=45 each): the remimazolam-mivacurium group (group R) and the propofol-mivacurium group (group P). Group allocation was kept confidential using sealed envelopes, and neither the follow-up researchers nor the patients were aware of the group assignments.

Inclusion criteria: (1) American Society of Anesthesiologists (ASA) classification I or II; (2) aged 18-60 years, body mass index (BMI) 18-28 kg/m^2; (3) willing to participate in the study and sign the relevant informed consent form.

Exclusion criteria: (1) history of severe cardiovascular, cerebrovascular, pulmonary, hepatic, renal, or metabolic diseases; (2) history of alcohol abuse or sedative use; (3) preoperative hypertension with systolic blood pressure >180 mmHg and/or diastolic blood pressure >110 mm Hg; (4) neurological or psychiatric disorders; (5) suspected abuse of anesthetic analgesics or sedatives; (6) known allergy to benzodiazepines or muscle relaxants; (7) difficult airway or difficulty exposing the vocal cords during suspension laryngoscopy.

1.3 Baseline data

One day before surgery, the Chinese version of the QoR-15 scale was used to assess the patients' condition as a baseline. The QoR-15 scale reflects the quality of patients' postoperative recovery from five dimensions: comfort, emotional state, physical independence, psychological support and pain [6]. Studies have shown that the validity and reliability of the Chinese version of the QoR-15 scale are comparable to the original scale [7].The postoperative recovery quality was influenced by various factors, such as the intensity of surgical stimulation, the size of the polyp, the amount of bleeding, and differences in patients' physical conditions. This study also used the Comprehensive Complication Index (CCI) and Surgical Apgar Score to assess patient complications and intraoperative conditions, ensuring that the baseline characteristics and surgical conditions of the two groups of patients were similar. There were no statistically significant differences in age, sex ratio, BMI, ASA classification, operative time, surgical Apgar score and preoperative QoR-15 score between the two groups (P > 0.05). **See Table 1.** The M (Q) of CCI score was 0 (0) in group P and 0 (0) in group R, with no statistical significance between the two groups (Z=-0.391, P=0.696).

Tab. 1 Comparison of patients' general conditions and operation duration between two groups (n=45, $\bar{x}\pm s$)

	Male /Female (case)	Age (year)	BMI (kg/m^2)	ASA (I/II)	Operation time (min)	Surgical Apgar score	Preoperative QoR-15 scores
Group P	27/18	40.2 ± 9.1	23.8 ± 1.9	35/10	9.3 ± 2.1	9.6 ± 0.6	142.5 ± 6.1
Group R	25/20	41.2 ± 10.9	24.2 ± 2.1	33/12	8.9 ± 2.7	9.4 ± 0.7	140.2 ± 6.8
χ^2/t value	0.182	0.474	0.947	0.240	0.784	1.455	1.689
***P* value**	0.669	0.636	0.346	0.623	0.434	0.149	0.094

1.4 Anesthesia methods

All patients were routinely instructed to fast for 4 hours and abstain from water for 8 hours before surgery. Upon arrival in the operating room, a peripheral venous line was opened, and the patient's electrocardiogram (ECG), non-invasive blood pressure (NIBP), saturated pulse oxygen (SpO2), bispectral index (BIS), and end-tidal CO_2 pressure were monitored. Patients were provided with oxygen at a flow rate of 2-3 L/min via a mask.

Anesthesia induction: Intravenous injection of propofol emulsion at a dose of 1.5-2.0 mg/kg for group P and intravenous bolus injection of remimazolam at a dose of 0.2-0.3 mg/kg for group R. After the disappearance of eyelash reflex, both groups received intravenous injections of midazolam 0.25 mg/kg and sufentanil 0.3 μg/kg, followed by the insertion of a 6.0 mm standard endotracheal tube by the anesthesiologist for mechanical ventilation. The tidal volume (VT) was set at 6-8 mL/kg, respiratory rate at 12-20 beats/min, and the inspiratory to expiratory ratio at 1:2. Ventilator parameters were adjuste to maintain the patient's end-tidal CO_2 pressure at 35-45 mmHg (1 mmHg = 0.133 kPa).

During surgery, anesthesia maintenance consists of continuous intravenous infusion of remimazolam at a rate of 0.5-1 mg/(kg•h) for group R and propofol emulsion at a rate of 4-6 mg/(kg•h) for group P to maintain the BIS value between 40 and 60. At the end of surgery, infusion of maintenance drugs was discontinued, and patients were transferred to the post-anesthesia care unit (PACU) for recovery.

1.5 Observation indicators

(1) The QoR-15 scale scores were recorded for patients on the day before surgery, postoperative day 1 (POD1), and postoperative day 2 (POD2).

(2) Mean arterial pressure (MAP), heart rate (HR), SpO2, Modified Observer's Assessment of Alertness/Sedation Scale were recorded (MOAA/S: with 0 indicating no response to any postoperative pain or stimulation and 5 indicating responsiveness) at various time points: before anesthesia induction (T0), after induction (T1), tracheal intubation (T2), insertion of laryngeal mask airway (T3), start of surgery (T4), end of surgery (T5), and extubation (T6).

