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CLINICAL TRIAL REPORT

The Influence of Piriform Recess Instillation with Lidocaine Before Bronchoscopy on Post-General Anesthesia Cough: A Randomized Controlled Trial

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Background and Importance: Postoperative cough is a common complication of general anesthesia after bronchoscopy. The aim of the present study was to determine the safety profile and efficacy of piriform recess instillation with lidocaine in reducing the incidence of coughing.

Objective: To what extent could piriform recess instillation with lidocaine decrease the incidence of cough at 10min after extubation?

Outcome Measures and Analysis: Eighty-eight consecutive patients were equally randomized to a lidocaine group receiving piriform recess instillation with 2mL 2% lidocaine, and a normal saline group receiving piriform recess instillation with 2mL saline. The primary outcome was the incidence of cough after extubation, and the secondary outcomes were throat score at 10 min and 6 h after extubation assessed by the numerical rating scale, cough severity at 10 min and 6 h after extubation assessed by the Visual Analog Scale (VAS), 24 h 40-item Quality of Recovery Score (QoR-40), and subject-rated satisfaction score on a VAS.

Main Results: Compared with saline group, the incidence of cough in lidocaine group was significantly lower (63.6% vs 86.4%, P=0.014). The sore throat score at 10 min after extubation was significantly lower (0[0,0] vs 1[0,2], P<0.001). The subject-rated overall anesthesia satisfaction score was significantly higher (84.8[±6.2] vs 76.6[±8.6], P<0.001). The severity of cough at 10 min after extubation was significantly lower (Mild: 36.4% vs 11.4%, P=0.006; Severe: 9.1% vs 43.2%, P<0.001). There was no significant difference in the sore throat score at 6 h after extubation, severity of cough at 6 h after extubation, or QoR-40 at 24 h after extubation between the two groups.

Conclusion: Piriform recess instillation with lidocaine before bronchoscopy is a simple and effective method for reducing early cough intensity and alleviating early sore throat. At 6 hours, there were no differences observed between the groups.

Clinical Trial Registration: Chinese Clinical Trial Registry (identifier: ChiCTR2200067087).

Keywords: piriform recess, lidocaine, general anesthesia, cough, bronchoscopy

Introduction

The incidence of cough after awakening from general anesthesia through endotracheal intubation is estimated to be between 38% and 96%,[1] the contributing causes of which include pharyngeal secretion and chemical irritation caused by volatile anesthetics and smoking.[2,3] Bronchoscopy has been the primary method for diagnosing and treating a variety of respiratory diseases, with a wide range of sedative options available.[4] General trials done under moderate sedation or local anesthesia show lidocaine use on the pharynx and larynx to be effective.[5,6] Effective intraoperative sedation and analgesia can improve patient comfort and facilitate the operation endoscopy. However, the practice may not be generalized when patients are under general anesthesia. Intense stimulation during the invasive process may evoke the

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airway to make strong responses after awakening, which manifest as cough, postoperative sore throat (POST) and dysphagia.[5,7,8] Multiple techniques have been identified as effective in reducing coughing, including the alkalinized lidocaine preloaded endotracheal tube cuff,[9] lidocaine infusion,[10] trans-cricothyroid membrane injection,[11] and ultrasound-guided internal superior laryngeal nerve (iSLN) block.[12]

The superior laryngeal nerve (SLN) is a branch of the vagus nerve that divides into an internal and external branch, with the internal branch innervating the tongue, epiglottis, and laryngeal mucous membrane down to the vocal cords. The mucosa of the laryngopharynx sinks to form a deep fossa known as the piriform recess between the sides of the aditus laryngis and the inner surface of the thyroid cartilage. Below is the iSLN.[13] The effectiveness of SLN block in reducing cough is debatable Some studies[14] showed that SLN block used as an adjuvant to general anesthesia could improve patient recovery and reduce the occurrence of postoperative cough, POST, and hoarseness of voice, but Wang et al[15] reported that ultrasound-guided iSLN block could not reduce the occurrence of cough. The efficacy of piriform recess lidocaine instillation on cough occurrence remains unknown.

The aim of this prospective randomized clinical trial was to see whether piriform recess instillation with lidocaine prior to bronchoscopy could reduce the incidence of cough during emergence from general anesthesia.

Patients and Methods

Study Design

This prospective, double-blinded, and randomized single-center clinical trial was conducted between December 2022 and February 2023, in the bronchoscopy suite of the Shanghai Pulmonary Hospital. The study protocol was approved by the Clinical Research Ethics Committee of Shanghai Pulmonary Hospital on December 8th, 2022 (L22-351-1). This trial was registered at https://www.chictr.org.cn/edit.aspx?pid=186944andhtm=4 on December 26th, 2022 (ChiCTR2200067087). All study participants provided written informed consent. This manuscript adhered to the applicable CONSORT guidelines. The study complied with the Declaration of Helsinki.

