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ORIGINAL RESEARCH **GENERAL ANESTHESIA**

Comparison of the effectiveness of lidocaine sprayed at the laryngeal inlet and the endotracheal tube cuff versus intravenous lidocaine for reducing cough during extubation: A prospective randomized controlled trial

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Abstract

Background & objective: Coughing during extubation of the endotracheal tube (ETT) may lead to poor surgical results. The aim of this study was to investigate the efficacy of a simple lidocaine application route to reduce coughing during ETT extubation.

Methodology: A prospective, randomized control trial was conducted. The topical group received four puffs of 10% lidocaine sprayed at the cuff of the ETT and four puffs at the laryngeal inlet, whereas the intravenous (IV) group received a 1.5 mg/kg intravenous injection of 2% lidocaine prior to extubation. The incidences of coughing during extubation, 24-h postoperative adverse events, and hemodynamic responses after extubation were analyzed.

Results: One hundred forty-eight patients met the criteria for analysis. The incidence of coughing during extubation between the topical group (44.6%) and the IV group (50.0%) was not significantly different ($p = 0.51$). However, the incidence of having a cough with a severity grade of 3 was significantly less likely to occur in the topical group (1.4%) compared to the IV group (9.5%) ($p = 0.02$). The incidence of having a sore throat was similar in both groups ($p > 0.99$), whereas hoarseness and dysphagia events were not found in the topical group. There was no statistically significant difference in the hemodynamic response between groups.

Conclusion: The combination of topical lidocaine spray on the laryngeal inlet and cuff of the ETT seems similarly effective in reducing cough during extubation compared to systemic IV lidocaine. However, the combined topical lidocaine application showed benefit outcomes, including reduced incidence of grade 3 cough severity and no dysphagia or hoarseness events.

Key words: Lidocaine; Endotracheal tube; Cough; Sore throat

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1. Introduction

Coughing during extubation of the endotracheal tube is a common problem that leads to poor surgical outcomes. The cough may produce hemodynamic changes, bronchospasms, and increased intraocular, abdominal and intracranial pressure.[1] These changes may cause cardiac ischemia, hypoxemia, rebleeding at the surgical wound, surgical wound dehiscence, and brain injury.[2,3] The incidence of coughing during extubation and emergence ranges from 38 to 96%.[4] There are many factors that affect coughing during the extubation and emergence period, including smoking, oropharyngeal secretions, and irritation from volatile anaesthetic.[5-7] Furthermore, the other major contributing factor is mechanical irritation of the tracheal mucosa from the endotracheal tube (ETT) cuff [8]; therefore, various strategies have been explored to reduce adverse coughing events due to tracheal mucosa irritation from the ETT, such as ETT cuff lubrication[9], fluticasone inhalation prior to intubation[10], opioid administration during an emergence period and extubation[11,12], intravenous lidocaine infusion[13], and applying alkalinized lidocaine in the ETT cuff[14]. However, there is no consensus on a simple, safe and efficient technique for reducing cough during extubation.

Recently, lidocaine administration has been widely used for reducing cough during extubation due to its simplicity and lack of serious adverse effects. There are two major routes for lidocaine administration; systemic intravenous injection and local direct application on the laryngeal inlets, such as spraying lidocaine on the supraglottic and subglottic regions or applying lidocaine jelly or sprayed lidocaine on the tip of the ETT. However, there is a lack of data comparing the efficacy between local lidocaine application and systemic lidocaine administration on reducing cough during extubation. Soltani et al.15 compared the five different methods of lidocaine application route with the normal saline application as a controlled method. They reported that using lidocaine to inflate the ETT cuff and lidocaine intravenous injection were more effective than the other methods at reducing cough during extubation. Regarding intracuff lidocaine use, the chance of lidocaine leakage or the cuff rupture may occur that lead to rapid airway absorption of lidocaine, thus resulting in lidocaine toxicity. Furthermore, the side effects of anesthetizing airway after applying lidocaine on the airway were concerned. The previous studies reported the mild postoperative sore throat (POST) of 11.7-26.9%.15-17 The other side effects (including postoperative nausea vomiting, dysphagia, and agitation) were also reported in patients who received topical lidocaine application; however, these side effects were not significantly different with applying a placebo.18 To prevent the risk of lidocaine leakage from intracuff lidocaine application, we introduced the modified technique with a dose of lidocaine sprayed on the ETT cuff and also sprayed lidocaine on the laryngeal inlet. Regarding anesthetizing airway complications, we adjusted the proper dose of lidocaine sprayed and modified application technique to introduce lidocaine on the true vocal cord. Hence, this study was conducted to investigate the efficacy of spraying lidocaine on both the laryngeal inlet and the ETT cuff for preventing cough during extubation. Moreover, the side effect of our modified applying lidocaine was evaluated as secondary outcomes.

