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Effect of aerosol inhalation of esketamine on postoperative sore throat in patients undergoing thoracoscopic radical resection of lung cancer

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Abstract: **Objective** To analyze the application value of aerosol inhalation of esketamine in patients undergoing thoracoscopic radical resection of lung cancer, evaluate its effect on postoperative sore throat (POST), and provide a reference for the clinical prevention and treatment of POST. **Methods** A total of 75 patients with non-small cell lung cancer (NSCLC) who underwent elective thoracoscopic radical resection of lung cancer at Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine from August 2022 to August 2024 were selected as the research subjects. They were divided into two groups using a random number table method: the aerosol inhalation group (n=39) received aerosol inhalation of 5 mL esketamine suspension [1 mL esketamine injection (2 mL∶50 mg) + 4 mL normal saline] before anesthesia induction, and the normal saline group (n=36) received aerosol inhalation of 5 mL normal saline before anesthesia induction. The heart rate and mean arterial pressure (MAP) at different time points during peri-tracheal intubation [before nebulization (T0), before tracheal intubation (T1), immediately after intubation (T2), 5 min after intubation (T3)], as well as blood glucose and blood lactate levels at T0, T1, and T2 were compared between the two groups. The incidence and duration of POST within 24 h after surgery, the degree of throat pain [Visual Analogue Scale (VAS)], and the incidence of adverse reactions during anesthesia induction were also compared between the two groups. **Results** At T2 and T3, heart rate and MAP in the aerosol inhalation group were lower than those in the normal saline group (P<0.05). At T2, the level of blood lactate in the aerosol inhalation group was lower than that in the normal saline group (P<0.05). There was no statistically significant difference in blood glucose levels between the two groups at each time point (P>0.05). Compared with the normal saline group, the aerosol inhalation group had a lower incidence of POST (15.38% *vs* 38.89%, $\chi2$=5.288, P= 0.021), shorter duration of POST [(9.67±2.73) h *vs* (13.43±3.48) h, t=2.344, P=0.031], and lower throat VAS score [(2.83±0.75) points *vs* (4.64±1.69) points, t=3.310, P=0.004] within 24 h after surgery (P<0.05). During anesthesia induction, the total incidence of adverse reactions in the nebulized inhalation group was lower than that in the normal saline group (7.69% *vs* 25.00%, $\chi2$=4.172, P=0.041). **Conclusion** Aerosol inhalation of esketamine can alleviate the cardiovascular response during peri-tracheal intubation, improve tissue perfusion, reduce the incidence of POST, and decrease adverse reactions during anesthesia induction in patients undergoing thoracoscopic radical resection of lung cancer.

Keywords: Non-small cell lung cancer; Thoracoscopic radical resection of lung cancer; Anesthesia; Esketamine; Postoperative sore throat

Thoracoscopic radical resection of lung cancer is the preferred surgical approach for the treatment of non-small cell lung cancer (NSCLC). Intraoperative double-lumen endobronchial intubation allows one-lung isolation and selective ventilation, providing a guarantee for uncomplicated surgery [1]. Postoperative sore throat (POST) is a common airway complication following general anesthesia with tracheal intubation. It not only aggravates postoperative discomfort, impairs oral intake and sleep, but also prolongs hospital stay and hinders postoperative recovery [2-3]. With the promotion of the concept of comfortable medical care, POST has attracted extensive attention from anesthesiologists. How to reduce the incidence of POST and improve postoperative comfort has become one of the urgent clinical problems to be solved in the department of anesthesiology [4]. Previous studies have confirmed that adjuvant topical anesthesia during general anesthesia can reduce the risk of POST after general anesthesia with tracheal intubation [5]. Esketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist with anti-inflammatory and analgesic effects, which can effectively alleviate airway irritation during the induction and emergence phases of general anesthesia [6]. At present, esketamine has become a commonly used sedative and analgesic drug in the preanesthetic period. Studies have shown that nebulized inhalation of esketamine acts directly on the respiratory tract and lung tissue with minimal impact on the systemic circulation. When used for one-lung ventilation anesthesia in thoracoscopic surgery, it significantly relieves airway irritation induced by general anesthesia induction [7]. This study aimed to analyze the application value of nebulized esketamine in patients undergoing thoracoscopic radical resection of lung cancer and to evaluate its effect on POST.

1 Materials and Methods

1.1 General Data

A total of 75 patients with NSCLC scheduled for elective thoracoscopic radical resection of lung cancer at Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, from August 2022 to August 2024 were enrolled.

Inclusion criteria: (1) Met the diagnostic criteria for NSCLC in the *Diagnosis and Treatment Specifications for Primary Lung Cancer (2018 Edition)* [8] and confirmed by histopathological examination; (2) Met the surgical indications for thoracoscopic radical resection of lung cancer; (3) Karnofsky Performance Status score > 80; (4) American Society of Anesthesiologists (ASA) physical status Grade I−III.

Exclusion criteria: (1) Cardiopulmonary dysfunction intolerant to surgery; (2) Acute myocardial infarction within 6 weeks preoperatively; (3) Complicated with severe cerebrovascular disease or organic neurological lesions; (4) Presence of thoracic adhesions; (5) Complicated with systemic infectious diseases; (6) Conversion to thoracotomy during surgery.