(3) Surgical time, time to recovery of spontaneous breathing (time from cessation of medication to recovery of spontaneous breathing), time to extubation, and PACU stay time (time from entry into PACU to achieving a Modified Aldrete Score of 9) were recorded.

(4) Adverse events during and after surgery were also documented, such as pain at injection site, hypotension (defined as a decrease in blood pressure of more than 20% relative to baseline upon entering the operating room), coughing, movement response, agitation during emergence, postoperative nausea and vomiting, awareness during surgery, and allergic reactions.

1.6 Statistical methods

Data were analyzed using SPSS 26.0 statistical software. The Shapiro-Wilk test was used for normality testing. Normally distributed and homoscedastic continuous data were presented as $\bar{x}\pm s$, and independent sample t-tests were used for between-group comparisons. For continuous data that do not meet the assumptions of homogeneity of variances, the t' test was employed. Non-normally distributed continuous data were presented as M (IQR), and between-group comparisons were conducted using the Mann-Whitney U test. Categorical data were presented as frequencies and percentages, and the chi-square test was used for comparison. A significance level of $P < 0.05$ was considered statistically significant.

2 Result

2.1 Comparwason of perioperative parameters between the two groups

There was no statistically significant difference in SpO_2 and HR at each time point between the two groups ($P > 0.05$). Compared with group R, the MAP at time points T1-T3 was lower than that in group P ($P < 0.05$). **See Table 2.** Both groups have a MOAA/S score of 5 at T0. At T1, the M (IQR) of MOAA/S score was 0 (0) for group P and 0 (0) for group R, with no statistically significant difference between two groups (Z = 1.334, P = 0.182). At T2-T5, the scores of the two groups were 0. At

T6, the M (IQR) of MOAA/S score was 5 (5) for group P and 5 (5) for group R, with no statistically significant difference between two groups (Z = 1.372, P = 0.170). **Table 3** showed that there was no statistically significant difference in PACU stay time between two groups (P > 0.05), but the time to recovery of spontaneous breathing and time to extubation were longer in group R than those in group P (P < 0.05).

2.2 Comparison of adverse reactions between two groups

Incidences of intraoperative hypotension and injection site pain in group R were lower than those in group P (P<0.01). There was no statistically significant difference in coughing, body movement reactions, agitation during emergence, postoperative nausea and vomiting (P> 0.05). No other adverse reactions such as intraoperative awareness and drug allergy were observed during the study. **See Table 4.**

2.3 Comparison of postoperative QoR-15 scores between two groups

On the first day postoperatively, QoR-15 scale scores in group R was lower than that in group P, with a statistically significant difference (P<0.05). However, since the minimum clinically significant difference for the QoR-15 scale score was 6 points, this difference was not clinically meaningful. There was no statistically significant difference in QoR-15 scale scores between the two groups on the second day postoperatively (P > 0.05). **See Table 5.**

Tab. 2 Comparison of MAP, HR and SpO2 of patients at each time point between two groups (n=45, $\bar{x}\pm s$)

Group	Indicators	T0	T1	T2	T3	T4	T5	T6
Group P	MAP(mmHg)	95.9±14.3	81.3±9.2	82.9±11.3	87.3±9.0	88.1±11.2	88.6±10.4	96.7±12.8
Group R	MAP(mmHg)	91.8±11.4	89.4±10.1	90.1±12.4	92.2±10.6	90.1±9.8	90.7±12.3	93.7±11.2
***t* value**		1.503	3.977	2.879	2.364	0.902	0.875	1.183
***P* value**		0.136	<0.001	0.005	0.020	0.370	0.384	0.240
Group P	HR(times/min)	74.6±10.2	76.4±9.1	76.9±11.7	79.2±11.0	73.8±12.9	75.9±8.8	81.1±13.7
Group R	HR(times/min)	76.6±12.8	77.4±10.2	78.8±8.8	82.0±12.5	77.8±10.3	74.8±10.9	78.3±9.0
***t* value**		0.820	0.491	0.871	1.128	1.625	0.527	1.131
***P* value**		0.415	0.625	0.386	0.262	0.108	0.600	0.260
Group P	SpO_2(%)	99.4±0.5	99.6±0.5	99.7±0.4	99.9±0.3	99.8±0.4	99.9±0.4	98.2±1.3
Group R	SpO_2(%)	99.5±0.5	99.5±0.5	99.6±0.5	99.8±0.4	99.7±0.5	99.8±0.4	97.6±1.6
***t* value**		0.948	0.948	1.047	1.341	1.047	1.186	1.952
***P* value**		0.345	0.345	0.297	0.183	0.297	0.239	0.054

Tab.3 Comparison of the time taken for two groups of patients to recover spontaneous breathing, remove tracheal catheters, and stay in PACU
(n=45, min, $\bar{x}\pm s$)

Group	Recover spontaneous breathing	Remove tracheal catheters	Stay in PACU
Group P	7.1±1.5	14.5±5.6	27.4±4.1
Group R	8.2±2.1	16.8±5.0	29.4±5.9
***t* value**	2.859	2.055	1.878
***P* value**	0.005	0.042	0.063

