中国临床研究 Chin J Clin Res, December 2024, Vol.37, No.12
Cite as: Kang CY, Kang CB, Ou XJ, et al. Effect of intravenous injection of different doses of lidocaine on cough during the recovery period after bronchoscopy under general anesthesia [J]. Chin J Clin Res, 2024, 37(12):1854-1859.
DOI: 10.13429/j.cnki.cjcr.2024.12.008

Effect of intravenous injection of different doses of lidocaine on cough during the recovery period after bronchoscopy under general anesthesia

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Abstract: Objective To evaluate the effect of intravenous injection of different doses of lidocaine on cough during the recovery period after bronchoscopy under general anesthesia, aiming to determine the optimal lidocaine dose. **Methods** Using prospective, single-center, randomized, controlled clinical trial methods, a total of 135 patients who underwent bronchoscopy in Shunde Hospital of Southern Medical University from September 2023 to June 2024 were selected, and they were randomly divided into group C (physiological saline), group L1.0 (1.0 mg/kg lidocaine), and the group L1.5 (1.5 mg/kg lidocaine), with 45 cases in each group. All patients received general anesthesia with laryngeal mask. After induction, lidocaine or saline was administered intravenously. The incidence and severity of cough within 30 minutes after removal of the laryngeal mask were recorded and analyzed, along with adverse events. Cough severity was categorized as mild (single episode), moderate (multiple episodes lasting over five seconds but not continuous), and severe (continuous coughing lasting over 5 s). **Results** There was a statistically significant difference in the incidence of cough during the recovery period after bronchoscopy among three groups: 42.2% in group C, 22.2% in group L1.0, and 8.9%group L1.5 (χ^2=13.72, P<0.01) After Bonferroni correction, the group L1.5 had a significantly lower incidence of cough than that in group C (χ^2=13.14, P<0.01). The incidence of severe cough was 17.8%, 4.4%, and 2.2%, respectively, and the difference among the three groups was statistically significant (χ^2=8.51, P<0.05). Compared with group C, incidences of postoperative nausea and vomiting and sore throat were fewer in both group L1.0 and group L1.5 (P < 0.017). **Conclusion** Intravenous injection of 1.5 mg/kg lidocaine can effectively reduce the incidence of cough during the resuscitation period after bronchoscopy under general anesthesia, and also can significantly decrease the occurrence of nausea, vomiting, and sore throat.

Keywords: Bronchoscopy; Lidocaine; Cough; Laryngeal mask anesthesia; Adverse reaction

Fund program: Basic and Applied Basic Research Joint Fund in Guangdong Province (2023A1515140142); Key Scientific Research Platform and Project of General Universities in Guangdong Province (2023ZDZX2008); Guangdong and Macao Young Talents Project of Science and Technology Department in Guangdong Province (YKZZ[2022] No.232); Foshan Self-funded Science and Technology Innovation Project (2320001007025).

Bronchoscopic examinations performed under general anesthesia with a laryngeal mask airway are a common diagnostic and therapeutic procedure in pulmonology [1]. However, postoperative cough is a frequent complication that may lead to adverse outcomes such as pneumothorax, bronchospasm, or airway obstruction [2]. Particularly under general anesthesia with intubation, the sensitivity of the cough reflex is increased, resulting in a significantly higher incidence of postoperative cough [3]. This reflex not only causes discomfort and distress for patients but may also increase the risk of bleeding and affect the therapeutic outcome.

As a local anesthetic, lidocaine has been widely recognized for its cough-suppressing effect when applied topically in the respiratory tract, and it is primarily administered through topical application clinically, such as spraying the throat, to reduce the cough reflex caused by the entry of the bronchoscope into the trachea. However, its effect on postoperative cough suppression is not significant [4]. Intravenous lidocaine has shown promise in reducing the sensitivity of the cough reflex both preoperatively and postoperatively [5]. The possible mechanism of action involves the inhibition of sodium ion channels, thereby reducing the excitability of cough reflex nerve fibers [6]. However, the optimal dose of intravenous lidocaine for alleviating cough after extubation during bronchoscopy is currently unclear and controversial. Therefore, this study aims to compare the effects of different doses of intravenous lidocaine on cough during the recovery period after bronchoscopy explore an optimized scheme that can maximize the suppression of cough after extubation during bronchoscopy under general anesthesia without causing significant adverse reactions, providing a reference for clinical practice.

1 Materials and Methods

1.1 Study Design

This study is a prospective, single-center, randomized controlled, double-blind clinical trial approved by the Ethics Committee of Shunde Hospital, Southern Medical University (approval number: KYLS20231022). All included patients or their family members who signed informed consent forms. This study selected patients who voluntarily underwent bronchoscopy from September 2023 to June 2024.

1.2 Inclusion and Exclusion Criteria

Inclusion Criteria: adults aged from 18 to 80 years old who were scheduled for elective bronchoscopy and classified within the American Society of Anesthesiologists (ASA) grade I to III.

Exclusion Criteria: Body Mass Index (BMI) exceeding 30 kg/m^2, require bronchoscopy for more than 1 hour, present with severe hepatic or renal impairment, suffer from chronic pain or psychiatric disorders, have significant cardiovascular or pulmonary conditions, possess known allergies to study drugs, were diagnosed with obstructive sleep apnea-hypopnea syndrome, have myasthenia gravis, or were in states of pregnancy or lactation.

1.3 Grouping and Blinding

Patients were randomized into three groups: group C (saline), group L1.0 (1.0 mg/kg lidocaine), and group L1.5 (1.5 mg/kg lidocaine). A computer-generated system facilitated randomization, with assignments securely sealed in opaque envelopes. Data collection and documentation were conducted by an independent observer blinded to group allocations. Both lidocaine and saline, being colorless and transparent, were uniformly prepared in 10 mL syringes, with a lidocaine concentration of 10 mg/mL. This ensured the blinding of the administering physician and the observer to the treatment. An anesthesiologist performed statistical analysis.