Patients were randomly divided into two groups using a random number table: the nebulization group (n=39, nebulized esketamine suspension before anesthesia induction) and the saline group (n=36, nebulized normal saline before anesthesia induction). This study was approved by the Ethics Committee of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine (Approval No.: 022070015). There were no significant differences in general data between the two groups (P > 0.05). See **Table 1.**

Tab.1 Comparison of general data between the two groups ($\bar{x}\pm s$)

Item	Saline group (n=36)	Nebulization group (n=39)	$\chi 2/t/Z$ Value	P Value
Gender [case(%)]			0.072	0.789
Male	22(61.11)	25(64.10)		
Female	14(38.89)	14(35.90)		
Age (years)	64.97±5.49	65.41±6.42	0.316	0.753
BMI (kg/m^2)	23.27±3.09	24.41±2.37	1.797	0.076
ASA Classification [case(%)]			0.704	0.481
Grade I	1(2.78)	2(5.13)		
Grade II	12(33.33)	15(38.46)		
Grade III	23(63.89)	22(56.41)		
Operation Time (min)	126.56±29.51	121.18±30.12	0.78	0.438
Intraoperative Blood Loss (mL)	72.83±14.20	75.62±13.69	0.864	0.391
One lung Ventilation Time (min)	103.19±15.10	108.95±16.27	1.584	0.118
Intubation Completion Time (s)	12.06±1.64	12.23±1.58	0.471	0.639
Extubation Time (s)	18.94±5.49	17.62±5.64	1.033	0.305

1.2 Anesthetic Methods

All patients received anesthesia and surgery performed by the same senior medical team. Patients fasted orally preoperatively. After entering the operating room, peripheral venous access was established, and routine monitoring included body temperature, electrocardiography, peripheral oxygen saturation (SpO_2), heart rate (HR), mean arterial pressure (MAP), and bispectral index (BIS). Patients were placed in the lateral decubitus position with the healthy side down, and radial artery cannulation was performed for continuous invasive arterial blood pressure monitoring. Patients in the nebulization group received nebulized inhalation of 5 mL esketamine suspension [1 mL esketamine injection (Jiangsu Hengrui Pharmaceuticals, Approval No.: H20193336, 2 mL:50 mg) + 4 mL normal saline] 15 min before anesthesia induction. Patients in the saline group received nebulized inhalation of 5 mL normal saline 15 min before anesthesia induction. All patients received a uniform anesthesia induction regimen: intravenous dexmedetomidine (Chenxin Pharmaceuticals, H20130027) 0.5-0.8 μg/kg, cyclopropofol (Shenyang Haisco Pharmaceuticals, H20200013) 0.5-0.6 mg/kg, rocuronium (Zhejiang Xianju Pharmaceuticals, H20093186) 1 mg/kg, and sufentanil (Yichang Renfu Pharmaceuticals, H20054171) 0.5 μg/kg. Three minutes after administration, double-lumen endobronchial intubation was performed, and mechanical ventilation was initiated via a ventilator. Intraoperative parameters were maintained as follows: inspired oxygen concentration 100%, oxygen flow 2 L/min, end-tidal partial pressure of carbon dioxide 35-40 mmHg, respiratory rate 12-18 breaths/min, tidal volume 4-6 mL/kg. Anesthesia was maintained using target-controlled infusion of propofol (Beijing Fresenius Kabi Pharmaceuticals, HJ20150655) and remifentanil (Yichang Renfu Pharmaceuticals, H20030197), with target plasma concentrations of 1-4 μg/mL and 3-5 ng/mL, respectively. Rocuronium 0.4 mg/kg was administered intermittently. Fluctuations in HR and systolic blood pressure were maintained within 20% of baseline values, and BIS was maintained at 40-60. At the end of surgery, a patient-controlled intravenous analgesia (PCIA) pump was connected. The analgesic formula consisted of sufentanil 1 μg/kg, dezocine (Yangtze River Pharmaceuticals, H20080329) 10 mg, and metoclopramide (Shanghai Hefeng Pharmaceuticals, H31021522) 20 mg in 100 mL normal saline. The infusion rate was 2 mL/h, with a PCIA bolus of 2 mL and a lockout interval of 15 min. Patients were transferred to the postanesthesia care unit. After full awakening and recovery of spontaneous respiration, airway and oral secretions were cleared, the double-lumen tube was removed, and patients were returned to the general ward after stable vital signs.

1.3 Observation Indexes

1.3.1 Cardiovascular Stress Response During Peri-intubation Period

HR and MAP were recorded before nebulization (T0), before tracheal intubation (T1), immediately after intubation (T2), and 5 min after intubation (T3).

1.3.2 Arterial Blood Gas Parameters

Two milliliters of radial arterial blood were collected at T0, T1, and T2 for blood gas analysis. Blood glucose and blood lactate levels were recorded.

1.3.3 Postoperative Sore Throat

Patients were followed up postoperatively and questioned about throat pain. The incidence and duration of POST within 24 h after surgery were recorded. The severity of throat pain was assessed using the Visual Analogue Scale (VAS): 0=no pain, 1-3=mild pain (tolerable, no sleep disturbance), 4-6=moderate pain (sleep disturbance), ≥7=severe pain (severe sleep disturbance).

1.3.4 Adverse Reactions

Adverse events during anesthesia induction were closely recorded, including choking cough, respiratory depression, chest wall rigidity, hypotension, and injection pain.