Tab.4 Comparison of adverse reaction rates between two groups of patients [n=45, case(%)]

Group	Injection site pain	Nausea and vomiting	Coughing	Hypotension	Restlessness during recovery period	Body movement reaction
Group P	38(84.4)	3(6.7)	6(13.3)	29(64.4)	10(22.2)	2(4.4)
Group R	3(6.7)	5(11.1)	2(4.4)	11(24.4)	6(13.3)	5(11.1)
χ^2 **value**	54.878	0.137	1.234	14.580	1.216	0.619
***P* value**	< 0.001	0.711	0.266	<0.001	0.270	0.431

Tab. 5 Comparison of postoperative QoR-15 scale scores between two groups of patients (point, $\bar{x}\pm s$)

QoR-15 scale scores	Case	POD 1	POD 2
Group P	45	126.2±11.0	138.0±6.2
Group R	45	121.3±10.2	136.8±6.9
***t* value**		2.191	0.867
***P* value**		0.031	0.387

3 Discussion

In clinical practice, the evaluation of postoperative recovery quality in patients often focuses on aspects such as rehabilitation outcomes, postoperative complications, and occurrence of adverse reactions. However, subjective patient experiences such as postoperative pain, insomnia, anxiety, poor physical comfort, and unstable emotional states are often overlooked. The Chinese version of the QoR-15 scale comprehensively assesses postoperative recovery quality from five dimensions: comfort, emotional state, physical independence, psychological support, and pain. With the promotion of ERAS, more aspects should be considered during diagnosis and treatment.

This study compared the effects of remimazolam and propofol on the postoperative recovery quality of patients undergoing vocal cord polypectomy. The results showed that patients in the remimazolam group had lower QoR-15 scale scores on the first day postoperatively compared to the propofol group, with a statistically significant difference. But there was no statistically significant difference between two groups on the second day postoperatively. This suggested that the use of midazolam may slightly reduce postoperative recovery quality compared to propofol, but overall, it is not inferior to propofol. This finding is consistent with related research [10]. Specific analysis of the five dimensions of the QoR-15 scale scores revealed that the decline in scores mainly occurred in terms of physical comfort and emotional state, which may be related to preoperative anxiety in patients and the effects of benzodiazepines on cognitive function. Remimazolam can be hydrolyzed into its inactive metabolite, midazolamic acid [11], which has minimal pharmacological activity and does not accumulate in the body, resulting in minimal impact on the neurological and mental functions of patients. However, attention should still be paid to the mental status of patients.

This study did not use flumazenil for sedation reversal therapy, so it is unclear whether the quality of recovery in patients can be improved when flumazenil is used for reversal. It is worth noting that Yamamoto *et al.* [12] found that after postoperative flumazenil administration, patients may re-enter a sedated state. Pharmacokinetic simulation studies by Masui [13] showed that when higher doses of flumazenil were used to antagonize the sedative effects of remimazolam, there was a higher risk of re-sedation in patients. This is because the antagonistic mechanism of flumazenil against benzodiazepines is only competitive antagonism, and as the blood concentration of flumazenil decreases, the sedative effects of midazolam may reappear. Therefore, when considering the possibility of excessive residual doses of midazolam and inability to continuously monitor patients' vital signs, it is not recommended to routinely administer high doses of flumazenil to antagonize midazolam, and a starting dose of 0.2 mg of flumazenil is recommended with slow injection.

In this study, the time to recovery of spontaneous breathing and extubation were longer in group R than those in group P, which may be improved after flumazenil antagonism. Although many studies have shown that midazolam cannot achieve the same depth of sedation as propofol, there were no differences in MOAA/S scores between the two groups at various time points in this study, and both groups met the sedation depth requirements for vocal cord polypectomy. The incidence of intraoperative hypotension and injection site pain were lower in the group R than those in the group P, and other adverse reactions during the perioperative period (including nausea and vomiting, drug allergies, and coughing reactions) did not differ between the groups. Therefore, remimazolam can maintain more stable hemodynamics, making it more advantageous in the elderly.

The operation time of vocal cord polypectomy under support laryngoscope is short, but the stimulation is large, which requires deep anesthesia during the operation and rapid recovery of neuromuscular function after operation. Therefore, this study used mivacurium chloride to achieve rapid extubation and reduce complications, decrease residual neuromuscular blockade, and improve postoperative recovery quality. Studies have shown that using 0.25 mg/kg of mivacurium chloride for anesthesia induction can meet intubation conditions without significant histamine release, making it safe for clinical use [14-15].

Limitations of this study include: firstly, the temporary decrease in postoperative recovery quality observed in patients after remimazolam administration for general anesthesia, although not clinically significant, the mechanism behind this phenomenon is unclear. Secondly, due to the limitations of the designated time for using the scale, this study did not evaluate the QoR-15 scale scores of patients during their stay in the PACU, which may provide more valuable results; thirdly, although previous studies have confirmed the safety and efficacy of midazolam in elderly patients and its lack of significant interference with postoperative recovery in elderly patients undergoing laparoscopic surgery[16-17], elderly

patients are still at high risk for postoperative delirium and cognitive dysfunction, and it is unclear how it affects postoperative recovery quality in elderly patients[18].