1.4 Anesthesia Procedure

Patients were required to fast for 8 hours and abstain from drinking for 2 hours before surgery. Upon entering the examination room, patients were connected to a multi-function monitor for routine monitoring of electrocardiogram (ECG), systolic blood pressure (SBP), diastolic blood pressure (DBP), and saturation of peripheral oxygen (SpO_2). Before induction, pure oxygen at a flow rate of 6 L/min was administered via a mask, and lactated Ringer's solution was infused intravenously through a peripheral vein at a rate of 6-8 mL/(kg·h). During the induction of general anesthesia, target-controlled infusion (TCI) of remifentanil was initially set to achieve a target effect-site concentration of 3 ng/ml. Once plasma and target compartment concentrations equilibrated, remimazolam was administered intravenously at a rate of 1200 mL/h with a dose of 0.3 mg/kg, followed by an intravenous administration of cisatracurium besylate 0.05 mg/kg. Finally, the corresponding dose of lidocaine or normal saline was administered intravenously at a slow rate. After the patient lost the eyelash reflex and jaw relaxation occurred, a laryngeal mask lubricated with petroleum jelly was inserted. Subsequently, volume-controlled positive-pressure ventilation was used to maintain end-tidal carbon dioxide ($EtCO_2$) levels between 35-45 mmHg. During the maintenance of anesthesia, the TCI target effect-site concentration of remifentanil was maintained at 2-4 ng/mL, and remimazolam was continuously infused intravenously at a rate of 0.3-1 mg/(kg·h). Mean arterial pressure (MAP) was maintained within ±20% of baseline with vasoactive drugs. A pulmonologist performed bronchoscopy. At the end of the procedure, remifentanil and remimazolam infusions were discontinued, and patients were transferred to the post-anesthesia care unit (PACU). After observing the patient's return of spontaneous respiration, neostigmine 1 mg and atropine 0.5 mg were routinely administered to counteract the effects of muscle relaxants. Gentle oral suction was performed before the patient was fully awake. When the patient could respond to verbal commands, breathe spontaneously with a SpO_2 over 95%, and maintain a fist above the head for more than 5 seconds, the laryngeal mask was removed. After at least 30 minutes of observation in the PACU, the patient was returned to the ward by an anesthesiologist.

1.5 Sample Size Estimation

This study conducted a preliminary trial, establishing a control group (administered normal saline) and an experimental group (administered 1.0 mg/kg lidocaine), with 10 patients in each group. The primary outcome measure was the incidence of coughing within 30 minutes after removal of the laryngeal mask. Preliminary results showed a cough incidence of 50% in the control group and 20% in the experimental group. To achieve a power of 80% (β=0.8) and a significance level (α) of 0.05, considering a dropout or loss to follow-up rate of 15%, it was calculated that 45 patients per group would be required, totaling 135 patients across three groups.

1.6 Outcomes

(1) Primary outcome: The incidence and severity of coughing were recorded within 30 minutes after patients emerged from general anesthesia and the laryngeal mask was removed. During this period, only moderate to severe coughing was considered effective and included in the analysis. The severity of coughing was categorized as mild (single cough), moderate (multiple coughs lasting more than 5 seconds but not continuous), and severe (continuous coughing for more than 5 seconds) [11].

(2) Other outcomes: MAP, heart rate (HR), and SpO_2 were recorded at the following time points: before anesthesia (T_0), 1 minute after laryngeal mask insertion (T_1), at the time of laryngeal mask removal (T_2), and upon departure from the post-anesthesia care unit (PACU) (T_3).

The duration of bronchoscopy, time to spontaneous respiration recovery, time to laryngeal mask removal, time to recovery of orientation, and time to discharge from the PACU were documented. Additionally, adverse events such as hypotension, hypertension, bradycardia, laryngospasm, hypoxemia, shivering, postoperative nausea and vomiting, emergence agitation, chest pain, and sore throat were recorded. Hypoxemia was defined as SpO_2 below 90% sustained for at least 5 seconds. The sore throat was defined as pain upon coughing when asked about its presence upon discharge from the PACU.

1.7 Statistical Analysis

Statistical analysis was performed using SPSS 22.0. The normality of data distribution was assessed using the Shapiro-Wilk test. Normally distributed continuous variables are expressed as $\bar{x}$ ±s, and comparisons among multiple groups were made using one-way analysis of variance (ANOVA). For comparisons of multiple groups at different time points, repeated measures analysis of variance was used, and pairwise comparisons were made using the least significant difference (LSD) method. Skewed continuous variables are expressed as M (Q_1, Q_3), and the Kruskal-Wallis rank sum test was used for comparisons, with pairwise comparisons made using the Bonferroni method. Categorical data are expressed as number or number (%), and the Pearson chi-squared test or Fisher's exact probability test was used for R*C contingency tables, with pairwise comparisons made using the Bonferroni correction method. All tests were two-tailed, with a significance level of α=0.05, and for pairwise comparisons in the chi-square test, α' was adjusted to 0.017.

2 Results

2.1 Patients' Baseline Characteristics

A total of 147 patients were initially included in the study, of which 6 were excluded for not meeting the inclusion criteria, leaving 141 patients who were divided into three groups: group C (n=45), group L1.0 (n=48), and group L1.5 (n=48). Due to missing data for 3 patients in group L1.0 and 3 patients in Group L1.5, the final analysis included 135 patients, with 45 patients in each group. There was no statistically significant difference in baseline characteristics such as age, height, weight, BMI, gender, ASA grade, medical history, and type of examination among three groups (P>0.05), as summarized in **Table 1**.

Tab. 1 Comparison of general information among three groups (n=45, case)

Index	Group C	Group L1.0	Group L1.5	$Z/F/\chi^2$ value	P value
Age (years)[a]	59(42, 70)	55 (37, 64)	56 (45, 69)	2.850	0.240
Height (cm, $\bar{x}$ ±s) [a]	164.1 ± 8.3	163.3 ± 8.8	160.4± 6.8	2.657	0.076
Weight (kg, $\bar{x}$ ±s) [a]	58.9 ± 12.1	59.6 ± 12.5	59.7 ± 9.0	0.067	0.932
BMI (kg/m^2, $\bar{x}$ ±s)[a]	21.8 ± 3.6	22.3 ± 4.2	23.2 ± 3.4	1.612	0.173
Gender (Male/Female)	30/15	22/23	24/21	3.131	0.209
ASA grading(I/II/III)	4/35/6	6/33/6	4/38/3	2.130	0.712
Personal and Medical History					
Smoking	11	8	8	0.833	0.660
Hypertension	7	3	2	3.841	0.146
Diabetes	1	0	1		1.000[b]
COPD[b]	0	1	0		1.000[b]
Asthma	0		0		1.000[b]
Type of Examination				7.124	0.523
Transbronchial Biopsy	18	12	14		
Transbronchial laser	0	0	2		
Bronchial Stent Placement	0	1	1		
Bronchial Brushing	7	9	6		
Bronchoalveolar Lavage	20	23	22		

Note: [a] indicated data presented as M (Q_1, Q_3); [b] signified the use of Fisher's exact probability test.

