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Effect of ketorolac tromethamine combined with lidocaine on the periextubation period of thyroid surgery in hypertensive patients

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Abstract: Objective To investigate the effect of ketorolac tromethamine combined with lidocaine on the mean arterial pressure (MAP), heart rate, 24-hour postoperative drainage volume, and Visual Analogue Scale (VAS) score for sore throat during the peri-extubation period in hypertensive patients undergoing thyroid surgery. **Methods** A total of 80 hypertensive patients scheduled for elective thyroid surgery at People's Hospital of Xinjiang Uygur Autonomous Region from December 2020 to March 2023 were randomly selected and divided into four groups: A, B, C, and D. Group A received 1 mL of normal saline before tumor resection and 10 mL of normal saline at the end of the surgery. Group B received 30 mg of ketorolac tromethamine in 1 mL before tumor resection and 10 mL of normal saline at the end of the surgery. Group C received 1 mL of normal saline before tumor resection and 1.5 mg/kg of lidocaine diluted to 10 mL at the end of the surgery. Group D received 30 mg of ketorolac tromethamine in 1 mL before tumor resection and 1.5 mg/kg of lidocaine diluted to 10 mL at the end of the surgery. All medications were administered as a single intravenous injection. MAP and heart rate were recorded before anesthesia induction, at extubation, 5 minutes after extubation, and 15 minutes after extubation. Coughing scores at extubation, postoperative adverse reactions, 24-hour postoperative drainage volume, and VAS scores for sore throat were also recorded. **Results** There was a significant difference in coughing scores at extubation among the four groups (H=31.658, P<0.01). The MAP and heart rates at 5 and 15 minutes after extubation in Groups B, C and D were lower than those in Group A(P<0.05). The VAS scores for sore throat 24 hours after extubation were 1.95±0.69 in Group A, 0.90±0.64 in Group B, 2.25±0.79 in Group C, and 0.75±0.64 in Group D, with a significant difference among the four groups (F=23.508, P<0.01). The VAS scores in Groups B and D were significantly lower than those in Groups A and C, respectively(P<0.05). There was a statistically significant difference in 24-hour postoperative drainage volume among the four groups (F=204.309, P<0.01). There was no statistically significant difference in the incidence of other adverse reactions after extubation among the four groups (P>0.05). **Conclusion** Intravenous administration of lidocaine combined with ketorolac tromethamine in hypertensive patients undergoing thyroid surgery can effectively reduce adverse reactions such as sore throat and coughing during the peri-extubation period while maintaining stable MAP and heart rate.

Keywords: Lidocaine; Ketorolac tromethamine; Thyroid tumor; Thyroid surgery; Hypertension; Sore throat; Coughing; Mean arterial pressure

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Thyroid surgery is one of the primary treatment modalities for thyroid tumors. The operative field in thyroid surgery involves complex anatomical structures and is highly vascular. Endotracheal intubation and extubation can easily induce significant hemodynamic changes [1-3]. Particularly in hypertensive patients, the peri-extubation period is prone to dramatic fluctuations in the circulatory system, which may even lead to postoperative hemorrhage, induce or exacerbate myocardial ischemia, stroke, and renal failure, among other complications [4]. This places higher demands on surgical anesthesia management. Lidocaine is an amide-type anesthetic agent widely used clinically for local anesthesia and anti-arrhythmic purposes [5-6]. Previous studies have shown that intravenous lidocaine can reduce postoperative pain, decrease coughing during extubation, and ameliorate hemodynamic fluctuations caused by intubation [7-8]. Ketorolac tromethamine is a novel non-steroidal anti-inflammatory drug widely used for the short-term treatment of acute moderate to severe pain, including postoperative pain, with distinct clinical advantages [9-10]. This study adopted an approach involving administration of ketorolac tromethamine before thyroid mass resection and intravenous injection of lidocaine at the end of surgery to investigate its effects on the peri-extubation period in hypertensive patients undergoing thyroid surgery. The aim is to provide clinical reference for improving the comfort and safety of such patients during general anesthesia recovery.

1 Materials and Methods

1.1 General Information

This study is a randomized controlled trial approved by the Ethics Committee of the People's Hospital of Xinjiang Uygur Autonomous Region. Eighty patients scheduled for elective thyroid surgery under general

anesthesia with endotracheal intubation at the People's Hospital of Xinjiang Uygur Autonomous Region between December 2020 and March 2023 were randomly selected. All patients had coexisting hypertension. Inclusion criteria: (1) American Society of Anesthesiologists (ASA) physical status classification II–III; (2) Age 35–70 years; (3) Coexisting primary hypertension, without severe target organ damage caused by hypertension; (4) Surgery duration 1–3 hours; (5) Body mass index (BMI) 21–28 kg/m². Exclusion criteria: (1) History of allergy to lidocaine or ketorolac tromethamine; (2) Coexisting diabetes, heart disease, or severe hepatic/renal dysfunction; (3) Difficult airway; (4) History of repeated intubation attempts and chronic pharyngitis.