Patients

Included in this study were 88 patients with American Society of Anesthesiologists (ASA) physical classification of I–III who were scheduled for bronchoscopy under general anesthesia with laryngeal mask ventilation. The exclusion criteria were pregnant and lactating women, patients who were allergic to narcotic drugs, and patients with heart failure (NYHA classes 3–4), drug abuse or severe neurological diseases that may impair cognition, and upper respiratory tract infections such as chronic obstructive pulmonary disease (COPD) and bronchiectasis. Details of patient enrolment are shown in Figure 1.

Randomization

The 88 included patients were equally randomized into a lidocaine group receiving piriform recess instillation with lidocaine (lidocaine group) and a normal saline group receiving piriform recess instillation with saline (saline group). The randomization sequence was generated by computer, and the assignments were put inside of sealed opaque envelopes. The local anesthetics were prepared by nurse anesthesiologists. The patients, statisticians, researchers, and endoscopists were blinded to the solution used for the procedure.

The Study Protocols

The demographic data of the patients including age, weight, height, smoking status, and previous medical histories were collected. Pre-oxygenation with 100% O_2 was achieved using a face mask, and general anesthesia was induced using propofol 1.0–1.5 mg/kg, sufentanil 0.1–0.3 μg/kg, rocuronium bromide 0.4–0.6mg/kg. After positioning the laryngeal mask correctly, a fresh syringe of either 2 mL of 2% lidocaine or 2 mL of saline was instilled into each side of the piriform recess using bronchoscopy. The intervention was performed by the same group of experienced endoscopists. Anesthesia was maintained with propofol and rocuronium. Atropine, ephedrine, and sufentanil were permitted to preserve hemodynamic values within 20% of preoperative baseline.

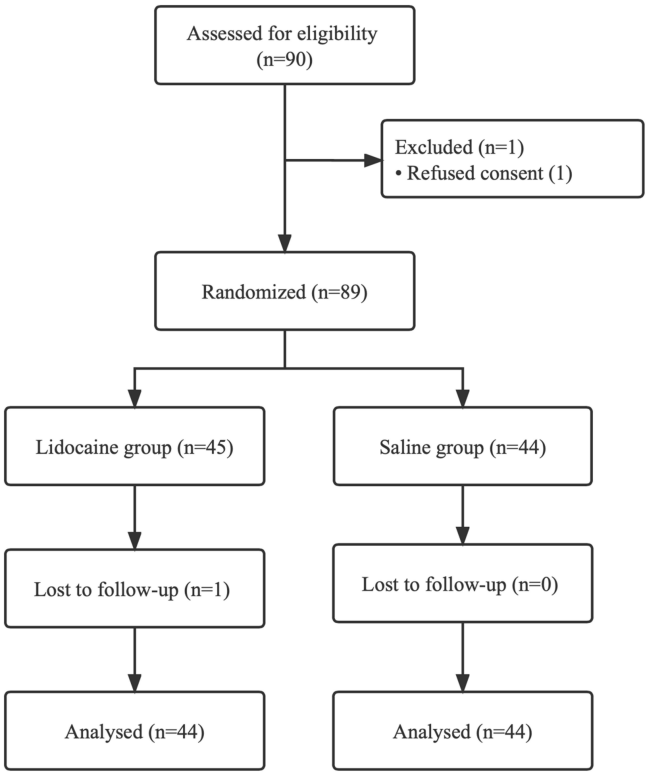

Figure 1 Flowchart of the study procedure.

Sugammadex sodium injection was used at the end of the procedure to antagonize when necessary. When there was a directed response to the command, extubation occurred. After subjects entered the post-anesthesia care unit, a dedicated researcher recorded the severity of the cough in the first 10 min and 6h. The number and grade of coughing episodes (0: no cough; 1: mild; single cough; 2: moderate; more than 1: cough lasting for less than 5 s; 3: severe, sustained for longer than 5 s).[16] The severity of POST was assessed on a numerical rating scale (NRS) from 0 to 10, where 0 = no pain and 10 = the worst imaginable pain. At 24 h after surgery, the QoR-40 questionnaire was evaluated by the same trained researcher. Subject-rated overall anesthesia satisfaction was evaluated using the Visual Analog Scale (VAS) from totally unsatisfactory (0 mm) to very satisfactory (100 mm).

Study Outcomes

The primary outcome was the incidence of cough. Secondary outcomes included cough severity and sore throat score at 10min and 6h, 24h QoR-40 score, and subject-rated satisfaction score.