2. Methodology

This prospective, randomized, double-blinded controlled trial was conducted at the Srinagarind Hospital, Khon Kaen University, Thailand, from September 2018 to June 2019. The study protocol adhered to the CONSORT guidelines. A sample size of 82 subjects in each group was deemed appropriate considering 95% confidence intervals, 2% error, and a meaningful estimated incidence of coughing in the topical lidocaine sprayed group of 0.2, whereas the incidence of coughing in the intravenous lidocaine group was 0.4 at the emergence period, based on a previous study.[19] Patients of either gender and age between 18 and 60 years were classified as I, II, or III using the American Society of Anesthesiologists physical status. Exclusion criteria included patients having a body mass index of more than 35 kg/m^2, a high risk of aspiration, chronic smokers (more than ten pack-years), patients with chronic cough or recent upper respiratory infection, suspected difficult airways, retained ETT from a prior surgery, previous surgery of the oral cavity, neck or thoracic region, an anticipated operative time of more than 120 min or less than 30 min, or a history of a lidocaine allergy. However, if patients could not be extubated after

finishing the procedure or presented with anaphylaxis from the anesthetic agents, they were withdrawn from the study. The study was reviewed and approved by the Khon Kaen University Ethics Committee for Human Research (HE611394).

This study was designed with a block of four randomizations. Random numbers were generated by a computer and placed in a sealed envelope. All patients were allocated (1:1) into two groups (topical group or IV group) after written informed consent was obtained by a research assistant; however, the patients were blinded from the allocated group results. The patients were asked to take nothing by mouth 6 h prior to surgery. In the operating room, the patients were monitored by blood pressure, electrocardiogram, pulse oximetry, and end-tidal carbon dioxide. The patients received 100% oxygen for 3-5 min before induction with 1-2 µg/kg fentanyl, 1.5-2.5 mg/kg propofol, 0.15-0.2 mg/kg cisatracurium or 1-1.5 mg/kg succinylcholine.

Subsequently, the ETT was intubated by an anesthesiologist, a nurse anesthetist, or an anesthesiology resident with more than 6 months of experience. The size of the ETT for intubation was 8.0 for males and 7.5 for females. Prior to insertion of the ETT, the topical lidocaine group received four puffs of 10% lidocaine sprayed on the cuff of the ETT and two puffs of 10% lidocaine sprayed on each true vocal cord during introduction of the laryngoscope (one puff of 10% lidocaine spray contains approximately 10 mg of lidocaine). For the IV group, the ETT was intubated as usual without the administration of lidocaine during this period.

After intubation, the ETT was connected to the anesthetic circuit with controlled ventilation. The ventilation settings were a respiratory rate of 10-16 breaths/min, a tidal volume of 6-8 ml/kg, and an end-tidal CO_2 of 30-35 mmHg. Ventilation was assisted with 2-2.5% sevoflurane in an adjusted fraction of inspired oxygen between 0.4-0.6 with air at a total flow of 1-2 L/min. After the surgical procedure was finished, 2% lidocaine at 1.5 mg/kg was intravenously injected into the IV group patients, whereas the topical group did not receive any intervention at this time. A dose of 0.05 mg/kg neostigmine and 0.02 mg/kg atropine was administered intravenously as reversal agents. Extubation was performed in patients who fulfilled the following criteria: normal vital signs, spontaneous breathing, a tidal volume of more than 5 ml/kg, voluntary eye-opening, following commands, and no secretions in the airway.