2.2 Comparison of the Incidence of Cough and Severe Cough among Three Groups

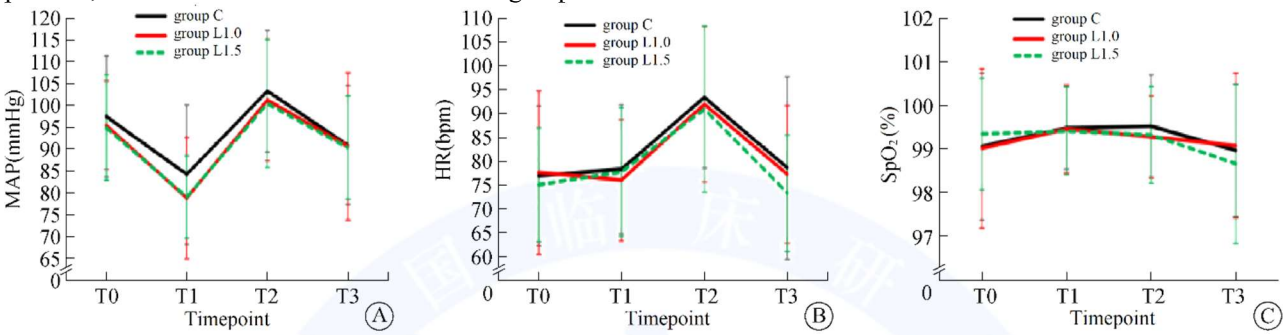
The severity of cough was observed as shown in **Table 2**. The incidence of severe cough showed statistically significant differences among the three groups (χ^2=8.512, P=0.014). Compared to group C, group L1.5 significantly reduced the incidence of severe cough (P<0.017). Moderate to severe cough was defined as effective cough, and its incidence was calculated. The incidence of cough in group C, group L1.0, and group L1.5 showed statistical differences, with rates of 42.2%, 22.2%, and 8.9%, respectively (χ^2=13.717, P=0.001). Compared to Group C, the incidence of cough in the L1.5 group was significantly reduced.

Tab2. Comparison of the incidence of cough and severe cough among three groups [n=45, case(%)]

Group	Non	Mild	Moderate	Severe
Group C	10(22.22)	16(35.56)	11(24.44)	8(17.78)
Group L1.0	19(42.22)	16(35.56)	8(17.78)	2(4.44)
Group L1.5	28(62.22)	13(28.89)	3(6.67)	1(2.22)
H value	19.498			
P value	<0.001			

2.3 Comparison of Hemodynamic Changes at Different Time Points

(1) After induction of general anesthesia, the mean arterial pressure (MAP) significantly decreased at time point T_1, with group L1.0 and group L1.5 showing a more pronounced reduction compared to group C (P<0.05). At time point T_2, MAP increased in all groups, and by time point T_3, it returned to normal levels. The three groups had no statistically significant differences at time points T_0, T_2, and T_3 (P>0.05). (2) Heart rate (HR) increased at time point T_2 and returned to normal levels by time point T_3, with no statistically significant differences between the three groups at any time point (P>0.05). (3) Oxygen saturation (SpO_2) levels remained stable, and no statistically significant differences were observed between the time points or among three groups (P>0.05). as illustrated in **Figure 1**.



Note: A, B, and C represent MAP, HR, and SpO_2, respectively.

Fig. 1 Comparison of hemodynamics changes at different time points among three groups

2.4 Comparison of Perioperative Time-related Outcomes Among Three Groups

The analysis showed no statistically significant differences in bronchoscopy duration, spontaneous ventilation recovery time, time to remove the laryngeal mask, orientation recovery time, or discharge time from the PACU among all groups (P>0.05) **[Table 3]**.

2.5 Comparison of Adverse Event Incidence in the Perioperative Period Among Three Groups

No bradycardia, laryngospasm, hypoxemia, or emergence agitation occurred in any of the three groups. There was a statistically significant difference in the incidence of postoperative nausea, vomiting, and sore throat among the three groups (P < 0.05); the incidence was significantly lower in groups L1.0 and L1.5 compared to group C (P < 0.017). Group L1.5 having an even lower incidence of sore throat. There was no statistically significant difference in the incidence of other adverse events among three groups (P>0.05) [**Table 4**].

Tab 3. Comparison of perioperative-related time indicators among three groups [n=45, $M(Q_1, Q_3)$]

Time Indicators (min)	group C	group L1.0	group L1.5	Z value	P value
Bronchoscopy Procedure Time	20(15,25)	19(17,23)	18(16,23)	0.17	0.92
Spontaneous Breathing Recovery Time	5(4,8)	6(5,9)	5(4,10)	1.81	0.40
Removal of Laryngeal Mask Airway Time	9(7,13)	12(8,15)	10(8,13)	2.01	0.37
Orienting Time	13(10,18)	15(10,17)	12(10,17)	0.76	0.68
Discharge Time from PACU	38(35,43)	40(38,45)	40(36,43)	3.17	0.20

Tab. 4 Comparison of adverse events among three groups (n=45, case)

Adverse Events	Group C	Group L1.0	Group L1.5	χ^2 value	P value
Hypotension	2(4.4)	4(8.9)	0	4.186	0.123
Hypertension	1(2.2)	0	0		1.000[a]
Shivering	1(2.2)	0	0		1.000[a]
Nausea and vomiting	8(17.8)	1(2.2)	1(2.2)	10.584	0.005
Chest Pain	2(4.4)	0	0		0.328[a]
Sore Throat	24(53.3)	8(17.8)	2(4.4)	30.507	<0.001

Note: [a] signified the use of Fisher's exact probability test. Compared with group C, [b]P<0.017.