Patients meeting the inclusion criteria were divided into four groups using a random number table, with 20 patients in each group. Group A was the control group, Group B was the ketorolac tromethamine group, Group C was the lidocaine group, and Group D was the lidocaine combined with ketorolac tromethamine group. There were no statistically significant differences among the four groups in terms of age, gender, BMI, ASA classification, or surgery duration (P>0.05). See **Table 1.**

Tab.1 Comparison of general data in four groups(n=20, $\bar{x}$ ±s)

Group	Age (years)	M/F (case)	BMI (kg/m²)	ASA II/III (case)	Surgery time(min)
Group A	52.00±6.88	8/12	23.62±2.96	12/8	122.25±22.45
Group B	51.70±5.27	7/13	22.53±1.73	13/7	114.50±21.7
Group C	55.35±5.88	6/14	22.11±1.99	14/6	126.25±19.19
Group D	54.50±5.93	7/13	22.64±2.53	14/6	120.75±18.01
***F*/χ^2 value**	1.816	0.440	1.465	0.615	1.142
***P* value**	0.151	0.932	0.231	0.893	0.337

1.2 Anesthesia Method

A comprehensive preoperative assessment of the patient's condition was conducted to formulate the anesthesia plan. Informed consent was obtained from the patients, who underwent routine fasting for 8 hours preoperatively. Upon entering the operating room, routine monitoring of electrocardiogram (ECG), blood pressure, heart rate, and saturation of peripheral oxygen (SpO_2) was established, along with monitoring of body temperature and the depth of anesthesia using the Bispectral Index (BIS).

The following drugs were administered in anesthesia induction: midazolam (Yichang Humanwell Pharmaceutical, H20067040) 0.03 mg/kg; propofol (Xi'an Libang Pharmaceutical, H20010368) 1.5 mg/kg; sufentanil (Jiangsu Enhua Pharmaceutical Co., Ltd., H20203650) 0.5 μg/kg; vecuronium (Chengdu Tiantai Mountain Pharmaceutical, H20063411) 0.1 mg/kg.

After loss of consciousness and muscle relaxation, the endotracheal tube was inserted, and controlled ventilation was initiated via the breathing circuit.

Anesthesia Maintenance: Propofol was infused at a rate of 4–12 $mg \cdot kg^{-1} \cdot h^{-1}$, and remifentanil (China National Pharmaceutical Group Industry, H20123421) was infused at a rate of 0.1–1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$. The infusion rates were adjusted based on the BIS value to maintain it between 40–60 during surgery. At the end of surgery, the infusion of propofol and remifentanil was stopped. Suctioning under low negative pressure (80–120 mmHg) was performed as needed. The endotracheal tube was removed when the patient was awake, spontaneous breathing had resumed, the BIS value returned to 85, the patient could follow commands such as opening eyes, opening mouth, and protruding tongue, and the spontaneous tidal volume exceeded 5 mL/kg.

1.3 Grouping

Group A: Received 1 mL of normal saline before tumor resection and 10 mL of normal saline at the end of surgery.

Group B: Received 30 mg ketorolac tromethamine in 1 mL before tumor resection and 10 mL of normal saline at the end of surgery.

Group C: Received 1 mL of normal saline before tumor resection and 1.5 mg/kg lidocaine diluted to 10 mL at the end of surgery.

Group D: Received 30 mg ketorolac tromethamine in 1 mL before tumor resection and 1.5 mg/kg lidocaine diluted to 10 mL at the end of surgery.

All experimental drugs were administered as single intravenous injections.

1.4 Observation Indicators

Coughing score at extubation: Coughing severity was graded as: Grade 1, no cough (0 times); Grade 2, mild cough (1–2 times); Grade 3, moderate cough (3–4 times); Grade 4, severe cough (≥5 times).

Hemodynamic parameters: Mean arterial pressure (MAP) and heart rate were recorded before anesthesia induction (T1), immediately after extubation (T2), 5 minutes after extubation (T3), and 15 minutes after extubation (T4).

Postoperative sore throat: Visual Analogue Scale (VAS) score for sore throat 24 hours postoperatively.

Other adverse reactions during the recovery period after extubation: Including nausea/vomiting, agitation, bradycardia, etc.

Postoperative drainage volume: Drainage volume 24 hours postoperatively.

1.5 Statistical Methods

Statistical analysis was performed using SPSS 26.0 software. Measurement data conforming to a normal distribution are expressed as $\bar{x} \pm s$. One-way analysis of variance (ANOVA) was used for comparisons among multiple groups, and the LSD-t test was used for pairwise comparisons. Repeated measures analysis of variance was used for multi-time-point comparisons. Count data are expressed as number (percentage) and compared using the chi-square test. Ordinal categorical variables were analyzed using non-parametric rank-sum tests; the Kruskal-Wallis H test was used for comparisons among multiple groups, and the Mann-Whitney U test was used for pairwise comparisons. A two-sided test was used with a significance level of α=0.05.