1.4 Statistical Analysis

Data were analyzed using SPSS 24.0 software. Normally distributed continuous data (confirmed by Shapiro-Wilk test) were expressed as $\bar{x}\pm s$. Between-group comparisons were performed using independent-samples *t*-test, and comparisons at multiple time points used repeated-measures analysis of variance with LSD-*t* test for post hoc analysis. Categorical data were expressed as cases (%) and analyzed using the χ^2 test. Ordinal data were analyzed using the rank-sum test. $P<0.05$ was considered statistically significant.

2 Results

2.1 Cardiovascular Responses

At T2 and T3, HR and MAP in the nebulization group were significantly lower than those in the saline group ($P<0.05$). See **Table 2**.

2.2 Blood Glucose and Lactate Levels

At T2, blood lactate level in the nebulization group was lower than that in the saline group ($P<0.05$). There were no significant differences in blood glucose levels between the two groups at any time point ($P>0.05$). See **Table 3**.

Tab.2 Comparison of heart rate and MAP during tracheal intubation between the two groups ($\bar{x}\pm s$)

Group	*n*	Heart Rate (beats/min)				MAP (mmHg)			
		T_0	T_1	T_2	T_3	T_0	T_1	T_2	T_3
Saline group	36	74.36±8.09	66.36±4.44	78.36±3.26	75.31±3.62	89.89±5.50	82.42±7.56	92.64±3.38	85.25±6.58
Nebulization group	39	73.64±7.68	64.90±3.16	72.95±4.21[a]	71.31±4.16[a]	89.10±7.42	80.59±5.14	86.31±5.81[a]	81.69±5.17[a]
***F* value**		F_{group}=11.203, F_{time}=88.867, $F_{interaction}$=5.345				F_{group}=16.283, F_{time}=39.245, $F_{interaction}$=3.397			
***P* value**		P_{group}=0.001, P_{time}<0.001, $P_{interaction}$=0.008				P_{group}<0.001, P_{time}<0.001, $P_{interaction}$=0.022			

Note: Compared with the saline group at the same time point, [a]$P<0.05$.

Tab.3 Comparison of blood glucose and blood lactate levels between the two groups ($\bar{x}\pm s$)

Group	*n*	Blood Glucose (mmol/L)			Blood Lactate (mmol/L)		
		T_0	T_1	T_2	T_0	T_1	T_2
Saline group	36	5.14±0.61	5.30±0.71	5.88±0.69	1.27±0.26	1.30±0.22	1.36±0.25
Nebulization group	39	5.15±0.56	5.45±0.59	6.09±0.74	1.22±0.23	1.21±0.20	1.22±0.16[a]
***F* value**		F_{group} =1.746, F_{time}=34.804, $F_{interaction}$=0.525			F_{group} =7.156, F_{time}=1.141, $F_{interaction}$=1.128		
***P* value**		P_{group}=0.190, P_{time}<0.001, $P_{interaction}$=0.590			P_{group}=0.009, P_{time}=0.318, $P_{interaction}$=0.322		

Note: Compared with the saline group at the same time point, [a]$P<0.05$.

2.3 Postoperative Sore Throat

Within 24 h postoperatively, POST occurred in 6 patients (15.38%) in the nebulization group and 14 patients (38.89%) in the saline group (χ^2=5.288, P=0.021). The nebulization group had shorter POST duration and lower throat VAS scores than the saline group ($P<0.05$). See **Table 4.**

Tab.4 Comparison of the duration of POST and pain degree between the two groups ($\bar{x}\pm s$)

Group	*n*	POST Duration (h)	POST Duration
Saline group	14[a]	13.43±3.48	4.64±1.69
Nebulization group	6[a]	9.67±2.73	2.83±0.75
***t* value**		2.344	3.310
***P* value**		0.031	0.004

Note: [a]indicates the number of cases with POST.

2.4 Adverse Reactions During Anesthesia Induction

The total incidence of adverse reactions during anesthesia induction was 7.69% (3/39) in the nebulization group, lower than 25.00% (9/36) in the saline group. See **Table 5**. Brief choking cough in both groups resolved after clearing foreign bodies and adjusting infusion speed. Respiratory depression was relieved by mask-assisted ventilation. Chest wall rigidity improved after adjusting infusion rate or administering muscle relaxants. Hypotension was treated with ephedrine. Injection pain was relieved by slowing administration or fentanyl after loss of consciousness

Tab.5 The occurrence of adverse reactions during anesthesia induction [case (%)]

Group	*n*	Choking Cough	Respiratory Depression	Chest Wall Rigidity	Hypotension	Injection Pain	Total
Saline Group	36	2(5.56)	1(2.78)	1(2.78)	2(5.56)	3(8.33)	9(25.00)
Nebulization Group	39	1(2.56)	0	0	1(2.56)	1(2.56)	3(7.69)
χ^2 Value							4.172
***P* Value**							0.041

3 Discussion

Double-lumen endotracheal tubes have a larger outer diameter and harder texture. Tracheal intubation and intraoperative fiberoptic bronchoscopic positioning may compress tracheal mucosa and pharyngolaryngeal tissue, inducing inflammatory mediator release and mucosal injury, leading to POST [9-10]. A study on POST after general anesthesia with double-lumen intubation reported that the incidence of POST reached 68.22% at 1 h postoperatively and increased to 76.74% at 24 h postoperatively [11]. POST is one of the main causes of postoperative discomfort in patients undergoing thoracoscopic radical lung cancer surgery. Preventing POST is of great significance for improving anesthetic comfort and promoting postoperative recovery. Current preventive strategies for POST include pharmacologic and physical methods. Esketamine, the dextrorotatory isomer of ketamine, inhibits inflammatory responses and central nociceptive sensitization and is widely used clinically as an analgesic [12]. However, whether nebulized esketamine reduces POST in patients undergoing general anesthesia with tracheal intubation remains to be confirmed.