3 Discussion

This study showed that lidocaine at a dose of 1.5 mg/kg (group L1.5) effectively reduced the incidence of cough and severe cough during the recovery period after bronchoscopy under general anesthesia, which indicated that the intravenous injection of 1.5 mg/kg lidocaine during induction is one of the effective methods to reduce the incidence and severity of cough during the recovery period after bronchoscopy.

Bronchoscopy is often performed by local spraying of lidocaine, primarily to prevent coughing induced by the passage of the bronchoscope through the pharynx. A meta-analysis has indicated that lidocaine can effectively reduce airway complications, including the incidence and severity of intraoperative and postoperative cough, as well as improve patient comfort; however, its effectiveness is related to the route of administration and dosage, with some variation in results among different studies [8]. This study investigated the effect of intravenous lidocaine administration at different doses on cough during the recovery period following bronchoscopy. The results indicated that lidocaine at a dosage of 1.5 mg/kg (group

L1.5) significantly reduced the incidence of cough and severe cough compared to the control group (group C), suggesting that intravenous lidocaine administration of 1.5 mg/kg during induction is an effective method for reducing the incidence and severity of cough during the recovery period after bronchoscopy. However, the cough suppressive effect appears to be dose-dependent, with the 1.5 mg/kg dosage being necessary to significantly reduce the incidence of cough. However, lidocaine has a narrow therapeutic window, and an excessive dose may lead to adverse reactions, including but not limited to systemic toxicity, hypotension, and arrhythmias [9-11]. Therefore, determining an optimized dosage regimen that maximizes efficacy while minimizing risk is crucial for clinical practice. A study suggests that the initial intravenous dose of lidocaine should not exceed 1.5 mg/kg to reduce the risk of drug-related adverse reactions due to an excessive dose [12]. Furthermore, the safety of intravenous lidocaine must be carefully considered, particularly for patients with pre-existing heart disease, liver dysfunction, or those with metabolic or excretory impairments of lidocaine [13]. Monitoring plasma concentrations and adhering to recommended dosages are key to minimizing potential risks [12,14].

In terms of hemodynamic parameters, the results of this study showed that intravenous administration of lidocaine led to a significant decrease in mean arterial pressure (MAP), with both the 1.0 mg/kg and 1.5 mg/kg doses resulting in approximately a 16.8% reduction, which was considered clinically acceptable. Importantly, the incidence of hypotension as an adverse event was relatively low, with no significant statistical differences observed between groups. The reduction in MAP induced by lidocaine administration may be related to its vasodilatory pharmacological effects [6,8], and this finding also indicated the need for further clinical investigation into the impact of intravenous lidocaine on hemodynamics, focusing on the balance between efficacy and minimizing adverse reactions. This also necessitates strict patient screening and personalized dosing strategies, particularly for patients at increased risk of cardiovascular complications. Although lidocaine has various applications in anesthesia, its effects on blood pressure must be carefully considered, especially in patients with unstable pre-existing cardiovascular conditions, and a comprehensive assessment of its risks and benefits is necessary [15].

The incidence of postoperative nausea and vomiting (PONV) after general anesthesia is approximately 30% [16]. Opioids are a major cause of PONV [17]. In this study, the incidence of PONV in group C was 17.8%, which may be attributed to the sole use of the short-acting opioid remifentanil, which has a duration of action of only 5 to 10 minutes. In contrast, the incidence of PONV in the two lidocaine groups was only 2.2%, showing a significant statistical difference compared to group C, indicating that intravenous lidocaine can effectively reduce the incidence of nausea and vomiting. A study suggested that intravenous lidocaine can reduce the incidence of postoperative nausea and vomiting [18]. However, the evidence supporting this claim is considered 'very low' [19]. Studies have shown that the incidence of sore throat after intubation can be as high as 60% [20], and using a laryngeal mask can significantly reduce its incidence [28]. Lidocaine, whether used topically or via intravenous administration, can effectively reduce the incidence and severity of postoperative sore throat [20-21]. However, some studies have shown that the effect of intravenous lidocaine is superior to topical use [7]. While this study did not classify the severity of sore throat, the incidence of cough-induced sore throat upon discharge from the PACU was 53.3%, 17.8%, and 4.4% for group C, group L1.0, and group L1.5, respectively, indicating that lidocaine significantly reduced the incidence of sore throat, with the higher dose group L1.5 having an even lower incidence. Additionally, it was observed that there were no significant differences in the incidence of other adverse events among the groups, further confirming the safety of intravenous lidocaine. However, due to its potential for systemic toxicity, especially at higher doses, the cautious use of lidocaine is also crucial [22].

This study has several limitations. First, although efforts were made to standardize the assessment of cough severity, it remains subjective, which could introduce bias. Therefore, the use of objective indicators could enhance the reliability of future studies. Second, this study primarily examined the outcomes observed in the PACU after bronchoscopy without assessing the effects of lidocaine over a longer period post-administration, which warrants further investigation. Third, the potential interactions between lidocaine and other perioperative medications were not explored, which could influence the efficacy and the occurrence of adverse reactions. Addressing these limitations in subsequent studies will help to gain a more comprehensive understanding of the role of lidocaine in cough suppression.

In summary, intravenous lidocaine at a dose of 1.5 mg/kg effectively reduces the incidence of cough and severe cough during the postoperative recovery period. It significantly decreases the occurrence of sore throat and postoperative nausea and vomiting. This approach markedly enhances patient comfort and safety during bronchoscopy under general anesthesia.