2 Results

2.1 Comparison of Cough Scores Among the Four Groups at Extubation

The Kruskal-Wallis *H* test showed that there were statistically significant differences in cough scores among the four groups at extubation ($P<0.01$). Pairwise comparisons revealed that Group A differed significantly from Group C and Group D (Z=3.512, $P<0.01$; Z=4.445, $P<0.01$), but not from Group B (Z=0.809, $P=0.419$). Group B also differed significantly from Group C and Group D (Z=3.093, $P=0.002$; Z=4.279, $P<0.01$). See **Table 2.**

2.2 Comparison of MAP and Heart Rate Among the Four Groups at Different Time Points

Within-group comparisons at different time points: In Group A, MAP and heart rate at T2, T3, and T4 were higher than those at T1 ($P<0.05$). In Group B, MAP at T2 was higher than that at T1 ($P<0.05$). In Groups C and D, there were no statistically significant differences in MAP and heart rate between T2–T4 and T1 ($P>0.05$). Between-group comparisons at the same time points: At T2, MAP and heart rate in Groups C and D were lower than those in Groups A and B, with statistically significant differences ($P<0.05$). At T3 and T4, MAP and heart rate in Groups B, C, and D were lower than those in Group A, with statistically significant differences ($P<0.05$). See **Table 3.**

2.3 Comparison of Sore Throat VAS Scores 24 Hours After Extubation

The sore throat VAS scores 24 hours after extubation were (1.95 ± 0.69) points in Group A, (0.90 ± 0.64) points in Group B, (2.25 ± 0.79) points in Group C, and (0.75 ± 0.64) points in Group D. There were statistically significant differences among the four groups ($F=23.508$, $P<0.01$). The VAS score in Group B was lower than that in Group A ($t=4.989$, $P<0.01$) and Group C ($t=5.938$, $P<0.01$), while the VAS score in Group D was lower than that in Group A ($t=5.702$, $P<0.01$) and Group C ($t=6.598$, $P<0.01$). However, there were no statistically significant differences in VAS scores between Group A and Group C ($t=1.279$, $P=0.209$) or between Group B and Group D ($t=0.741$, $P=0.463$).

2.4 Comparison of Postoperative Drainage

The drainage volumes at 24 hours postoperatively were (104.50 ± 6.47) mL in Group A, (102.75 ± 7.16) mL in Group B, (70.25 ± 4.99) mL in Group C, and (69.00 ± 5.76) mL in Group D. There were statistically significant differences in drainage volume among the four groups ($F=204.309$, $P<0.01$). The drainage volume in Group C was lower than that in Group A ($t=18.746$, $P<0.01$) and Group B ($t=5.938$, $P<0.01$), and the drainage volume in Group D was lower than that in Group A ($t=18.746$, $P<0.01$) and Group B ($t=16.654$, $P<0.01$), with all differences being statistically significant.

2.5 Comparison of Other Adverse Reactions

The incidence rates of other adverse reactions (such as nausea and vomiting, agitation, bradycardia, etc.) after extubation among the four groups were as follows: 15% (3 cases) in Group A, 15% (3 cases) in Group B, 10% (2 cases) in Group C, and 5% (1 case) in Group D. There was no statistically significant difference among the groups ($\chi^2=1.377$, $P=0.711$).

Tab.2 Comparison of the cough scores after extubation among four groups of patients[case(%)]

Group	Case	Grade 1	Grade 2	Grade 3
Group A	20	2(10.0)	7(35.0)	11(55.0)
Group B	20	2(10.0)	10(50.0)	8(40.0)
Group C	20	9(45.0)	10(50.0)	1(5.0)
Group D	20	16(80.0)	3(15.0)	1(5.0)
***H* value**			31.658	
***P* value**			<0.001	

Tab.3 Comparison of MAP and heart rate at different time points among four groups ($n=20$, $\bar{x}$ ±s)

Group	MAP (mmHg)				Heart rate (times/min)			
	T1	T2	T3	T4	T1	T2	T3	T4
Group A	96.65±5.23	106.75±4.20[a]	105.9±4.01[a]	104.95±4.66[a]	73.2±5.34	86.55±3.85[a]	83.25±3.73[a]	77.9±5.31[a]
Group B	98.1±4.12	105.75±3.77[a]	101.1±4.46[b]	98.35±4.33[b]	72.1±5.66	84.25±4.78[a]	75.4±5.83[ba]	74.3±5.74[ba]
Group C	96.25±4.91	96.10±4.54[bc]	96.7±4.34[b]	96.45±4.57[b]	73.35±6.32	73.65±5.62[bc]	73.45±6.79[b]	73.3±5.91[b]
Group D	97.45±4.66	97.20±4.19[bc]	97.9±4.24[b]	98.25±4.33[b]	72.95±5.8	72.9±5.81[bc]	72.75±5.95[b]	72.45±5.45[b]
F_{group}/P_{group} **value**	20.434/<0.001				13.645/<0.001			
F_{time}/P_{time} **value**	21.857/<0.001				33.214/<0.001			
$F_{interaction}/P_{interaction}$ **value**	11.191<0.001				11.947/<0.001			

Note: Compared with T1, [a]$P<0.05$; Compared with Group A, [b] $P<0.05$; Compared with Group B, [c] $P<0.05$.