Sample Size Calculation

The sample size was calculated with the model of Test for Two Means in PASS V11 software (NCSS, Kaysville, Utah, USA) based on the incidence of cough in our pre-experiment study (90% in saline group, 73% in lidocaine group). At a power of 80% and a significance level of 0.05, considering a 10% withdrawal rate, 45 participants were required in each group.

Statistical Analysis

All analyses were performed using SPSS 21 (International Business Machines Inc., USA). Continuous variables were presented as mean ± standard deviation (SD) for normally distributed data or median (interquartile range, IQR) for non-normally distributed data. Continuous variables were compared using the *t* test (normally distributed data) or the Wilcoxon rank sum test (non-normally distributed data). Categorical variables are presented as number (percentage) and compared using the $\chi 2$ test/Fisher exact test. *P* value less than 0.05 was considered statistically significant.

Results

The study flowchart is shown in Figure 1. A total of 90 patients were assessed for eligibility. One was excluded due to refusal of consent, and one was lost for follow-up. Finally, 88 patients were included for analysis. Their baseline demographic and clinical characteristics are summarized in Table 1, showing no significant differences in gender distribution, age, body mass index (BMI), smoking, indications for bronchoscopy, and the diagnostic process between the two groups.

The incidence of cough at 10 min post-operation in lidocaine group was significantly lower than that in saline group (63.6% vs 86.4% P=0.014) (Table 2). The sore throat score in lidocaine group was significantly lower than that in saline group (0[0,0] vs 1[0,2], P<0.001). But the sore throat score at 6h was comparable between the two groups. In addition, the subject-rated overall anesthesia satisfaction in lidocaine group was significantly higher than that in saline group (84.8

Table 1 Patient Demographic and Clinical Parameters

Variables	Lidocaine Group (n=44)	Saline Group (n=44)	*P* value
Age, mean± SD	60.7(±10.3)	61.8(±11.2)	0.658
Males, n (%)	28(63.6)	31(70.5)	0.496
BMI (kg /m2), mean± SD	22.7(±2.0)	23.0(±1.7)	0.415
Smoker, n (%)	21(47.7)	18(40.9)	0.668
Indication for bronchoscopy, n (%)			
Infection	9(20.5)	5(11.5)	0.383
Chronic cough	7(15.9)	9(20.5)	0.783
Hemoptysis	8(18.2)	5(11.4)	0.549
Suspicion of malignancy	15(34.1)	18(40.9)	0.660
Cancer follow-up	2(4.5)	4(9.1)	0.676
Chest pain	1(2.3)	3(6.8)	0.616
Atelectasis	2(4.5)	0(0)	0.153
Procedures performed, n (%)			
Bronchial brushing	4(9.1)	6(13.6)	0.739
Bronchial washing and brushing	12(27.3)	8(18.2)	0.446
EBUS-TBNA	17(38.6)	15(34.1)	0.825
BAL	3(6.8)	5(11.4)	0.713
EBB	8(18.2)	10(22.7)	0.597

Note: Data are presented as mean (±SD) or n (%).
Abbreviations: EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; EBB, endobronchial biopsy; BAL, bronchoalveolar lavage.

Table 2 Primary and Secondary Outcome Measures

Outcomes	Lidocaine Group (n=44)	Saline Group (n=44)	*P* value
Primary outcome			
Incidence of cough, n (%)	28(63.6%)	38(86.4%)	0.014
Secondary outcomes			
Sore throat score			
10min	0(0,0)	1(0,2)	<0.001
6h	0(0,1)	1(0,1)	0.252
24h QoR-40 score	181.2(±1.9)	180.5(±1.8)	0.083
Subject-rated overall anesthesia satisfaction	84.8(±6.2)	76.6(±8.6)	<0.001
10min	0(0,0)	1(0,2)	<0.001
6h	0(0,1)	1(0,1)	0.252
24h QoR-40 score	181.2(±1.9)	180.5(±1.8)	0.083

Notes: Data are presented as median (IQR), mean ± SD or n (%). QoR-40, Quality of Recovery-40.

Table 3 Severity of Cough

Severity of Cough	Lidocaine Group (n=28)	Saline Group (n=38)	*P* value
Severity of cough (10min), n (%)			
Mild	16(36.4)	5(11.4)	0.006
Moderate	8(18.2)	14(31.8)	0.14
Severe	4(9.1)	19(43.2)	<0.001
Severity of cough (6h), n (%)			
Mild	7(15.9)	10(22.7)	0.418
Moderate	2(4.5)	4(9.1)	0.398
Severe	0	0	1

Note: Data are presented as n (%).

vs 76.6, $P<0.001$). The severity of cough at 10min in lidocaine group was significantly lower than that in NS group (Mild: 36.4% vs 11.4%, $P=0.006$; Severe: 9.1% vs 43.2%, $P<0.001$), but there was no significant difference at 6 h post-operation between the two groups (Table 3).