In summary, the combination of remimazolam and mivacurium chloride can safely be used for supporting vocal cord polypectomy. While meeting the requirements for anesthesia induction, supporting laryngoscopy exposure, and surgical needs, it can maintain more stable hemodynamics compared to propofol, and does not affect the postoperative recovery quality of patients compared to propofol.

Conflict of Interest None

Author Contributions Statement

JIAO Zhongyu, WANG Peishan, MENG Ruixia, and WANG Kai proposed the main research objectives, were responsible for the conception and design of the study, implementation of the research, and writing of the paper; WANG Kai and XIAO Ran collected and organized the data; JIAO Zhongyu and YUAN Mengyi conducted the statistical analysis, and prepared the figures and tables for presentation; JIAO Zhongyu revised the paper; WANG Peishan and MENG Ruixia were responsible for the quality control and review of the article, overall responsibility for the article, and supervision and management.

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·论　著·

瑞马唑仑联合米库氯铵对声带息肉切除术后患者恢复质量的影响

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摘要：目的　采用 15 项恢复质量评分量表(QoR-15)评估对比瑞马唑仑与丙泊酚对支撑喉镜下声带息肉切除术患者术后恢复质量的影响。**方法**　选择 2022 年 12 月至 2023 年 10 月新乡医学院第四临床学院行支撑喉镜下声带息肉切除术患者 90 例，采用随机区组设计法随机分为瑞马唑仑联合米库氯铵组(R 组)和丙泊酚联合米库氯铵组(P 组)，每组 45 例。通过静脉给药，R 组患者给予瑞马唑仑 0.2～0.3 mg/kg，P 组患者给予丙泊酚 1.5～2.0 mg/kg，待患者睫毛反射消失后，均给予舒芬太尼 0.3 μg/kg、米库氯铵 0.25 mg/kg。于手术前 1 d、术后第 1 天、术后第 2 天，采用 QoR-15 量表评估患者术后恢复质量。记录两组患者不同时间点的平均动脉压、心率、脉搏血氧饱和度、改良警觉/镇静量表(MOAA/S)评分；记录各项所需时间[包括手术、术后自主呼吸恢复、气管导管拔除以及麻醉后监测治疗室(PACU)停留]；记录术中及术后不良反应发生情况。**结果**　R 组患者术后 1 d 的 QoR-15 量表评分低于 P 组($P<0.05$)，由于 QoR-15 量表评分最小临床意义变化值为 6 分，所以其不具有临床意义；R 组患者恢复自主呼吸时间、拔管时间长于 P 组($P<0.05$)，两组 PACU 停留时间差异无统计学意义($P>0.05$)；R 组患者低血压、注射部位疼痛发生率低于 P 组(24.4% *vs* 64.4%，$\chi^2=14.580$，$P<0.01$；6.7% *vs* 84.4%，$\chi^2=54.878$，$P<0.01$)，其他不良反应发生率差异无统计学意义($P>0.05$)。**结论**　在支撑喉镜下声带息肉切除术麻醉中，使用瑞马唑仑的患者术后恢复质量与丙泊酚相当，在满足围术期需要的同时，能够维持更加稳定的血流动力学，且无明显的注射部位疼痛情况，能提高患者围术期的舒适度。

关键词： 声带息肉切除；术后恢复质量；瑞马唑仑；米库氯铵；丙泊酚；15 项恢复质量量表
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Effects of remimazolam combined with mivacurium on recovery quality of patients after vocal cord polypectomy

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Abstract: Objective　To evaluate the effects of remimazolam versus propofol on the quality of postoperative recovery in patients undergoing vocal cord polypectomy with supportive laryngoscopy by the 15-item quality of recovery scale (QoR-15). **Methods**　A total of 90 patients who underwent vocal cord polypectomy with supported laryngoscopy from the Fourth Clinical College of Xinxiang Medical University from December 2022 to October 2023 were divided into remimazolam combined with mivacurium group (group R) and propofol combined with mivacurium group (group P) by random block design method, with 45 cases in each group. By intravenous administration, patients in group R and group P were given remiazolam 0.2 to 0.3 mg/kg and propofol 1.5 to 2.0 mg/kg, respectively. After the disappearance of eyelash reflex, sufentanil 0.3 g/kg and mivacurium 0.25 mg/kg were given to all patients. The quality of postoperative