3 Discussion

Thyroid surgery involves complex anatomy and a rich vascular supply in the operative field. During the peri-extubation period, as the depth of anesthesia lightens, stimuli such as pain and coughing activate the sympathetic-adrenal medullary system, leading to a massive release of catecholamines and causing abnormal hemodynamic fluctuations [11-12]. In patients with coexisting hypertension, severe hemodynamic fluctuations may lead to postoperative hemorrhage and, in severe cases, can induce various cardiovascular complications such as myocardial ischemia, stroke, and cerebral hemorrhage, thereby reducing the quality of early postoperative recovery and prolonging hospital stay [4]. Previous studies have shown that intravenous lidocaine helps alleviate postoperative pain, reduce the coughing response during general anesthesia extubation, and improve hemodynamic fluctuations [13-15]. In a

randomized controlled study on thyroid cancer surgery, Shu et al. [16] administered intravenous lidocaine before anesthesia induction. The results showed that compared to the control group, this led to satisfactory postoperative analgesia and reduced the dosage of general anesthetics and the incidence of adverse reactions such as postoperative vomiting. Administering intravenous lidocaine 2 minutes after thyroidectomy helped improve the incidence of coughing and hemodynamic fluctuations in patients [17]. Previous research found that intravenous lidocaine at doses of 1.0–1.5 mg/kg results in blood concentrations within a safe range, while exceeding 2.0 mg/kg may pose risks [18]. In this study, a single injection of 1.5 mg/kg lidocaine at the end of surgery reduced coughing in hypertensive patients during the peri-extubation period, maintained hemodynamic stability during extubation, and reduced postoperative blood loss (drainage volume). However, regarding sore throat, there was no statistically significant difference in the 24-hour postoperative sore throat VAS score between the lidocaine group and the control group, suggesting its analgesic duration is short, which is consistent with previous studies.

Ketorolac tromethamine is a non-steroidal anti-inflammatory drug (NSAID) with potent analgesic effects. It inhibits prostaglandin synthesis to achieve analgesia and can be used for short-term treatment of acute moderate to severe pain, with fewer adverse reactions [19-20]. Studies have shown that pretreatment with intravenous ketorolac tromethamine before anesthesia induction can significantly reduce the incidence of sufentanil-induced coughing during general anesthesia induction and also significantly alleviate postoperative incisional pain and recovery agitation [21]. However, there is limited research on the effects of ketorolac tromethamine on the peri-extubation period in thyroid surgery. One study involving female patients undergoing thyroidectomy found that intravenous injection or infusion of ketorolac tromethamine before anesthesia induction reduced the incidence of adverse reactions such as post-extubation sore throat, coughing, and wound pain [22]. The results of this study indicate that intravenous injection of ketorolac tromethamine before tumor resection can reduce postoperative sore throat at 24 hours, but it does not show significant advantages in reducing postoperative coughing or maintaining hemodynamic stability. This may be due to the short half-life of ketorolac tromethamine and the relatively small dose used. Therefore, this study innovatively adopted a combined drug approach, administering intravenous ketorolac tromethamine before tumor resection and intravenous lidocaine at the end of surgery. The results showed no significant differences in MAP and heart rate immediately after extubation, 5 minutes after extubation, and 15 minutes after extubation compared to before induction. Furthermore, the 24-hour postoperative sore throat VAS score was lower than that in the lidocaine group. These results suggest that in thyroid surgery, compared to using lidocaine or ketorolac tromethamine alone, the combined approach of intravenous ketorolac tromethamine before tumor resection and lidocaine injection at the end of surgery offers more comprehensive advantages in reducing coughing, maintaining hemodynamic stability, and providing analgesia during the peri-extubation period.

In conclusion, the combination of lidocaine and ketorolac tromethamine can effectively reduce adverse reactions such as post-extubation sore throat, circulatory fluctuations, and coughing at extubation in hypertensive patients undergoing thyroid surgery. This helps improve the comfort and safety of such patients during the peri-extubation period.