Esketamine can be administered intranasally, intravenously, or via nebulization. Intranasal administration is mainly used for depression, and intravenous injection for perioperative analgesia, but may prolong sedation. Nebulization targets the respiratory tract and lungs, allowing uniform drug distribution in the oral cavity, glottis, and airway [7,12]. Therefore, this study used nebulized esketamine before anesthesia induction to investigate its effect on POST in patients undergoing thoracoscopic radical lung cancer surgery. Our results showed that HR and MAP at T2 and T3 were lower in the nebulization group than in the saline group, indicating that nebulized esketamine before induction attenuates cardiovascular responses to tracheal intubation, likely by inhibiting sympathetic activation and maintaining hemodynamic stability [13]. Chen et al. [14] also found that esketamine reduces fluctuations in HR and MAP and stabilizes hemodynamics during intubation in laparoscopic surgery.

Blood glucose reflects metabolic status and stress level, while blood lactate indicates organ perfusion and anaerobic metabolism. Monitoring both is valuable for evaluating tissue perfusion and cellular oxygenation under stress [15]. In this study, blood lactate at T2 was lower in the nebulization group, with no between-group difference in blood glucose, suggesting that esketamine improves organ perfusion and reduces anaerobic metabolism without inducing stress-related metabolic disturbance. This may be related to the inhibition of nuclear factor-κB signaling and subsequent alleviation of inflammation and improvement of microperfusion [16]. Stimuli from intubation and incision peak within 1-2 min [17], resulting in non-significant changes in blood glucose within the sampling interval.

Compared with the saline group, the nebulization group had a lower incidence, shorter duration, and lower VAS score of POST within 24 h postoperatively, demonstrating that nebulized esketamine prevents POST, shortens pain duration, and reduces pain intensity. Esketamine non-competitively binds to the phencyclidine site of the NMDA receptor to prevent central nociceptive sensitization, inhibits monoamine neurotransmitters, acts on nitric oxide synthase, activates descending pain inhibitory pathways, and reduces inflammatory mediator release, thereby exerting analgesic effects [18-19]. Liang et al. [20] reported that esketamine reduced POST from 47.1% to 12.9% in patients with double-lumen intubation without obvious adverse reactions. In our study, the nebulization group had a lower incidence of choking cough and respiratory depression, indicating that nebulized esketamine reduces adverse events during induction. Increased vagal tone induced by intravenous opioids contributes to bronchoconstriction and coughing [21]. Esketamine relaxes bronchial smooth muscle and inhibits the medullary cough center, thus reducing coughing [22]. Its sympathomimetic property and lack of significant respiratory depression counterbalance propofol-related respiratory and circulatory depression, lowering the risk of respiratory depression [23]. Furthermore, nebulization allows direct deposition in the airway, enhancing local analgesic and antitussive effects [7].

Nebulized inhalation of esketamine before anesthesia induction in patients undergoing thoracoscopic radical resection of lung cancer attenuates cardiovascular responses to tracheal intubation, improves tissue perfusion, reduces the incidence of POST, and lowers the rate of adverse reactions during anesthesia induction.

Conflict of Interest: None

Reference

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·临床麻醉专题·论著·

艾司氯胺酮雾化吸入对胸腔镜肺癌根治术患者术后咽喉痛的影响

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摘要：目的 分析艾司氯胺酮雾化吸入在胸腔镜肺癌根治术患者中的应用价值，评估其对患者术后咽喉痛（POST）的影响，为临床防治POST提供参考依据。**方法** 选取2022年8月至2024年8月上海中医药大学附属岳阳中西医结合医院择期行胸腔镜肺癌根治术的非小细胞肺癌（NSCLC）患者75例作为研究对象，采用随机数字表法将患者分为两组：雾化吸入组39例，于麻醉诱导前雾化吸入5 mL艾司氯胺酮混悬液[1 mL艾司氯胺酮注射液（2 mL∶50 mg）+4 mL生理盐水]；生理盐水组36例，麻醉诱导前雾化吸入5 mL生理盐水。比较两组围气管插管期不同时间点[雾化前（T_0）、气管插管前（T_1）、插管后即刻（T_2）、插管后5 min（T_3）]的心率、平均动脉压（MAP）和T_0、T_1、T_2时的血糖、血乳酸水平，比较两组术后24 h内POST发生率、持续时间、咽喉部疼痛程度[视觉模拟评分（VAS）]及麻醉诱导期间不良反应发生率。**结果** T_2、T_3时，雾化吸入组心率和MAP均低于生理盐水组（P<0.05）。T_2时，雾化吸入组血乳酸水平低于生理盐水组（P<0.05）；两组各时间点血糖水平比较差异无统计学意义（P>0.05）。与生理盐水组比较，术后24 h内雾化吸入组POST发生率低（15.38% *vs* 38.89%，χ^2=5.288，P=0.021）、POST持续时间短[（9.67±2.73）h *vs*（13.43±3.48）h，t=2.344，P=0.031]、咽喉部VAS评分低[（2.83±0.75）分 *vs*（4.64±1.69）分，t=3.310，P=0.004]。麻醉诱导期间，雾化吸入组总不良反应发生率低于生理盐水组（7.69% *vs* 25.00%，χ^2=4.172，P=0.041）。**结论** 艾司氯胺酮雾化吸入可减轻胸腔镜肺癌根治术患者围气管插管期心血管反应，改善组织灌注，降低POST发生率，并减少麻醉诱导期间不良反应。