Conflict of Interest None

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Submission received: 2024-07-24 / **Revised**:2024-08-06

·论　著·

静脉注射不同剂量利多卡因对全麻下行支气管镜检查后复苏期咳嗽的影响

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摘要：目的　评估静脉注射不同剂量利多卡因在全麻下行支气管镜检查后对复苏期咳嗽的影响，以确定利多卡因最佳剂量。**方法**　采用前瞻性、单中心、随机对照临床试验方法，选取 2023 年 9 月至 2024 年 6 月南方医科大学顺德医院 135 例行支气管镜检查的患者，随机分为 C 组（生理盐水）、L1.0 组（1.0 mg/kg 利多卡因）、L1.5 组（1.5 mg/kg 利多卡因），每组 45 例。采用喉罩插管的全身麻醉，诱导后，分别静脉注射利多卡因和生理盐水。记录并分析拔除喉罩后 30 min 内咳嗽的发生情况，同时记录不良事件。咳嗽严重程度分为：轻度（单次咳嗽）、中度（持续超过 5 s 的多次咳嗽但无连续性）、重度（连续咳嗽超过 5 s）。**结果**　C 组、L1.0 组、L1.5 组患者复苏期咳嗽发生率分别为 42.2%、22.2%和 8.9%，三组间差异有统计学意义（$\chi^2=13.72$，$P<0.01$），两两比较经 Bonferroni 校正，L1.5 组显著低于 C 组（$\chi^2=13.14$，$P<0.01$）。重度咳嗽发生率分别为 17.8%、4.4%和 2.3%，三组间差异有统计学意义（$\chi^2=8.51$，$P<0.05$）。与 C 组相比，L1.0 组和 L1.5 组的术后恶心呕吐和咽喉痛发生率均显著降低（$P<0.017$）。**结论**　静脉注射 1.5 mg/kg 利多卡因能有效降低全麻下行支气管镜检查后复苏期咳嗽和重度咳嗽发生率，且显著减少恶心呕吐和咽喉痛的发生。

关键词：支气管镜检查；利多卡因；咳嗽；喉罩全身麻醉；不良反应
中图分类号：R614.2　**文献标识码：**A　**文章编号：**1674-8182(2024)12-1855-06

Effect of intravenous injection of different doses of lidocaine on cough during the recovery period after bronchoscopy under general anesthesia

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Abstract: Objective　To evaluate the effect of intravenous injection of different doses of lidocaine on cough during the recovery period after bronchoscopy under general anesthesia, aiming to determine the optimal lidocaine dose. **Methods**　Using prospective, single-center, randomized controlled clinical trial methods, a total of 135 patients who underwent bronchoscopy in Shunde Hospital of Southern Medical University from September 2023 to June 2024 were selected, and they were randomly divided into group C (normal saline), group L1.0 (1.0 mg/kg lidocaine), and group L1.5 (1.5 mg/kg lidocaine), with 45 cases in each group. All patients received general anesthesia with laryngeal mask. After induction, lidocaine or saline was administered intravenously. The incidence and severity of cough within 30 minutes after removal of the laryngeal mask were recorded and analyzed, along with adverse events. Cough severity was categorized as mild (single episode), moderate (multiple episodes lasting over 5 s but not continuous), and severe (continuous coughing lasting over 5 s). **Results**　There was a statistically significant difference in the incidence of cough during the recovery period after bronchoscopy among the three groups: 42.2% in group C, 22.2% in group L1.0,

DOI: 10.13429/j.cnki.cjcr.2024.12.008
基金项目：广东省基础与应用基础研究联合基金（2023A1515140142）；广东省普通高校重点科研平台和项目（2023ZDZX2008）；广东省科学技术厅粤澳青年人才项目（粤科智字〔2022〕232 号）；佛山市科技创新项目（2320001007025）
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出版日期：2024-12-20

QR code for English version

and 8.9% in group L1.5 (χ^2 = 13.72, P<0.01), and after Bonferroni correction, that in group L1.5 was significantly lower than that in group C (χ^2 = 13.14, P < 0.01). The incidence of severe cough was 17.8%, 4.4% and 2.3% respectively, and the difference among the three groups was statistically significant (χ^2 = 8.51, P<0.05). Compared with group C, the incidence of postoperative nausea, vomiting and sore throat significantly reduced in group L1.0 and group L1.5 (P<0.017). **Conclusion** Intravenous injection of 1.5 mg/kg lidocaine can effectively decrease the incidence of cough during the recovery period after bronchoscopy under general anesthesia, and also can significantly reduce the occurrences of nausea, vomiting and sore throat.

Keywords: Bronchoscopy; Lidocaine; Cough; Laryngeal mask anesthesia; Adverse reaction

Fund program: Basic and Applied Basic Research Joint Fund in Guangdong Province (2023A1515140142); Key Scientific Research Platform and Project of General Universities in Guangdong Province (2023ZDZX2008); Guangdong and Macao Young Talents Project of Science and Technology Department in Guangdong Province (YKZZ〔2022〕No. 232); Foshan Science and Technology Innovation Project (2320001007025)

喉罩插管全身麻醉下进行的支气管镜检查是呼吸科常见的诊疗手段[1]。然而,术后咳嗽是常见的并发症,可能导致气胸、支气管痉挛或呼吸道受阻等不良后果[2]。特别是在插管的全身麻醉状态下,咳嗽反射敏感性增加,导致术后咳嗽的发生率显著上升[3]。这种反射会增加出血风险,影响治疗效果。

利多卡因在呼吸道局部应用时的镇咳作用已被广泛认可,临床上主要通过局部使用(即喷喉)的方式进行,以降低支气管镜进入气管过程中引起的呛咳反射,但对术后镇咳效果并不显著[4]。而静脉注射利多卡因在降低术前和术后的咳嗽反射敏感性方面均有良好的应用前景[5]。其可能的作用机制是抑制钠离子通道,从而降低咳嗽反射神经纤维的兴奋性[6]。但是,用于减轻在支气管镜检查拔除喉罩后咳嗽的静脉注射利多卡因的最佳剂量,目前尚存在争议,因此,本研究旨在通过比较静脉注射不同剂量利多卡因对支气管镜检查后复苏期咳嗽的影响,探讨一种既能最大限度地抑制全麻下行支气管镜检查拔除喉罩后的咳嗽,又不会引起显著不良反应的优化方案。

1　资料与方法

1.1　研究设计　本研究为一项前瞻性、单中心、随机对照临床试验,获得南方医科大学顺德医院伦理委员会批准(编号:KYLS20231022)。所有纳入的患者或其家属签署了知情同意书。本研究选取了 2023 年 9 月至 2024 年 6 月自愿接受支气管镜检查的患者。