During extubation, the severity of the cough was determined by an investigator who was blinded to the study. Severity of the cough[18] was evaluated as follows: 0 = no cough; 1 = slight cough (cough without obvious contraction of abdomen); 2 = moderate cough (strong and sudden contraction of the abdomen lasting less than 5 sec); 3 = severe cough (strong and sudden contraction of the abdomen sustained more than 5 sec). Blood pressure, heart rate, and oxygen saturation were monitored prior to extubation, during extubation, and after extubation. Secondary outcomes, such as postoperative sore throat, dysphonia, and dysphagia, were evaluated at 24 h after extubation by two blinded nurse anesthetists who had a Cohen's Kappa inter-rater reliability coefficient of more than 0.8; therefore, the double-blinded study (including blinded patients and blinded data collectors) was conducted for preventing bias. We evaluated sore throat with numeric rating scale (0 = no, 10 = extreme). The sore throat was considered a significant adverse event if the numeric rating was more than 3.

Descriptive data are presented as frequency and percentages. Analysis used the Chi-square test for an expected cell frequency of more than five; the Fisher's exact test was used for expected cell frequencies less than five. Continuous normally distributed data were analyzed using the Student's t-test, whereas the Mann-Whitney test was used for nonnormally distributed continuous data. All statistics were calculated with STATA (v 10.0: StataCorp., Texas, USA).

3. Results

One hundred sixty-four patient's enrolment, randomization, and analysis are demonstrated in the CONSORT flow diagram (Figure 1). Sixteen patients were dropped out due to longer operation than 120 min; therefore, 148 patient demographics were shown in (Table 1). Patients in both groups were similar in their basic demographics (gender, age) and physical status characteristics. The incidence of cough during extubation between the topical group (44.6%) and the IV group (50.0%) was not significantly different ($p = 0.51$). However, cough severity levels were

significantly different between the two groups. The incidence of having a cough with a severity grade of 3 was significantly less likely to occur in the topical group (1.4%) compared to the IV group (9.5%) ($p = 0.02$) (Table 2). The incidence of a postoperative sore throat was similar in both groups ($p > 0.99$), whereas hoarseness and dysphagia events were not found in the topical group (Table 3). Only, 7% of patients developed hoarseness and dysphagia in IV group. Furthermore, we observed that no patients had local anesthetic toxicity in both groups. Hemodynamic response after extubation was examined. Initial hemodynamic parameter values and values 1, 2, 3, 4, and 5 min after extubation were not significantly different between the topical and IV groups ($p > 0.05$) (Figure 2).

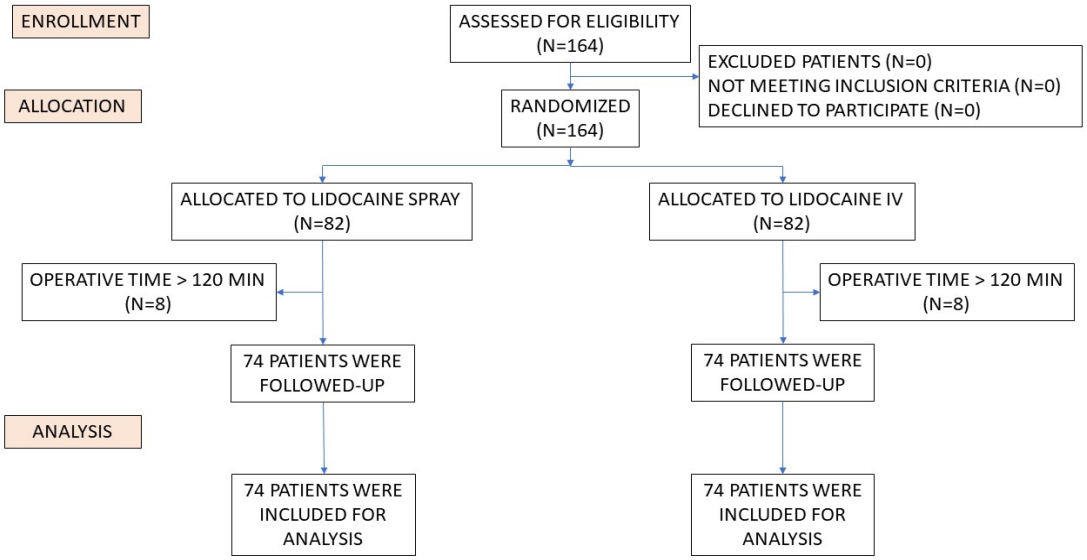

Figure 1 Flow diagram of the study

Table 1 Demographic data

Characteristics	Topical group	IV group
Gender: n (%)		
Male	32	28
Female	42	46
Age (yr): Median (range)	42 (19-60)	41 (19-60)
Weight (kg): Median (range)	61 (30-99)	59 (41-90)
Height (cm): Mean ± SD	162 ± 8.5	161 ± 8.2
BMI (kg/m^2): Median (range)	23 (12-32)	23 (17-35)
ASA physical status		
Class I: n (%)	45	57
Class II: n (%)	27	14
Class III: n (%)	2	3
Operation time (min): Mean ± SD	84 ± 27.7	80 ± 28.8