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recovery was evaluated by the QoR-15 scale 1 day before, 1 day and 2 days after surgery. Mean arterial pressure, heart rate, pulse oxygen saturation, and Modified Observer's Assessment of Alertness/Sedation Scale (MOAA/S) scores of the two groups were recorded at different time points. The time required including surgery, recovery of spontaneous breathing, endotracheal tube removal, and post anesthesia care unit (PACU) stay after surgery, and the occurrence of intra- and post-operative adverse reactions were recorded. **Results** The QoR-15 scale score of group R was lower than that of group P ($P<0.05$) on the first day after surgery, but it was not clinically significant because the minimum clinically significant change value of QoR-15 scale score was 6 points. The recovery time of spontaneous breathing and extubation time in group R were longer than those in group P ($P<0.05$), but there was no significant difference in PACU stay time between the two groups ($P>0.05$). The incidences of hypotension and injection site pain in group R were lower than those in group P (24.4% *vs* 64.4%, $\chi^2=14.580$, $P<0.01$; 6.7% *vs* 84.4%, $\chi^2=54.878$, $P<0.01$), and no significant difference was found in the incidence of other adverse reactions ($P>0.05$). **Conclusion** In the anesthesia of vocal cord polypectomy under supported laryngoscopy, the quality of patients recovery using remimazolam is comparable to that of propofol. While meeting perioperative needs, it can maintain more stable hemodynamics, without significant injection site pain, and can improve perioperative patient's comfort.

Keywords: Vocal cord polypectomy; Postoperative recovery quality; Remimazolam; Mivacurium; Propofol; The 15-item quality of recovery scale

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支撑喉镜下声带息肉切除术为耳鼻喉科常见手术之一，其具有时间短、对患者咽喉部刺激强烈等特点。麻醉医生常规会选择深度麻醉诱导方案来减轻插支撑喉镜时对患者产生的刺激以及术中局部使用肾上腺素而引起的应激反应，但也因此造成患者术后苏醒时间延长、苏醒质量不佳、肌松药代谢不全、易发生烦躁、麻醉后监测治疗室(post anesthesia care unit，PACU)停留时间过长等问题。随着加速康复外科(enhanced recovery after surgery，ERAS)理念的提倡，其核心是强调以患者为中心的诊疗理念，对涉及围术期处理的临床路径予以优化，通过缓解患者围术期各种应激反应，达到减少患者术后并发症的发生、缩短患者住院时间及促进康复的目的[1]。因此，近年来对于声带息肉切除主张选择起效快、代谢快的麻醉药物，或行超声引导下喉上神经阻滞，来减少支撑喉镜引起的应激反应[2]，减少麻醉药物的用量，以缩短患者复苏时间，保证患者高苏醒质量，提高患者围术期的满意度。目前常用的全麻药物丙泊酚对患者呼吸抑制较为明显，且有注射痛、对血流动力学影响较大等缺点。常用的肌肉松弛药物顺阿曲库铵及罗库溴铵半衰期长于声带息肉切除术时间，而米库氯铵是短效非去极化肌松药，起效迅速，消除半衰期短，可达深度肌松要求，提供满意的气管插管和手术条件，与耳鼻喉科短小手术相契合[3]。瑞马唑仑是新型苯二氮䓬类镇静药，其不良反应小、代谢快，在全麻诱导中使用的安全性和有效性已得到证实[4]，适用于耳鼻喉科短小手术的镇静与麻醉诱导。本研究拟观察使用瑞马唑仑联合米库氯铵作用于声带息肉切除术中的效果及对患者术后恢复质量的影响，为临床麻醉诱导方案提供参考。

1　资料与方法

1.1　*研究设计*　本研究已获得新乡市中心医院伦理委员会批准(伦理号：2022-276-01)，于中国临床试验中心注册(注册号：ChiCTR2300068097)，并与患者及家属签署知情同意书。

本研究主要结局指标为术后 15 项恢复质量量表(the 15-item quality of recovery scale，QoR-15)评分，根据已经进行的预实验结果以及参考既往研究，术后第 1 天的 QoR-15 量表评分差异具有临床意义(根据 QoR-15 量表制作者发表的最新文章显示，其最小临床意义差值为 6 分[5])。笔者以术后第 1 天 QoR-15 量表评分情况估算样本量，预估瑞马唑仑组 QoR-15 量表评分比丙泊酚组低 10 分，标准差为 13，以检验效能(1−β)为 90%，检验水准 α 为 0.05。用 PASS 15.0 软件计算得出，每组需要 37 例患者，在考虑 20%的脱落率后，得出每组需要 45 例患者。

1.2　*研究对象*　按照上述研究设计的样本量计算结果及以下纳入排除标准，并剔除因生理解剖结构异常，导致支撑喉镜下声门暴露困难、手术操作时间过长或术后随访配合度较差等问题的患者，从 2022 年 12 月至 2023 年 10 月新乡医学院第四临床学院拟行支撑喉镜下声带息肉切除术患者中选择，最终纳入研究 90 例。由 1 名不参与麻醉诱导及随访的研究者负责招募对象，采用随机区组设计法随机分为两组($n=45$)：瑞

马唑仑—米库氯铵组(以下简称 R 组)和丙泊酚—米库氯铵(以下简称 P 组),分组安排采用信封保存,随访研究者以及患者对分组情况并不知晓。纳入标准:(1) 美国麻醉医师协会(ASA)分级为Ⅰ或Ⅱ级;(2) 年龄 18~60 岁,身体质量指数(BMI)为 18~28 kg/m^2;(3) 愿意接受试验研究并签署相关知情同意书。排除标准:(1) 有严重心、脑、肺、肝、肾和代谢疾病病史者;(2) 有酗酒史、安眠药服用史者;(3) 术前高血压患者收缩压>180 mmHg 和(或)舒张压>110 mmHg;(4) 有神经肌肉系统疾病、精神疾病者;(5) 怀疑有滥用麻醉性镇痛药或镇静药者;(6) 已知对苯二氮䓬类药物和肌肉松弛药物过敏者;(7) 存在困难气道、支撑喉镜暴露困难者。