1.2　纳入和排除标准　纳入标准:年龄 18~80 岁,择期行支气管镜检查,美国麻醉医师协会(American Society of Anesthesiologists, ASA)分级为Ⅰ~Ⅲ。排除标准:身体质量指数(body mass mdex, BMI)超过 30 kg/m^2;超过 1 h 的支气管镜检查;严重肝肾功能不全;患有慢性疼痛或精神障碍;有严重的心血管或肺部疾病;对相关药物过敏;患有阻塞性睡眠呼吸暂停综合征、重症肌无力;妊娠或哺乳状态。

1.3　分组和盲法　患者被随机分为三组:C 组(生理盐水)、L1.0 组(1.0 mg/kg 利多卡因)和 L1.5 组(1.5 mg/kg 利多卡因)。使用计算机生成的系统进行随机分组,分组信息保存在不透明信封中。数据收集和记录由独立观察者完成,对分组信息不知情。药物由不参与研究的护士进行配置。利多卡因和生理盐水均为无色透明液体,制备成 10 mL 注射器中,利多卡因浓度为 10 mg/mL,以确保给药麻醉医师和观察者对治疗方案的不知情。

1.4　麻醉操作　术前要求患者禁食 8 h,禁饮 2 h。进入检查室后,患者连接多功能监护仪,常规监测心电图、血压和血氧饱和度(saturation of peripheral oxygen, SpO_2)。诱导前,面罩吸入流速为 6 L/min 的纯氧,通过外周静脉输注乳酸林格溶液,速度为 6~8 mL/(kg·h)。在全麻诱导阶段,首先设置靶控输注瑞芬太尼以达到室浓度 3 ng/mL。当血浆和靶室浓度达到平衡后,以 1 200 mL/h 的速度静脉泵注瑞马唑仑,剂量为 0.3 mg/kg,再静脉给予苯磺酸顺阿曲库铵 0.05 mg/kg,最后以缓慢的速度静脉注射相应剂量的利多卡因或生理盐水,待患者失去睫毛反射及下颌松弛后,置入以石蜡油润滑的喉罩。随后,采用容量控制正压通气以维持呼吸末二氧化碳(end-tidal carbon dioxide concentration, $EtCO_2$)水平在 35~45 mmHg。麻醉维持期间,靶控输注(target-controlled infusion, TCI)瑞芬太尼靶室浓度维持在 2~4 ng/mL,以 0.3~1 mg/(kg·h)的速度连续静脉输注瑞马唑仑,应用血管活性药物将平均动脉压(mean arterial pressure, MAP)维持在基础值的±20%内。由呼吸内科医师执行支气管镜检查操作。术毕,停止输注瑞芬

太尼和瑞马唑仑,将患者转移至麻醉复苏室(postanaesthesia care unit, PACU),在观察患者至恢复自主呼吸后,常规给予 1 mg 新斯的明和 0.5 mg 阿托品以对抗肌肉松弛剂的影响。在患者完全清醒之前进行温和的口腔吸引,当患者能够清醒并对语言提示作出反应,自主呼吸空气且保持 SpO_2 超过 95%,并能在头部上方保持握拳状态超过 5 s 时,拔除喉罩。在 PACU 至少观察 30 min 后,由麻醉医生将患者送回病房。

1.5　样本量估算　本研究进行了预试验,设立了两组:对照组(给予生理盐水)和试验组(给予 1.0 mg/kg 利多卡因),每组 10 例患者。主要观察指标是在拔除喉罩后 30 min 内咳嗽的发生率。初步结果显示,对照组咳嗽发生率为 50%,试验组为 20%。为了达到 80%的研究功效($\beta=0.8$)和显著性水平(α)为 0.05,考虑到数据丢失或失访率为 15%,计算出需要每组 45 例患者,三组共 135 例患者。

1.6　观察指标　(1) 主要结果:在患者从全麻中苏醒并拔除喉罩后 30 min 内,记录咳嗽的发生率和严重程度。在此期间,仅将中至重度咳嗽作为有效咳嗽,并纳入分析。咳嗽严重程度分为:轻度(单次咳嗽)、中度(持续超过 5 s 的多次咳嗽但无连续性)、重度(连续咳嗽超过 5 s)[7]。(2) 其他结果:麻醉前(T0)、置入喉罩后 1 min 时(T1)、拔除喉罩时(T2)、离开 PACU 时(T3)的 MAP、心率(heart rate, HR)及 SpO_2。记录支气管镜检查时间、自主呼吸恢复时间、拔除喉罩时间、定向力恢复时间、出 PACU 时间等。此外,还记录低血压、高血压、心动过缓、喉痉挛、低氧血症、寒战、术后恶心呕吐、苏醒期躁动、胸痛、咽喉痛等不良事件。低氧血症定义为 SpO_2 低于 90%且维持 5 s。咽喉痛定义为出 PACU 时询问是否存在咳嗽时疼痛。

1.7　统计学方法　使用 SPSS 22.0 进行统计分析。通过 Shapiro-Wilk 检验评估数据正态分布,正态连续变量以 $\bar{x}\pm s$ 表示,多组间比较采用单因素 ANOVA,多组不同时间点比较采用重复测量的方差分析, 两两比较采用 LSD 法;偏态连续变量以 $M(Q_1,Q_3)$ 表示,采用 Kruskal-Wallis 秩和检验, 两两比较采用 Bonferroni 法;分类数据以例或例(%)表示,采用 Pearson χ^2 检验或 Fisher 确切概率法,两两比较采用 Bonferroni 校正法。均行双侧检验,检验水准 $\alpha=0.05$,χ^2 检验两两比较时,$\alpha'=0.017$。

2　结　果

2.1　一般资料比较　共有 147 例患者最初被纳入研究,其中 6 例因不符合纳入标准而被排除,余 141 例患者分为三组:C 组($n=45$)、L1.0 组($n=48$)和 L1.5 组($n=48$)。因 L1.0 组和 L1.5 组各有 3 例患者数据缺失,最终为 135 例患者,每组各 45 例。各组的年龄、BMI、性别、ASA 分级、病史和检查类型等基线特征差异均无统计学意义($P>0.05$)。见表 1。