Conflict of Interest None

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·论　著·

酮咯酸氨丁三醇联合利多卡因对高血压患者甲状腺手术围拔管期的影响

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摘要：目的　探讨酮咯酸氨丁三醇联合利多卡因对高血压患者行甲状腺手术围拔管期平均动脉压（MAP）、心率、术后24 h引流量及咽喉痛VAS评分的影响。**方法**　随机选取2020年12月至2023年3月于新疆维吾尔自治区人民医院择期行甲状腺手术的高血压患者80例，随机分为A、B、C、D四组。A组，肿物切除前给予1 mL生理盐水，手术结束时给予10 mL生理盐水；B组，肿物切除前给予30 mg酮咯酸氨丁三醇1 mL，手术结束时给予10 mL生理盐水；C组，肿物切除前给予1 mL生理盐水，手术结束时给予1.5 mg/kg利多卡因稀释至10 mL；D组，肿物切除前给予30 mg酮咯酸氨丁三醇1 mL，手术结束时给予1.5 mg/kg利多卡因稀释至10 mL。药物均采用单次静脉注射的方式。分别记录各组患者麻醉诱导前、拔管时、拔管后5 min及拔管后15 min的MAP和心率；记录拔管时呛咳评分、术后不良反应情况、术后24 h引流量和咽喉痛视觉模拟评分（VAS）。**结果**　四组患者拔管时的呛咳评分比较差异有统计学意义（H=31.658，P<0.01）。B组、C组和D组拔管后5 min和15 min的MAP和心率均低于A组（P<0.05）。拔管后24 h咽痛VAS评分A组为（1.95±0.69）分，B组为（0.90±0.64）分，C组为（2.25±0.79）分，D组为（0.75±0.64）分，四组间差异有统计学意义（F=23.508，P<0.01），且B组和D组VAS评分分别低于A组和C组，差异均有统计学意义（P<0.05）。四组术后24 h引流量差异有统计学意义（F=204.309，P<0.01）。四组患者拔管后其他不良反应发生率差异无统计学意义（P>0.05）。**结论**　合并高血压患者行甲状腺手术时静脉注射利多卡因联合酮咯酸氨丁三醇能有效减轻围拔管期的咽喉痛、呛咳等不良反应，同时维持MAP和心率的平稳。

关键词：利多卡因；酮咯酸氨丁三醇；甲状腺肿瘤；甲状腺手术；高血压；咽喉痛；呛咳；平均动脉压
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Abstract: Objective　To investigate the effect of ketorolac tromethamine combined with lidocaine on the mean arterial pressure (MAP), heart rate, 24-hour postoperative drainage volume, and Visual Analogue Scale (VAS) score for sore throat during the peri-extubation period in hypertensive patients undergoing thyroid surgery. **Methods**　A total of 80 hypertensive patients scheduled for elective thyroid surgery at People's Hospital of Xinjiang Uygur Autonomous Region from December 2020 to March 2023 were randomly selected and divided into four groups: A, B, C, and D. Group A received 1 mL of normal saline before tumor resection and 10 mL of normal saline at the end of the surgery. Group B received 30 mg of ketorolac tromethamine in 1 mL before tumor resection and 10 mL of normal saline at the end of the surgery. Group C received 1 mL of normal saline before tumor resection and 1.5 mg/kg of lidocaine diluted to 10 mL at the

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end of the surgery. Group D received 30 mg of ketorolac tromethamine in 1 mL before tumor resection and 1.5 mg/kg of lidocaine diluted to 10 mL at the end of the surgery. All medications were administered as a single intravenous injection. MAP and heart rate were recorded before anesthesia induction, at extubation, 5 minutes after extubation, and 15 minutes after extubation. Coughing scores at extubation, postoperative adverse reactions, 24-hour postoperative drainage volume, and VAS scores for sore throat were also recorded. **Results** There was a significant difference in coughing scores at extubation among the four groups (H=31.658, P<0.01). The MAP and heart rates at 5 and 15 minutes after extubation in Groups B, C and D were lower than those in Group A (P<0.05). The VAS scores for sore throat 24 hours after extubation were 1.95±0.69 in Group A, 0.90±0.64 in Group B, 2.25±0.79 in Group C, and 0.75±0.64 in Group D, with a significant difference among the four groups (F=23.508, P<0.01). The VAS scores in Groups B and D were significantly lower than those in Groups A and C, respectively (P<0.05). There was a statistically significant difference in 24-hour postoperative drainage volume among the four groups (F=204.309, P<0.01). There was no statistically significant difference in the incidence of other adverse reactions after extubation among the four groups (P>0.05). **Conclusion** Intravenous administration of lidocaine combined with ketorolac tromethamine in hypertensive patients undergoing thyroid surgery can effectively reduce adverse reactions such as sore throat and coughing during the peri-extubation period while maintaining stable MAP and heart rate.