关键词：非小细胞肺癌；胸腔镜肺癌根治术；麻醉；艾司氯胺酮；术后咽喉痛

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Effect of aerosol inhalation of esketamine on postoperative sore throat in patients undergoing thoracoscopic radical resection of lung cancer

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Abstract: Objective To analyze the application value of aerosol inhalation of esketamine in patients undergoing thoracoscopic radical resection of lung cancer, evaluate its effect on postoperative sore throat (POST), and provide a reference for the clinical prevention and treatment of POST. **Methods** A total of 75 patients with non-small cell lung cancer (NSCLC) who underwent elective thoracoscopic radical resection of lung cancer at Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine from August 2022 to August 2024 were selected as the research subjects. They were divided into two groups using a random number table method: the aerosol inhalation group (n=39) received aerosol inhalation of 5 mL esketamine suspension [1 mL esketamine injection (2 mL∶50 mg) + 4 mL normal saline] before anesthesia induction, and the normal saline group (n=36) received aerosol inhalation of 5 mL normal saline before anesthesia induction. The heart rate and mean

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arterial pressure (MAP) at different time points during peri-tracheal intubation [before nebulization (T_0), before tracheal intubation (T_1), immediately after intubation (T_2), 5 min after intubation (T_3)], as well as blood glucose and blood lactate levels at T_0, T_1, and T_2 were compared between the two groups. The incidence and duration of POST within 24 h after surgery, the degree of throat pain [Visual Analogue Scale (VAS)], and the incidence of adverse reactions during anesthesia induction were also compared between the two groups. **Results** At T_2 and T_3, heart rate and MAP in the aerosol inhalation group were lower than those in the normal saline group (P<0.05). At T_2, the level of blood lactate in the aerosol inhalation group was lower than that in the normal saline group (P<0.05). There was no statistically significant difference in blood glucose levels between the two groups at each time point (P>0.05). Compared with the normal saline group, the aerosol inhalation group had a lower incidence of POST (15.38% *vs* 38.89%, χ^2=5.288, P=0.021), shorter duration of POST [(9.67±2.73)h *vs* (13.43±3.48)h, t=2.344, P=0.031], and lower throat VAS score [(2.83±0.75)points *vs* (4.64±1.69) points, t=3.310, P=0.004] within 24 h after surgery (P<0.05). During anesthesia induction, the total incidence of adverse reactions in the nebulized inhalation group was lower than that in the normal saline group (7.69% *vs* 25.00%, χ^2=4.172, P=0.041). **Conclusion** Aerosol inhalation of esketamine can alleviate the cardiovascular response during peri-tracheal intubation, improve tissue perfusion, reduce the incidence of POST, and decrease adverse reactions during anesthesia induction in patients undergoing thoracoscopic radical resection of lung cancer.

Keywords: Non-small cell lung cancer; Thoracoscopic radical resection of lung cancer; Anesthesia; Esketamine; Postoperative sore throat

胸腔镜肺癌根治术是外科治疗非小细胞肺癌(non-small cell lung cancer,NSCLC)的首选术式,术中采用双腔支气管插管可实现单肺隔离与选择性通气,为手术顺利开展提供保障[1]。术后咽喉痛(post-operative sore throat,POST)是气管插管全身麻醉术后常见的气道并发症,不仅会加重患者术后不适感,影响进食与睡眠,还会延长住院时长,不利于患者术后康复[2-3]。随着舒适化医疗理念的推广,POST受到麻醉医师的广泛关注,如何降低POST发生率、提升患者术后舒适度,成为现阶段麻醉科亟需解决的临床问题之一[4]。既往研究证实,全身麻醉期间辅助应用表面麻醉,可降低气管插管全身麻醉后POST的发生风险[5]。艾司氯胺酮属于N-甲基-D-天冬氨酸(N-methyl-D-aspartate,NMDA)受体拮抗剂,兼具抗炎、镇痛功效,能有效减轻全身麻醉诱导期及苏醒期的气道刺激反应[6]。目前,艾司氯胺酮已成为围麻醉期常用的镇静镇痛药物,已有研究表明,艾司氯胺酮雾化吸入可直接作用于呼吸道与肺组织,对机体循环系统影响轻微,用于胸腔镜手术单肺通气麻醉,能显著缓解全身麻醉诱导引发的气道刺激[7]。本研究旨在分析艾司氯胺酮雾化吸入在胸腔镜肺癌根治术患者中的应用价值,评估其对患者POST的影响。