1.3　基线资料　术前 1 d,采用中文版 QoR-15 量表评估患者情况,并以此作为基线。QoR-15 量表[6]从患者的舒适度、情绪状态、身体独立、心理支持和疼痛 5 个维度来反映其术后恢复质量。经有关研究检验显示:中文版 QoR-15 量表的有效性和可靠性与 QoR-15 量表相当[7]。患者术后恢复质量受多种因素的影响,如手术操作刺激的强弱、息肉的大小、出血量的多少、患者身体素质差异等。本研究进一步使用综合并发症指数(comprehensive complication index, CCI)[8]及外科 Apgar 评分[9]来简易评估患者的并发症以及术中操作情况,确保两组患者基本特征及手术情况相近。两组患者的年龄、性别比、BMI 值、ASA 分级、手术时长、外科 Apgar 评分、术前 QoR-15 评分比较,差异无统计学意义(P>0.05)。见表 1。两组患者 CCI 分值的 $M(Q)$ P 组为 0(0),R 组为 0(0),组间比较差异无统计学意义(Z=0.391, P=0.696)。

1.4　麻醉方法　所有患者常规术前禁水 4 h、禁食 8 h。入手术室后,开放外周静脉通路,监测患者心电图、无创血压(NIBP)、脉搏血氧饱和度(SpO_2)、脑电双频指数(BIS)、呼气末 CO_2 分压($P_{ET}CO_2$),给予患者氧流量为 2~3 L/min 面罩吸氧。麻醉诱导:P 组予以静脉注射丙泊酚乳状液 1.5~2.0 mg/kg,R 组予以患者静脉推注苯磺酸瑞马唑仑 0.2~0.3 mg/kg,待患者睫毛反射消失后,两组患者静脉推注米库氯铵 0.25 mg/kg、舒芬太尼 0.3 μg/kg,后由麻醉医师插入 6.0 普通气管导管,行机械通气。设定潮气量(VT)为 6~8 mL/kg,呼吸频率 12~20 次/min,吸呼比 1∶2,调整呼吸机参数,维持患者正常 $P_{ET}CO_2$ 于 35~45 mmHg(1 mmHg=0.133 kPa)。术中麻醉维持:R 组静脉持续泵注苯磺酸瑞马唑仑 0.5~1 mg/(kg·h),P 组泵注丙泊酚乳状液 4~6 mg/(kg·h),维持 BIS 值在 40~60,手术结束停止维持药物的输注,将患者转入 PACU 进行复苏。

1.5　观察指标　(1) 记录患者术前 1 d、术后第 1 天(POD1)、术后第 2 天(POD2)的 QoR-15 量表评分。(2) 记录麻醉诱导前(T0)、诱导后(T1)、插入气管导管(T2)、插支撑喉镜(T3)、手术开始(T4)、手术结束(T5)和拔除气管导管时(T6)的平均动脉压(MAP)、心率(HR)、SpO_2、改良警觉/镇静量表评分(MOAA/S;0 分为对术后任何疼痛和刺激无反应,5 分为反应灵敏。(3) 记录手术时间、恢复自主呼吸时间(停药至患者恢复自主呼吸时间)、拔除气管导管时间、PACU 停留时间(进入 PACU 至改良 Aldrete 恢复评分满足 9 分的时间)。(4) 记录术中及术后不良反应发生情况,如注射部位疼痛、低血压情况(血压相对入室基础值降低幅度超过 20%)、呛咳反应、体动反应、苏醒期躁动情况、术后恶心呕吐情况、术中知晓以及过敏反应等。

1.6　统计学方法　所有数据采用 SPSS 26.0 软件分析处理。用 Shapiro-Wilk 法进行正态性检验,满足正态性和方差齐性的计量资料以 $\bar{x}\pm s$ 表示,组间比较采用独立样本 t 检验,不满足方差齐性的采用 t' 检验;非正态分布的计量资料采用 $M(IQR)$ 表示,组间比较采用 Mann-Whitney U 检验;计数资料以例数和百分数表示,采用 χ^2 检验。P<0.05 表示差异有统计学意义。

2　结　果

2.1　两组患者围术期相关指标情况比较　两组间各时间点 SpO_2、HR 比较,差异无统计学意义(P>0.05)。与 R 组相比,P 组患者 T1~T3 时间点的 MAP 降低(P<0.05)。见表 2。两组 T0 时 MOAA/S 评分均为 5 分;T1 时 MOAA/S 评分的 $M(IQR)$ P 组为 0(0),R 组为 0(0),组间差异无统计学意义(Z=1.334, P=0.182);T2~T5 时 MOAA/S 评分两组均为 0 分;T6 时的 $M(IQR)$ P 组为 5(5),R 组为 5(5),组间差异无统计学意义(Z=1.372, P=0.170)。表 3 可见,两组患者 PACU 停留时间比较,差异无统计学意义(P>0.05),但 R 组恢复自主呼吸时间、拔除气管导管时间均长于 P 组(P<0.05)。