Keywords: Lidocaine; Ketorolac tromethamine; Thyroid tumor; Thyroid surgery; Hypertension; Sore throat; Coughing; Mean arterial pressure

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甲状腺手术是甲状腺肿瘤的主要治疗方式之一，而甲状腺手术的操作区域解剖结构复杂、血管丰富，气管插管及拔管易引起剧烈的血流动力学改变[1-3]。尤其高血压患者，在围拔管期容易出现循环系统剧烈波动，甚至导致术后出血，诱发或加重心肌缺血、脑卒中以及肾功能衰竭等[4]，这对手术麻醉管理提出了更高的要求。利多卡因是一种酰胺类麻醉药，在临床上被广泛用于局部麻醉和抗心律失常[5-6]。既往研究表明，静脉注射利多卡因具有降低术后疼痛、减少拔管期呛咳、改善插管引起的血流动力学波动等作用[7-8]。而酮咯酸氨丁三醇是一种新型的非甾体抗炎药，广泛用于急性中度和重度疼痛的短期治疗，包括术后疼痛，临床优势明显[9-10]。本研究采用甲状腺肿物切除前给予酮咯酸氨丁三醇，手术结束时静脉注射利多卡因的方式，探讨其对行甲状腺手术的高血压患者围拔管期的影响，为提高此类患者在全身麻醉恢复期的舒适度和安全性提供临床参考。

1　资料与方法

1.1　一般资料　本研究为随机对照试验，已通过新疆维吾尔自治区人民医院伦理委员会批准，伦理审批号：KY202412020263(GZ2024)。随机选择2020年12月至2023年3月于新疆维吾尔自治区人民医院择期进行全身麻醉下气管插管的甲状腺手术患者80例，患者均合并高血压。纳入标准：(1) 美国麻醉医师学会(American Society of Anesthesiologists, ASA)分级Ⅱ~Ⅲ级；(2) 年龄35~70岁；(3) 合并原发性高血压，无高血压引起的靶器官严重受损；(4) 手术时间1~3 h；(5) 身体质量指数(body mass index, BMI)21~28 kg/m^2。排除标准：(1) 有利多卡因或酮咯酸氨丁三醇过敏史；(2) 合并糖尿病、心脏病、肝肾功能严重异常；(3) 困难气道；(4) 反复多次插管并有慢性咽炎。

采用随机数字表法将纳入的患者分为四组，每组20例。A组为对照组，B组为酮咯酸氨丁三醇组，C组为利多卡因组，D组为利多卡因联合酮咯酸氨丁三醇组。四组患者的年龄、性别、BMI、ASA分级和手术时间差异均无统计学意义(P>0.05)。见表1。

表1　四组患者一般情况比较　(n=20, $\bar{x}\pm s$)

Tab.1　Comparison of general data in four groups　(n=20, $\bar{x}\pm s$)

组别	年龄(岁)	男/女(例)	BMI(kg/m^2)	ASAⅡ/Ⅲ级(例)	手术时间(min)
A组	52.00±6.88	8/12	23.62±2.96	12/8	122.25±22.45
B组	51.70±5.27	7/13	22.53±1.73	13/7	114.50±21.70
C组	55.35±5.88	6/14	22.11±1.99	14/6	126.25±19.19
D组	54.50±5.93	7/13	22.64±2.53	14/6	120.75±18.01
F/χ^2值	1.816	0.440	1.465	0.615	1.142
P值	0.151	0.932	0.231	0.893	0.337

1.2　麻醉方法　术前全面评估患者情况，制定麻醉方案，患者签署知情同意书，术前常规禁食、禁饮8 h。入室常规监测患者的心电图、血压、心率、外周血氧饱和度，同时监测体温以及麻醉深度指标脑电双频指数(bispectral index, BIS)。麻醉诱导：药物

均使用咪达唑仑（宜昌人福药业，国药准字H20067040）0.03 mg/kg、丙泊酚（西安力邦制药，国药准字H20010368）1.5 mg/kg、舒芬太尼（江苏恩华药业，国药准字H20203650）0.5 μg/kg、维库溴铵（成都天台山制药，国药准字H20063411）0.1 mg/kg，待患者意识消失、肌肉松弛后置入气管导管，连接呼吸管路控制通气。麻醉维持：丙泊酚泵注速度为4~12 mg·kg^{-1}·h^{-1}，瑞芬太尼（国药集团工业，国药准字H20123421）泵注速度为0.1~1.0 μg·kg^{-1}·min^{-1}，根据BIS值调整泵速，术中维持BIS值在40~60。术毕停止泵入丙泊酚和瑞芬太尼。按需要对患者进行低负压（80~120 mmHg）下吸痰，待患者清醒，自主呼吸恢复，BIS值恢复至85，能完成睁眼、张嘴、伸舌等指令，且自主呼吸潮气量大于5 mL/kg时拔除气管导管。

1.3　分组　A组：肿物切除前给予1 mL生理盐水，手术结束时给予10 mL生理盐水。B组：肿物切除前给予30 mg酮咯酸氨丁三醇1 mL，手术结束时给予10 mL生理盐水。C组：肿物切除前给予1 mL生理盐水，手术结束时给予1.5 mg/kg利多卡因稀释至10 mL。D组：肿物切除前给予30 mg酮咯酸氨丁三醇1 mL，手术结束时给予1.5 mg/kg利多卡因稀释至10 mL。实验药物均采用单次静脉注射的方式。