1　资料与方法

1.1　*一般资料*　选取2022年8月至2024年8月上海中医药大学附属岳阳中西医结合医院择期行胸腔镜肺癌根治术的NSCLC患者75例作为研究对象。纳入标准:(1) 经临床检查符合《原发性肺癌诊疗规范(2018年版)》[8]中NSCLC诊断标准,且经组织病理学检查确诊;(2) 符合胸腔镜肺癌根治术手术指征;(3) Karnofsky功能状态评分>80分;(4) 美国麻醉医师协会(American Society of Anesthesiologists,ASA)分级Ⅰ~Ⅲ级。排除标准:(1) 心肺功能不耐受手术;(2) 术前6周内发生急性心肌梗死;(3) 合并严重脑血管疾病、神经系统器质性病变;(4) 存在胸腔粘连;(5) 合并全身感染性疾病;(6) 术中转为开胸手术。采用随机数字表法将患者分为两组:雾化吸入组(n=39,麻醉诱导前雾化吸入艾司氯胺酮混悬液)和生理盐水组(n=36,麻醉诱导前雾化吸入生理盐水)。本研究经上海中医药大学附属岳阳中西医结合医院伦理委员会审核批准(审批号:022070015)。两组患者一般资料比较差异无统计学意义(P>0.05)。见表1。

1.2　*麻醉方法*　所有患者均由同一组高年资医师实施麻醉与手术。患者术前常规禁饮禁食,入室后建立外周静脉通路,常规监测体温、心电图、外周血氧饱和度(saturation of peripheral oxygen,SpO_2)、心率、平均动脉压(mean arterial pressure,MAP)、脑电双频指数(bispectral index,BIS);患者取健侧卧位,行桡动脉穿刺,持续监测有创动脉血压。雾化吸入组于麻醉诱导前15 min雾化吸入5 mL艾司氯胺酮混悬液[艾司氯胺酮注射液(江苏恒瑞医药,国药准字:H20193336,规格2 mL∶50 mg)1 mL+生理盐水4 mL],

生理盐水组于麻醉诱导前15 min雾化吸入5 mL生理盐水。两组患者均接受统一麻醉诱导方案：静脉推注右美托咪定（辰欣药业，国药准字H20130027）0.5~0.8 μg/kg、环泊酚（沈阳海思科制药，国药准字：H20200013）0.5~0.6 mg/kg、罗库溴铵（浙江仙琚制药，国药准字H20093186）1 mg/kg、舒芬太尼（宜昌人福药业，国药准字H20054171）0.5 μg/kg，给药3 min后行双腔支气管插管，连接呼吸机行机械通气。术中维持吸入氧浓度100%，氧流量2 L/min，呼气末二氧化碳分压35~40 mmHg，呼吸频率12~18次/min，潮气量4~6 mL/kg；采用靶控输注模式持续输注丙泊酚（北京费森尤斯卡比医药，国药准字HJ20150655）、瑞芬太尼（宜昌人福药业，国药准字H20030197）维持麻醉，维持丙泊酚血浆靶浓度1~4 μg/mL、瑞芬太尼血浆靶浓度3~5 ng/mL，间断静脉注射罗库溴铵0.4 mg/kg，维持患者心率、收缩压波动幅度不超过基础值的20%，BIS值维持于40~60。术毕连接患者自控静脉镇痛泵，镇痛方案：100 mL生理盐水中加入舒芬太尼1 μg/kg、地佐辛（扬子江药业，国药准字H20080329）10 mg、甲氧氯普胺（上海禾丰制药，国药准字H31021522）20 mg；镇痛泵输注速率2 mL/h，患者自控静脉镇痛单次剂量2 mL，锁定时间15 min。术后将患者转入麻醉恢复室，待患者完全清醒、自主呼吸功能恢复后，清除气道及口腔内分泌物，拔除双腔气管导管，生命体征平稳后送回普通病房。

1.3 观察指标

1.3.1 围气管插管期心血管应激反应 分别记录雾化前（T_0）、气管插管前（T_1）、插管后即刻（T_2）、插管后5 min（T_3）各时间点患者的心率、MAP水平。

1.3.2 动脉血气指标 分别于T_0、T_1、T_2时间点采集桡动脉血2 mL，行动脉血气分析，记录血糖、血乳酸水平。

1.3.3 POST发生情况 术后随访患者，询问咽喉部疼痛感受，记录术后24 h内POST发生率、POST持续时长；采用视觉模拟评分法（Visual Analogue Scale，VAS）评估咽喉部疼痛程度，评分标准：0分为无痛，1~3分为轻度疼痛（尚可忍受，不影响睡眠），4~6分为中度疼痛（影响睡眠），≥7分为重度疼痛（严重影响睡眠）。

1.3.4 不良反应 严密记录患者麻醉诱导期间呛咳、呼吸抑制、胸壁强直、低血压、注射痛等不良反应的发生情况。

1.4 统计学方法 采用SPSS 24.0软件分析数据。计量资料经Shapiro-Wilk检验呈正态分布，采用$\bar{x}\pm s$表示，两组间比较行独立样本t检验，多时间点比较采用重复测量资料的方差分析及两两比较的LSD-t检验。计数资料以例（%）表示，行χ^2检验，等级资料采用秩和检验。P<0.05为差异有统计学意义。