2.2　两组患者不良反应情况比较　R 组患者术中低血压、注射部位疼痛发生率低于 P 组(P<0.01)。两组患者呛咳、体动反应、苏醒期躁动、术后恶心呕吐情况等差异无统计学意义(P>0.05),见表 4。研究过程中未见术中知晓、药物过敏等其他不良反应。

2.3　两组患者间术后 QoR-15 量表评分比较　术后第 1 天 R 组患者 QoR-15 量表评分低于 P 组患者,差

异有统计学意义(P<0.05),由于 QoR-15 量表评分最小临床意义为 6 分,所以其并不具有临床意义。术后第 2 天两组患者 QoR-15 量表评分差异无统计学意义(P>0.05)。见表 5。

表 1　两组患者一般情况和手术时长的比较　(n=45, $\bar{x}\pm s$)

Tab. 1　Comparison of patients' general conditions and operation duration between two groups　(n=45, $\bar{x}\pm s$)

组别	男/女(例)	年龄(岁)	BMI(kg/m^2)	ASA 分级(Ⅰ/Ⅱ,例)	手术时间(min)	外科 Apgar 评分(分)	术前 QoR-15 量表评分(分)
P 组	27/18	40.2±9.1	23.8±1.9	35/10	9.3±2.1	9.6±0.6	142.5±6.1
R 组	25/20	41.2±10.9	24.2±2.1	33/12	8.9±2.7	9.4±0.7	140.2±6.8
χ^2/t 值	0.182	0.474	0.947	0.241	0.784	1.455	1.689
P 值	0.669	0.636	0.346	0.624	0.434	0.149	0.094

表 2　两组间各时间点 MAP、HR 和 SpO_2 的比较　(n=45, $\bar{x}\pm s$)

Tab. 2　Comparison of MAP, HR and SpO_2 of patients at each time point between two groups　(n=45, $\bar{x}\pm s$)

组别	指标	T0	T1	T2	T3	T4	T5	T6
P 组	MAP(mmHg)	95.9±14.3	81.3±9.2	82.9±11.3	87.3±9.0	88.1±11.2	88.6±10.4	96.7±12.8
R 组	MAP(mmHg)	91.8±11.4	89.4±10.1	90.1±12.4	92.2±10.6	90.1±9.8	90.7±12.3	93.7±11.2
t 值		1.503	3.977	2.879	2.364	0.902	0.875	1.183
P 值		0.136	<0.001	0.005	0.020	0.370	0.384	0.240
P 组	HR(次/min)	74.6±10.2	76.4±9.1	76.9±11.7	79.2±11.0	73.8±12.9	75.9±8.8	81.1±13.7
R 组	HR(次/min)	76.6±12.8	77.4±10.2	78.8±8.8	82.0±12.5	77.8±10.3	74.8±10.9	78.3±9.0
t 值		0.820	0.491	0.871	1.128	1.625	0.527	1.131
P 值		0.415	0.625	0.386	0.262	0.108	0.600	0.260
P 组	SpO_2(%)	99.4±0.5	99.6±0.5	99.7±0.4	99.9±0.3	99.8±0.4	99.9±0.4	98.2±1.3
R 组	SpO_2(%)	99.5±0.5	99.5±0.5	99.6±0.5	99.8±0.4	99.7±0.5	99.8±0.4	97.6±1.6
t 值		0.948	0.948	1.047	1.341	1.047	1.186	1.952
P 值		0.345	0.345	0.297	0.183	0.297	0.239	0.054

表 3　两组患者恢复自主呼吸、拔除气管导管、PACU 停留的时间比较　(n=45, min, $\bar{x}\pm s$)

Tab. 3　Comparison of the time taken for two groups of patients to recover spontaneous breathing, remove tracheal catheters, and stay in PACU　(n=45, min, $\bar{x}\pm s$)

组别	恢复自主呼吸时间	拔除气管导管时间	PACU 停留时间
P 组	7.1±1.5	14.5±5.6	27.4±4.1
R 组	8.2±2.1	16.8±5.0	29.4±5.9
t 值	2.859	2.055	1.878
P 值	0.005	0.042	0.063

表 4　两组患者不良反应发生率比较　[n=45, 例(%)]

Tab. 4　Comparison of adverse reaction rates between two groups of patients　[n=45, case(%)]

组别	注射部位疼痛	恶心呕吐	呛咳反应	低血压	苏醒期躁动	体动反应
P 组	38(84.4)	3(6.7)	6(13.3)	29(64.4)	10(22.2)	2(4.4)
R 组	3(6.7)	5(11.1)	2(4.4)	11(24.4)	6(13.3)	5(11.1)
χ^2 值	54.878	0.137	1.234	14.580	1.216	0.619
P 值	<0.001	0.711	0.266	<0.001	0.270	0.431

表 5　两组患者术后 QoR-15 量表评分比较　(分, $\bar{x}\pm s$)