1.4　观察指标　拔管时呛咳评分，呛咳等级评定：1级为无呛咳（0次）；2级为轻度呛咳（1~2次）；3级为中度呛咳（3~4次）；4级为重度呛咳（≥5次）。记录患者麻醉诱导前（T1）、拔管即刻（T2）、拔管后5 min（T3）、拔管后15 min（T4）的平均动脉压（mean arterial pressure，MAP）和心率；术后24 h患者咽痛的视觉模拟评分（Visual Analogue Scale，VAS）；拔管后苏醒期其他不良反应发生情况（包括恶心呕吐、躁动、心动过缓等）；患者术后24 h的引流量。

1.5　统计学方法　应用SPSS 26.0软件进行统计分析。符合正态分布的计量资料以$\bar{x}\pm s$表示，多组间比较采用单因素方差分析，多时点比较采用重复测量资料方差分析，两两比较采用LSD-t检验。计数资料以例（%）表示，比较采用χ^2检验。有序分类变量采用非参数秩和检验，多组间比较采用Kruskal-Wallis H检验，两两比较采用Mann-Whitney U检验。采用双侧检验，检验水准α=0.05。

2　结　果

2.1　四组拔管时患者的呛咳评分比较　Kruskal-Wallis H检验结果显示，四组患者拔管时的呛咳评分比较差异有统计学意义（P<0.01）。两两比较结果显示A组与C组和D组比较差异有统计学意义（Z=3.512，P<0.01；Z=4.445，P<0.01），与B组比较差异无统计学意义（Z=0.809，P=0.419）。B组与C组和D组比较，差异有统计学意义（Z=3.093，P=0.002；Z=4.279，P<0.01）。见表2。

2.2　四组患者不同时点MAP和心率比较　组内不同时间点比较：A组患者T2、T3、T4时的MAP和心率较T1时的MAP升高（P<0.05）。B组患者T2时的MAP较T1时的MAP升高（P<0.05）。C、D组患者T2~T4时的MAP和心率与T1时比较，差异均无统计学意义（P>0.05）。相同时间点组间比较：在T2时，C组、D组患者的MAP和心率均低于A组、B组，差异有统计学意义（P<0.05）；在T3、T4时B组、C组和D组患者的MAP水平和心率均低于A组，差异有统计学意义（P<0.05）。见表3。

表2　四组患者拔管时的呛咳评分比较　［例（%）］

Tab.2　Comparison of the cough scores at extubation among four groups of patients　［case（%）］

组别	例数	1级	2级	3级
A组	20	2（10.0）	7（35.0）	11（55.0）
B组	20	2（10.0）	10（50.0）	8（40.0）
C组	20	9（45.0）	10（50.0）	1（5.0）
D组	20	16（80.0）	3（15.0）	1（5.0）
H值			31.658	
P值			<0.001	

表3　四组患者不同时点MAP和心率比较　（n=20，$\bar{x}\pm s$）

Tab.3　Comparison of MAP and heart rate at different time points among four groups　（n=20，$\bar{x}\pm s$）

组别	MAP（mmHg）				心率（次/min）			
	T1	T2	T3	T4	T1	T2	T3	T4
A组	96.65±5.23	106.75±4.20^{a}	105.90±4.01^{a}	104.95±4.66^{a}	73.20±5.34	86.55±3.85^{a}	83.25±3.73^{a}	77.90±5.31^{a}
B组	98.10±4.12	105.75±3.77^{a}	101.10±4.46^{b}	98.35±4.33^{b}	72.10±5.66	84.25±4.78^{a}	75.40±5.83^{ab}	74.30±5.74^{ab}
C组	96.25±4.91	96.10±4.54^{bc}	96.70±4.34^{b}	96.45±4.57^{b}	73.35±6.32	73.65±5.62^{bc}	73.45±6.79^{b}	73.30±5.91^{b}
D组	97.45±4.66	97.20±4.19^{bc}	97.90±4.24^{b}	98.25±4.33^{b}	72.95±5.80	72.90±5.81^{bc}	72.75±5.95^{b}	72.45±5.45^{b}
$F_{组间}/P_{组间}$值	20.434/<0.001				13.645/<0.001			
$F_{时间}/P_{时间}$值	21.857/<0.001				33.214/<0.001			
$F_{交互}/P_{交互}$值	11.191<0.001				11.947/<0.001			