2 结 果

2.1 围气管插管期心血管反应比较 T_2、T_3时，雾化吸入组心率、MAP水平均低于生理盐水组（P<0.05）。见表2。

2.2 血糖、血乳酸水平比较 T_2时，雾化吸入组血乳酸水平低于生理盐水组（P<0.05）；两组不同时间点血糖水平比较差异无统计学意义（P>0.05）。见表3。

2.3 POST发生情况比较 术后24 h内，雾化吸入组6例患者发生POST，生理盐水组14例患者发生POST；雾化吸入组POST发生率为15.38%，低于生理盐水组的38.89%（χ^2=5.288，P=0.021）。雾化吸入组POST持续时间短于生理盐水组，咽喉部VAS评分低于生理盐水组（P<0.05）。见表4。

2.4 麻醉诱导期间不良反应发生情况 麻醉诱导期间，雾化吸入组总不良反应发生率为7.69%（3/39），低于生理盐水组的25.00%（9/36）。见表5。两组患者发生呛咳的患者持续时间较短，经清除口腔内异物、调整给药速度后症状消失；呼吸抑制患者给予面罩辅助呼吸后呼吸抑制解除；胸壁强直患者经调整给药速度或给予肌肉松弛药后缓解；低血压患者予以麻黄碱治疗；注射痛患者经调整给药速度或于意识消失后予以芬太尼缓解。

表1 两组患者一般资料比较 （$\bar{x}\pm s$）

Tab.1 Comparison of general data between the two groups （$\bar{x}\pm s$）

项目	生理盐水组（n=36）	雾化吸入组（n=39）	$\chi^2/t/Z$值	P值
性别[例（%）]			0.072	0.789
男	22（61.11）	25（64.10）		
女	14（38.89）	14（35..90）		
年龄（岁）	64.97±5.49	65.41±6.42	0.316	0.753
身体质量指数（kg/m²）	23.27±3.09	24.41±2.37	1.797	0.076
ASA分级[例（%）]			0.704	0.481
Ⅰ级	1（2.78）	2（5.13）		
Ⅱ级	12（33.33）	15（38.46）		
Ⅲ级	23（63.89）	22（56.41）		
手术时间（min）	126.56±29.51	121.18±30.12	0.780	0.438
术中出血量（mL）	72.83±14.20	75.62±13.69	0.864	0.391
单肺通气时间（min）	103.19±15.10	108.95±16.27	1.584	0.118
插管完成时间（s）	12.06±1.64	12.23±1.58	0.471	0.639
拔管时间（s）	18.94±5.49	17.62±5.64	1.033	0.305

表2　两组患者气管插管期心率、MAP比较　($\bar{x}\pm s$)

Tab.2　Comparison of heart rate and MAP during tracheal intubation between the two groups　($\bar{x}\pm s$)

组别	例数	心率(次/min)				MAP(mmHg)			
		T_0	T_1	T_2	T_3	T_0	T_1	T_2	T_3
生理盐水组	36	74.36±8.09	66.36±4.44	78.36±3.26	75.31±3.62	89.89±5.50	82.42±7.56	92.64±3.38	85.25±6.58
雾化吸入组	39	73.64±7.68	64.90±3.16	72.95±4.21[a]	71.31±4.16[a]	89.10±7.42	80.59±5.14	86.31±5.81[a]	81.69±5.17[a]
F值		$F_{组间}$=11.203, $F_{时间}$=88.867, $F_{交互}$=5.345				$F_{组间}$=16.283, $F_{时间}$=39.245, $F_{交互}$=3.397			
P值		$P_{组间}$=0.001, $P_{时间}$<0.001, $P_{交互}$=0.008				$P_{组间}$<0.001, $P_{时间}$<0.001, $P_{交互}$=0.022			

注：与同时间点生理盐水组比较，[a]P<0.05。

表3　两组患者血糖、血乳酸水平比较　($\bar{x}\pm s$)

Tab.3　Comparison of blood glucose and blood lactate levels between the two groups　($\bar{x}\pm s$)

组别	例数	血糖(mmol/L)			血乳酸(mmol/L)		
		T_0	T_1	T_2	T_0	T_1	T_2
生理盐水组	36	5.14±0.61	5.30±0.71	5.88±0.69	1.27±0.26	1.30±0.22	1.36±0.25
雾化吸入组	39	5.15±0.56	5.45±0.59	6.09±0.74	1.22±0.23	1.21±0.20	1.22±0.16[a]
F值		$F_{组间}$=1.746, $F_{时间}$=34.804, $F_{交互}$=0.525			$F_{组间}$=7.156, $F_{时间}$=1.141, $F_{交互}$=1.128		
P值		$P_{组间}$=0.190, $P_{时间}$<0.001, $P_{交互}$=0.590			$P_{组间}$=0.009, $P_{时间}$=0.318, $P_{交互}$=0.322		

注：与同时间点生理盐水组比较，[a]P<0.05。

表4　两组患者POST持续时间、疼痛程度比较　($\bar{x}\pm s$)

Tab.4　Comparison of the duration of POST and pain degree between the two groups　($\bar{x}\pm s$)

组别	例数	POST持续时间(h)	VAS(分)
生理盐水组	14[a]	13.43±3.48	4.64±1.69
雾化吸入组	6[a]	9.67±2.73	2.83±0.75
t值		2.344	3.310
P值		0.031	0.004

注：[a]表示发生POST的例数。

表5　麻醉诱导期间不良反应发生情况　[例(%)]

Tab.5　The occurrence of adverse reactions during anesthesia induction [case(%)]