表 1　三组患者一般资料比较　($n=45$, 例)
Tab. 1　Comparison of general information among three groups　($n=45$, case)

指标	C 组	L1.0 组	L1.5 组	$Z/F/\chi^2$ 值	P 值
年龄(岁)[a]	59(42, 70)	55(37, 64)	56(45, 69)	2.850	0.240
身高(cm, $\bar{x}\pm s$)	164.1±8.3	163.3±8.8	160.4±6.8	2.657	0.074
体重(kg, $\bar{x}\pm s$)	58.9±12.1	59.6±12.5	59.7±9.0	0.067	0.935
BMI(kg/m^2, $\bar{x}\pm s$)	21.8±3.6	22.3±4.2	23.2±3.4	1.612	0.203
性别(男/女)	30/15	22/23	24/21	3.131	0.209
ASA 分级(Ⅰ/Ⅱ/Ⅲ)	4/35/6	6/33/6	4/38/3	2.130	0.712
个人史和病史					
吸烟	11	8	8	0.833	0.660
高血压	7	3	2	3.841	0.146
糖尿病	1	0	1		1.000[b]
慢性阻塞性肺疾病	0	1	0		1.000[b]
哮喘	0	1	0		1.000[b]
检查类型				7.124	0.523
经支气管活检	18	12	14		
经激光治疗	0	0	2		
支气管支架置入术	0	1	1		
刷检术	7	9	6		
支气管肺泡灌洗	20	23	22		

注:[a] 表示数据形式为 $M(Q_1,Q_3)$,[b] 为 Fisher 确切概率法。

2.2　三组患者咳嗽和重度咳嗽发生率比较　咳嗽严重程度观察见表 2。重度咳嗽发生率三组比较差异有统计学意义($\chi^2=8.512$, $P=0.014$),与 C 组相比,L1.5 组显著降低了重度咳嗽的发生率($P<0.017$)。将中等至重度咳嗽定义为有效咳嗽,计算其发生率,C 组、L1.0 组和 L1.5 组咳嗽发生率具有统计学差异,分别为 42.2%、22.2% 和 8.9% ($\chi^2=13.717$, $P=0.001$);与 C 组相比,L1.5 咳嗽的发生率组显著降低($P<0.017$)。

2.3　不同时间点的血流动力学变化比较　(1) 全麻诱导后,MAP 在 T1 时点明显下降,且 L1.0 组和 L1.5 组的 MAP 降低显著低于 C 组($P<0.05$),T2 时点各组均回升,T3 时点回到正常水平; T0、T2、T3 时点三组间差异无统计学意义($P>0.05$)。(2) HR 在 T2 时点升高,T3 时点回到正常水平,各时点三组间差异均无统计学意义($P>0.05$)。(3) SpO_2 水平一直平稳,各时点间、各组间均未观察到统计学差异($P>0.05$)。见图 1。

2.4　三组患者围术期相关时间结果比较　分析显

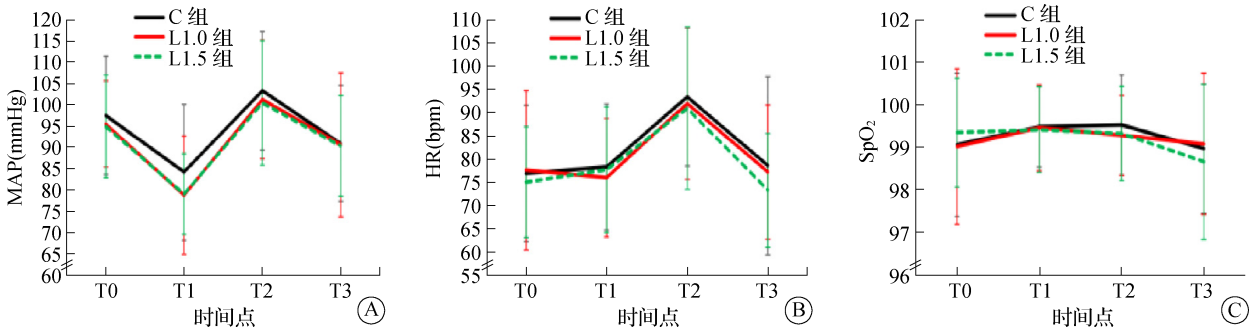
示,在所有组别中,支气管镜检查持续时间、自主呼吸恢复时间、拔除喉罩时间、定向力恢复时间以及出 PACU 时间差异均无统计学意义(P >0.05)。见表 3。

2.5　三组患者不良事件发生情况比较　三组均未发生心动过缓、喉痉挛、低氧血症和苏醒期躁动。三组在术后恶心呕吐、咽喉痛发生率上差异有统计学意义(P<0.01),L1.0 组和 L1.5 组显著低于 C 组(P<0.017)。其他不良事件三组间差异无统计学意义(P>0.05)。见表 4。

表 2　三组咳嗽情况比较　[n=45, 例(%)]

Tab. 2　Comparison of cough conditions among three groups　[n=45, case (%)]

组别	无咳嗽	轻度咳嗽	中度咳嗽	重度咳嗽
C 组	10(22.22)	16(35.56)	11(24.44)	8(17.78)
L1.0 组	19(42.22)	16(35.56)	8(17.78)	2(4.44)
L1.5 组	28(62.22)	13(28.89)	3(6.67)	1(2.22)
H 值	19.498			
P 值	<0.001			



注:A、B、C 分别为 MAP、HR、SpO_2。

图 1　三组患者不同时间点血流动力学比较

Fig. 1　Comparison of hemodynamics changes at different time pointsamong three groups

表 3　三组患者围术期相关时间指标比较　[n=45, min, $M(Q_1, Q_3)$]

Tab 3　Comparison of perioperative related time indicators among three groups　[n=45, min, $M(Q_1, Q_3)$]

时间指标	C 组	L1.0 组	L1.5 组	Z 值	P 值
支气管镜检查时间	20(15, 25)	19(17, 23)	18(16, 23)	0.17	0.92
自主呼吸恢复时间	5(4, 8)	6(5, 9)	5(4, 10)	1.81	0.40
拔除喉罩时间	9(7, 13)	12(8, 15)	10(8, 13)	2.01	0.37
定向力恢复时间	13(10, 18)	15(10, 17)	12(10, 17)	0.76	0.68
出离 PACU 时间	38(35, 43)	40(38, 45)	40(36, 43)	3.17	0.20