注：与同组T1时比较，^{a}P<0.05；与A组比较，^{b}P<0.05；与B组比较，^{c}P<0.05。

2.3 拔管后24 h咽痛VAS评分比较 拔管后24 h咽痛VAS评分A组为(1.95±0.69)分,B组为(0.90±0.64)分,C组为(2.25±0.79)分,D组为(0.75±0.64)分,四组间差异有统计学意义(F=23.508,P<0.01)。B组VAS评分低于A组(t=4.989,P<0.01)和C组(t=5.938,P<0.01),D组VAS评分低于A组(t=5.702,P<0.01)和C组(t=6.598,P<0.01)。而A组和C组(t=1.279,P=0.209)以及B组和D组(t=0.741,P=0.463)VAS评分比较差异均无统计学意义。

2.4 术后引流量比较 术后24 h的引流量分别为A组(104.50±6.47) mL, B组(102.75±7.16) mL, C组(70.25±4.99)mL,D组(69.00±5.76)mL。四组引流量差异有统计学意义(F=204.309,P<0.01)。C组引流量低于A组(t=18.746,P<0.01)和B组(t=5.938,P<0.01),D组引流量低于A组(t=18.746,P<0.01)和B组(t=16.654,P<0.01),差异均有统计学意义。

2.5 其他不良反应发生情况比较 四组患者拔管后其他不良反应(恶心呕吐、躁动、心动过缓等)发生率:A组15%(3例),B组15%(3例),C组10%(2例),D组5%(1例),差异无统计学意义(χ^2=1.377,P=0.711)。

3 讨 论

甲状腺手术操作部位的解剖复杂、血管丰富,在围拔管期随着麻醉深度变浅,疼痛、呛咳等刺激激活交感-肾上腺髓质系统,儿茶酚胺大量释放,导致血流动力学异常波动[11-12]。对于合并高血压患者,剧烈血流动力学波动可能导致术后出血,严重时可诱发多种心血管反应,如心肌缺血、脑卒中及脑出血等,降低术后早期恢复质量,延长住院时间[4]。既往研究表明,静脉注射利多卡因有助于减轻术后疼痛、减少全身麻醉拔管期呛咳反应、改善血流动力学波动[13-15]。在一项甲状腺癌手术的随机对照研究中,Shu等[16]在麻醉诱导前给予静脉注射利多卡因,结果显示,与对照组相比,术后镇痛效果满意,减少了全身麻醉药物的用量和术后呕吐等不良反应的发生率。在甲状腺切除术后2 min静脉注射利多卡因,有助于改善患者呛咳的发生率和血流动力学波动[17]。既往研究发现,静脉注射利多卡因剂量在1.0~1.5 mg/kg时,其血药浓度在安全范围内,超过2.0 mg/kg可能存在风险[18]。本研究中手术结束时单次注射利多卡因1.5 mg/kg,结果显示可以减轻高血压患者围拔管期的呛咳、维持拔管期血流动力学平稳以及减少术后出血量(引流量)。但在咽喉痛方面,利多卡因组在术后24 h的咽喉痛VAS评分与对照组差异无统计学意义,提示其镇痛时间较短,这与先前的研究一致。

酮咯酸氨丁三醇酮是目前镇痛效果最好的非甾体抗炎药,可抑制前列腺素合成,达到镇痛效果,可用于急性中重度疼痛的短期治疗,且不良反应较少[19-20]。研究表明,麻醉诱导前静脉注射酮咯酸氨丁三醇预处理可显著降低全身麻醉诱导期间舒芬太尼诱导的呛咳发生率,也可显著减轻术后切口疼痛和恢复期躁动[21]。但酮咯酸氨丁三醇对甲状腺手术围拔管期的影响研究较少。在一项女性患者行甲状腺切除术的研究中发现,麻醉诱导前静脉注射或静脉滴注酮咯酸氨丁三醇能降低拔管后咽喉痛、呛咳、伤口疼痛等不良反应的发生率[22]。本研究结果表明,肿物切除前静脉注射酮咯酸氨丁三醇,可以减轻患者术后24 h咽喉痛,但在减轻术后呛咳、维持血流动力学稳定方面无明显优势。这可能是由于酮咯酸氨丁三醇半衰期短,且用量较小。因此,本研究采用联合用药的方式,在肿物切除前静脉注射酮咯酸氨丁三醇,手术结束时静脉注射利多卡因,结果显示,拔管即刻、拔管后5 min、拔管后15 min的MAP、心率较诱导前无明显差异,且术后24 h咽喉痛VAS评分低于利多卡因组。以上结果表明,在甲状腺手术中,与单用利多卡因或酮咯酸氨丁三醇相比,联合用药即肿物切除前静脉注射酮咯酸氨丁三醇、手术结束时注射利多卡因,在围拔管期减少呛咳、维持血流动力学平稳、镇痛等综合层面更有优势。

综上所述,利多卡因联合酮咯酸氨丁三醇能有效减轻行甲状腺手术的高血压患者拔管后的咽喉痛、循环波动和拔管时呛咳等不良反应,有助于提高此类患者围拔管期的舒适度和安全性。

利益冲突 无

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