Tab. 5　Comparison of postoperative QoR-15 scale scores between two groups of patients　(point, $\bar{x}\pm s$)

QoR-15 量表评分	例数	POD 1	POD 2
P 组	45	126.2±11.0	138.0±6.2
R 组	45	121.3±10.2	136.8±6.9
t 值		2.191	0.867
P 值		0.031	0.387

3　讨　论

临床工作中,常从患者康复效果、术后并发症、不良反应等方面评估患者术后的恢复质量,但也容易忽略患者的主观感受,如患者术后疼痛、失眠、焦虑、身体舒适度较差、情绪状态不稳定等。中文版 QoR-15 量表,从舒适度、情绪状态、身体独立性、心理支持和疼痛 5 个维度来全面评估患者的术后恢复质量,随着 ERAS 的提倡,在诊疗过程中,应考虑更多方面。

本研究比较了使用瑞马唑仑与丙泊酚对声带息肉切除术中患者术后恢复质量的影响。结果显示,瑞马唑仑组患者在术后第 1、2 天的 QoR-15 量表评分低于丙泊酚组,但术后第 2 天组间差异无统计学意义,亦即使用瑞马唑仑后患者术后恢复质量稍有降低,但整体并不差于丙泊酚。这与相关研究结果相近[10]。对 QoR-15 量表评分的 5 个维度分析发现,评分下降主要发生在身体舒适度和情绪状态两个方面,这可能与患者术前焦虑及苯二氮䓬类药物对人体认知功能的影响有关,瑞马唑仑在体内可被组织脂酶水解为唑仑丙酸,唑仑丙酸几乎无药理活性[11],不存在药物蓄积,对患者神经精神功能影响较小,但仍需关注患者的精神状态。

本研究未使用氟马西尼进行镇静拮抗治疗,所以

尚不清楚当使用氟马西尼进行拮抗后，患者的恢复质量能否得到提高。值得警惕的是，Yamamoto 等[12]发现术后使用氟马西尼对瑞马唑仑进行拮抗后，患者会再次进入镇静状态。Masui[13]的药代动力学模拟研究显示，当给予较高剂量氟马西尼拮抗瑞马唑仑镇静效果时，患者发生再镇静的风险更高，这是由于氟马西尼对苯二氮䓬类药物的拮抗机制仅表现为竞争性拮抗，随着氟马西尼血药浓度的降低，瑞马唑仑的镇静效果可能会再次出现，所以当瑞马唑仑残余剂量过高，且无法持续监护患者生命体征时，不建议常规给予高剂量氟马西尼去拮抗瑞马唑仑，推荐以 0.2 mg 的氟马西尼作为初始剂量并缓慢注射。

本研究中 R 组患者恢复自主呼吸时间及拔除气管导管时间稍长于 P 组，可能给予氟马西尼拮抗后，会改善这种情况。虽有不少研究结果表明瑞马唑仑并不能达到丙泊酚同样的镇静深度，但本研究中各时间点两组患者 MOAA/S 评分无差异，且均能满足声带息肉切除术所需的镇静深度。R 组患者术中低血压、注射部位疼痛发生率低于 P 组，其他围术期的不良反应无差异，因此，瑞马唑仑能够维持更加稳定的血流动力学，在老年患者的应用中更具优势。

支撑喉镜下声带息肉切除术手术时间短，但刺激大，术中需要深度麻醉以及术后神经肌肉功能的快速恢复，因此本研究使用米库氯铵来达到术后快速拔管、降低并发症、减少发生术后肌松残余问题，提高了患者术后恢复质量。有研究表明，全麻诱导中使用 0.25 mg/kg的米库氯铵，能够满足插管条件，且无明显的组胺释放，可安全应用于临床[14-15]。

本研究存在以下局限性：首先，笔者发现瑞马唑仑用于全身麻醉后，患者术后恢复质量短暂下降，虽不具有临床意义，但其背后的机制尚不清楚。其次，由于量表规定使用时间的局限性，本研究未评估患者苏醒后在 PACU 停留时的 QoR-15 量表评分，可能其间的结果更具有价值；第三，既往研究虽已证实瑞马唑仑作用于老年患者的安全性与有效性[16-17]，且对老年患者腹腔镜手术后苏醒无明显干扰[18]，但老年患者仍是术后谵妄、认知功能障碍的高危人群，其对老年患者术后恢复质量影响如何，尚不清楚。

综上所述，瑞马唑仑联合米库氯铵可安全作用于支撑喉镜下声带息肉切除术中，在满足麻醉诱导、支撑喉镜暴露及手术需要的同时，能够维持更加稳定的血流动力学，且与丙泊酚相比，并不会影响患者的术后恢复质量。

利益冲突　本文不涉及相关利益冲突

作者贡献声明　焦钟雨、王培山、孟瑞霞、王凯提出主要研究目标，负责研究的构思与设计，研究的实施，撰写论文；王凯、肖燃进行数据收集与整理；焦钟雨、袁梦依进行统计学处理，图、表的绘制；焦钟雨进行论文的修订；王培山、孟瑞霞负责文章的质量控制，对文章整体负责，监督管理。

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