表 4　三组患者不良事件比较　[n=45, 例(%)]

Tab. 4　Comparison of adverse events among three groups　[n=45, case (%)]

不良事件	C 组	L1.0 组	L1.5 组	χ^2/t 值	P 值
低血压	2(4.4)	4(8.9)	0	4.186	0.123
高血压	1(2.2)	0	0		1.000[a]
寒战	1(2.2)	0	0		1.000[a]
恶心呕吐	8(17.8)	1(2.2)[b]	1(2.2)[b]	10.584	0.005
胸痛	2(4.4)	0	0		0.328[a]
咽喉痛	24(53.3)	8(17.8)[b]	2(4.4)[b]	30.507	<0.001

注:[a] 为比较采用 Fisher 确切概率法;与 C 组相比,[b]P<0.017。

3　讨　论

本研究结果显示,1.5 mg/kg 的利多卡因(L1.5 组)利多卡因能有效地降低全麻下行支气管镜检查术后复苏期咳嗽和重度咳嗽发生率,表明诱导期静脉注射 1.5 mg/kg 的利多卡因是降低支气管镜检查术后复苏期咳嗽频率及严重程度的有效方法之一。

支气管镜检查多通过局部喷洒利多卡因的方式进行,主要为预防支气管镜通过咽喉部时引起的呛咳。有 Meta 分析研究表明,利多卡因能有效减少气道并发症,包括术中及术后咳嗽的发生率和严重程度,提高患者舒适度,但其效果与给药途径和剂量相关,不同研究结果存在一定差异[8]。本研究是通过静脉注射利多卡因方式,主要目的就是为减少术后复苏期发生的咳嗽。研究结果显示,与 C 组相比,L1.5 组咳嗽和重度咳嗽的发生率明显更低,L1.0 组稍低,但差异无统计学意义,表明静脉注射利多卡因能有效降低患者复苏期咳嗽发生率,但需要达到 1.5 mg/kg 剂量,方能发挥抑制咳嗽发生的作用。然而,利多卡因的治疗窗较窄,过量剂量可能导致不良反应,包括但不仅限于系统性毒性、低血压和心律失常[9-11]。因此,确定一种最大限度提高疗效,同时最大限度减少风险的优化剂量方案对临床实践至关重要。有研究建议利多卡因的初始静脉剂量不应超过 1.5 mg/kg,以降低因剂量过大引起的药物不良反应的风险[12]。此外,静脉注射利多卡因的安全性需要谨慎考虑,尤其是对于有预先存在的心脏病、肝功能不全或可能改变利多卡因代谢或排泄的并发药物的患者[13]。监测

血浆浓度并遵守推荐剂量是降低潜在风险的关键[12, 14]。

本研究结果显示,利多卡因静脉给药导致了 MAP 显著降低,1.0 mg/kg 和 1.5 mg/kg 剂量均出现约 16.8%的下降,但这种降低幅度被认为是临床可接受的。重要的是,在不良事件方面,低血压的发生率相对较低,但组间差异无统计学意义。利多卡因给药引起的 MAP 降低可能与其扩张血管的药理作用相关[6, 8],这一结果也促使临床需要关注疗效和减少不良反应之间的平衡。这也要求对患者进行严格的筛选和个性化的给药策略,特别是对心血管并发症风险增加的患者。尽管利多卡因在麻醉中有各种应用,但其对血压的影响需要谨慎考虑,特别是对于原有心血管状况不稳定的患者,有必要全面考虑其风险和益处[15]。

全麻后术后恶心呕吐的发生率约为 30%[16]。使用阿片类药物是术后恶心呕吐的主要原因[17]。本研究中,C 组术后恶心呕吐的发生率为 17.8%,这可能归因于单独使用作用持续时间仅为 5 至 10 min 的短效阿片类药物瑞芬太尼。相反,两个利多卡因组术后恶心呕吐的发生率仅为 2.2%,与 C 组比较差异有统计学意义,表明静脉注射利多卡因可以有效降低恶心呕吐的发生率。有研究表明,静脉注射利多卡因会降低术后恶心呕吐的发生率[18]。然而,支持这一说法的证据质量被认为是“非常低”[19]。有研究显示,气管插管后引发的咽喉痛比例高达 60%[20],使用喉罩可以明显降低其发生率。利多卡因不管是局部使用还是静脉注射使用,都能有效降低术后咽喉痛发生率和程度[20-21]。但有研究显示,静脉注射利多卡因的效果优于局部使用[7]。虽然本研究没有对咽喉痛的严重程度进行分类,但离开 PACU 时患者咳嗽引起的咽喉痛发生率,C 组、L1.0 组、L1.5 组分别为 53.3%、17.8%和4.4%,可见利多卡因能显著降低咽喉痛发生率,且剂量高的 L1.5 组发生率更低。本研究还观察到,各组间其他不良事件发生率相近,证实了静脉注射利多卡因的安全性。然而,由于潜在的全身毒性,特别是在较高剂量下,谨慎使用利多卡因也至关重要[22]。

本研究存在几个局限性。首先,咳嗽严重程度评估尽管已经尽力标准化,但依然存在主观性,这可能引入偏见。因此,使用客观指标可以提高未来研究的可靠性。其次,本研究主要是了解支气管镜检查后在 PACU 观察到的结果,而未评估利多卡因使用后更长时间内的应用效果。第三,未探讨利多卡因与其他围手术期药物之间可能存在的相互作用,这可能影响疗效和不良反应的发生。

总之,静脉注射利多卡因 1.5 mg/kg 可有效降低术后复苏期咳嗽和重度咳嗽发生率,且可显著减少咽喉痛和恶心呕吐的发生。这种方法在全身麻醉下进行支气管镜检查时,显著提高了患者的舒适度和安全性。

利益冲突　无

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收稿日期:2024-07-24　**修回日期**:2024-08-06　**编辑**:石嘉莹

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收稿日期:2024-06-14　**修回日期**:2024-07-11　**编辑**:李方