Discussion

The results of this randomized controlled trial demonstrated that the piriform recess instillation lidocaine could lower the incidence of cough, attenuate cough severity, reduce POST score in 10min postoperatively, and improve subject-rated satisfaction score as compared with saline group.

It was reported[17] that laryngotracheal topicalization with lidocaine before intubation could reduce the incidence of cough both before and after tracheal extubation as compared with the placebo group (26% vs 66% and 4% vs 30%). In our study, the 28% incidence of cough in lidocaine group was slightly higher. The reason might be explained by the fact that the glottis and airway may be damaged during bronchoscopy.

The application of SLN block for vocal cord polypectomy during suspension laryngoscopy had a significantly lower incidence of perioperative cough in the early period (1 hour after extubation).[18] When compared to local spray, perineural injection surrounding the iSLN performed better in suppressing cough during thyroidectomy.[19] Similarly, the attenuation of refractory cough by SLN block has been demonstrated in COVID-19 patients undergoing extracorporeal membrane oxygenation.[20] A more recent study[21] showed that SLN block in bariatric surgery could blunt fiberscope-associated cough during awake endotracheal intubation. These studies demonstrate that SLN block can safely and effectively attenuate cough occurrence. In our study, piriform recess instillation with lidocaine to block iSLN before bronchoscopy significantly decreased the incidence of cough in the early postoperative period.

Cough frequency is reported to increase during nebulized lidocaine administration due to pharyngeal sensory fiber activation, which induces spontaneous cough frequency.[22] It was found in our study that intubation with a laryngeal mask and airway movement caused by a bronchoscope were the two main causes of cough. Additionally, when lidocaine was instilled into the piriform recess after successful induction of general anesthesia, the patient has lost the initial painful burning sensation and therefore coughing was unaffected by sensory fiber activation. During emergence from general anesthesia, various reflexes gradually recover. Piriform recess instillation with lidocaine was only effective for early cough suppression. Lidocaine, with a very short half-life of 1.85 hours,[23] resulted in no difference at 6 hours.

Previous studies reported that 24–70% patients under general anesthesia had sore throat after extubation.[24] iSLN blockade with lidocaine can not only block noxious stimulation but also provide an analgesic effect. Lidocaine has analgesic and anti-inflammatory properties due to its actions on potassium and calcium channels, as well as G protein-coupled receptors.[25] Because of its actions on potassium and calcium channels, as well as G protein-coupled receptors, lidocaine has analgesic and anti-inflammatory properties.[12] POST most frequently occurred 2–4 hours after extubation.[26] It was found in our study that the NRS score of POST was reduced in the early postoperative period (10min after extubation). Coughing was thought to worsen the tracheal mucosa injury caused by POST.[27] The higher incidence of cough in saline group might have contributed to the higher POST NRS score. The half-life of topical lidocaine in

children aged 3 months to 9.5 years is 109 min.[28] This could explain why the saline group had slightly higher NRS scores, but there was no statistical difference between the two groups at 6h post-operation.

The current study has a few limitations. Firstly, the bronchoscope was utilized to administer lidocaine into the piriform recess, suggesting that the procedure may not be easily applicable to other surgeries. Secondly, the POST NRS score was subjective. Airway management, including intubation and extubation, may have an impact on POST. Finally, we did not measure the actual serum concentrations of lidocaine.

Conclusion

Piriform recess instillation of lidocaine before bronchoscopy decreases the early cough intensity and alleviates the early sore throat.

Abbreviations

ASA = American Society of Anesthesiologists; BAL = Bronchoalveolar Lavage; BMI, Body Mass Index; COPD = Chronic Obstructive Pulmonary Disease; EBB = Endobronchial Biopsy; EBUS-TBNA=Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration; IQR = Interquartile Range; iSLN = Internal Superior Laryngeal Nerve; NRS = Numerical Rating Scale; POST = Postoperative Sore Throat; SD = Standard Deviation; SLN = Superior Laryngeal Nerve; TRPV1 = Transient Receptor Potential Vanilloid Type-1; TRPA1 = Transient Receptor Potential Ankyrin-1; VAS = Visual Analog Scale; Vgscs=Voltage-Gated Sodium Channels.

Guarantor Statement

X. L takes responsibility for the content of the manuscript, including the data and analysis.

Data Sharing Statement

All data generated or analyzed during this study have been included in the published article. For further inquiries regarding the datasets, they are available from Xin Lv upon request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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