组别	例数	呛咳	呼吸抑制	胸壁强直	低血压	注射痛	合计
生理盐水组	36	2(5.56)	1(2.78)	1(2.78)	2(5.56)	3(8.33)	9(25.00)
雾化吸入组	39	1(2.56)	0	0	1(2.56)	1(2.56)	3(7.69)
χ^2值							4.172
P值							0.041

3　讨　论

双腔气管导管外径较大、质地较硬，气管插管操作及术中纤维支气管镜定位可能会压迫气管黏膜和咽喉部，引起炎性介质释放及咽喉部损伤，导致POST的发生[9-10]。一项有关全身麻醉双腔气管插管术后POST现状的研究发现，术后1 h患者POST发生率可达68.22%，术后24 h患者POST发生率上升至76.74%[11]。POST是胸腔镜肺癌根治术患者术后不适的主要原因之一，预防POST的发生对提高患者麻醉舒适度、促进术后恢复具有重要意义。当前，POST的预防措施主要包括药物预防、物理预防等，艾司氯胺酮是氯胺酮的右旋异构体，具有抑制炎症反应、减轻痛觉中枢敏化等作用，是临床常用的镇痛药物[12]。但艾司氯胺酮在雾化吸入给药方式下能否减少气管插管全麻患者POST的发生，有待进一步证实。

艾司氯胺酮的给药方式主要有经鼻给药、经静脉给药、雾化吸入等，经鼻给药主要用于抑郁症的治疗，经静脉给药可用于围手术期镇痛，但可能导致镇静延长；雾化吸入的给药方式以呼吸道和肺为靶器官，可使药物均匀分布于口腔、声门及气道[7,12]。因此，本研究选取麻醉诱导前雾化吸入的给药方式分析艾司氯胺酮对胸腔镜肺癌根治术患者POST的影响。本研究结果显示，与生理盐水组比较，雾化吸入组T_2、T_3时的心率和MAP较低，提示麻醉诱导前艾司氯胺酮雾化吸入可减轻患者气管插管期间的心血管反应，考虑与艾司氯胺酮抑制了交感神经的兴奋，从而维持麻醉诱导后的血流动力学稳定有关。气管插管期心血管反应与患者麻醉风险增加密切相关，维持围手术期血流动力学稳定具有重要意义[13]。Chen等[14]研究亦发现，艾司氯胺酮可降低气管插管期间腹腔镜手术患者的心率、MAP波动，维持血流动力学稳定。

血糖不仅可反映机体糖代谢水平，亦可作为应激的重要指标；血乳酸水平变化能够反映器官灌注是否充足和无氧代谢程度，评估围手术期血糖和血乳酸水平可作为评价应激状态下组织灌注、细胞氧合的重要方法[15]。本研究中，雾化吸入组T_2时血乳酸水平低于生理盐水组，两组各时间点血糖水平比较差异无统计学意义，提示艾司氯胺酮可改善胸腔镜肺癌根治术患者的器官灌注，降低无氧代谢水平，且不会引发应激性代谢紊乱。分析原因可能为，气

管插管对咽喉部及气管黏膜的损伤会引发一系列炎症反应，艾司氯胺酮可通过抑制核因子-κB途径的活性，减轻炎症反应，从而改善微灌注水平[16]。此外，气管插管、切皮等手术操作引起的刺激在1~2 min内即可达到峰值[17]，血糖在本研究检测间隔时间内的变化不明显，因此组间比较差异无统计学意义。

本研究结果发现，与生理盐水组相比，雾化吸入组术后24 h内POST发生率更低、疼痛持续时间更短、咽喉部VAS评分更低，表明艾司氯胺酮雾化吸入可在预防胸腔镜肺癌根治术患者POST发生的同时，缩短咽喉部疼痛持续时间并减轻疼痛程度。艾司氯胺酮一方面可非竞争性结合NMDA受体的苯环己哌啶位点，预防疼痛中枢敏化；另一方面可抑制单胺类神经递质，并作用于一氧化氮合酶，激活疼痛下行抑制通路，减少炎症介质释放，发挥镇痛作用[18-19]。Liang等[20]的随机对照试验研究发现，艾司氯胺酮可缓解双腔支气管导管插管导致的POST，患者POST发生率由47.1%下降至12.9%，且无明显不良反应。本研究中，雾化吸入组麻醉诱导期间呛咳、呼吸抑制等不良反应发生率低于生理盐水组，提示艾司氯胺酮雾化吸入可降低胸腔镜肺癌根治术患者麻醉诱导期间不良反应发生率。静脉注射阿片受体激动剂引起的迷走神经功能增强是导致支气管收缩、引发呛咳的主要原因之一[21]，艾司氯胺酮可舒张支气管平滑肌、抑制延髓咳嗽中枢，从而减少麻醉诱导期间呛咳的发生[22]。同时，艾司氯胺酮具有拟交感神经特性且无明显呼吸抑制作用，可平衡丙泊酚引起的呼吸循环抑制，降低麻醉期间呼吸抑制风险[23]。此外，雾化吸入的给药方式可使艾司氯胺酮直接作用于呼吸道，促进药物在呼吸道局部沉积，进而发挥更好的镇痛、抑制呛咳反射作用[7]。

综上所述，胸腔镜肺癌根治术患者麻醉诱导前给予艾司氯胺酮雾化吸入，可减轻气管插管期心血管反应，改善组织灌注，降低POST发生率，并降低麻醉诱导期间不良反应发生率。

利益冲突 无

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