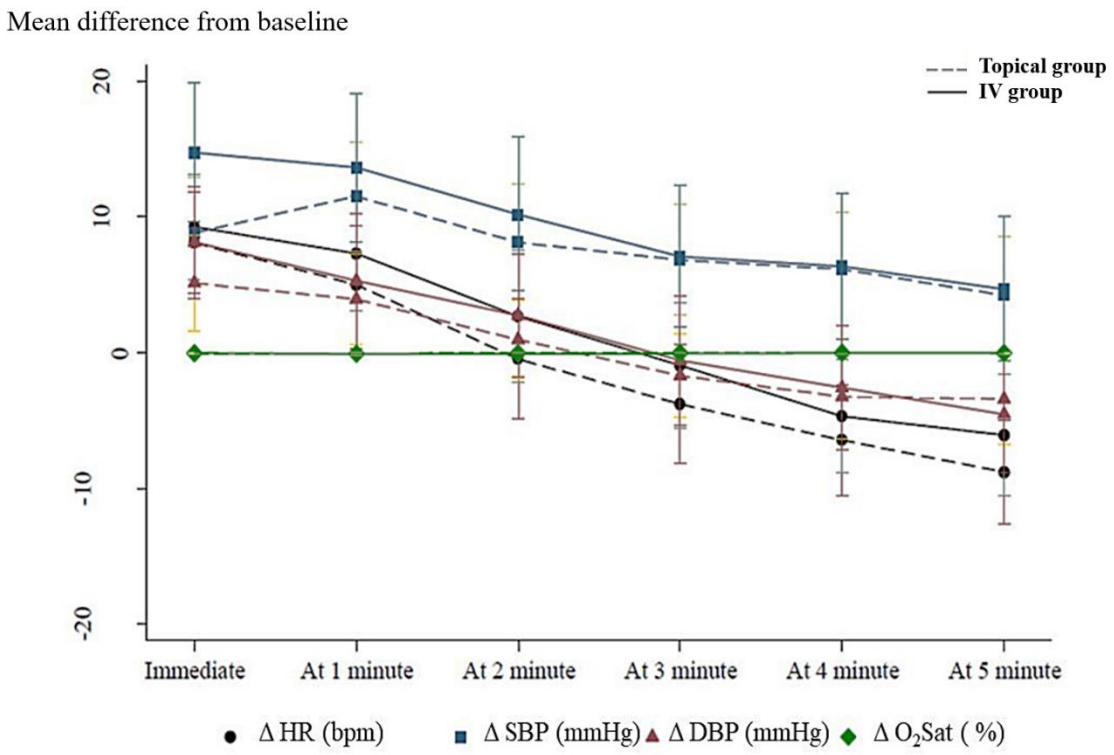

Figure 2 Comparison of the hemodynamic response, including heart rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation, between the topical group and the IV group immediately and at 1, 2, 3, 4, and 5 min after extubation. All values were calculated as the mean difference from baseline and there were no statistically significant differences between the groups ($p > 0.05$). (HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; O_2Sat: oxygen saturation).

Table 2 Incidence and severity of cough during extubation

Adverse event:	Topical group: n (%)	IV group: n (%)	p-value
Cough	33 (44.6) (95% CI: 33.8-55.9)	37 (50.0) (95% CI: 38.9-61.1)	0.51
Severity			
Grade 0	41 (55.4) (95% CI: 44.1-66.2)	37 (50.0) (95% CI: 38.9-61.1)	0.51
Grade 1	24 (32.4) (95% CI: 22.9-43.7)	26 (35.1) (95% CI: 25.2-4.5)	0.56
Grade 2	8 (10.8) (95% CI: 5.5-19.9)	4 (5.4) (95% CI: 2.1-13.1)	0.23
Grade 3	1 (1.4) (95% CI: 0.2-7.3)	7 (9.5) (95% CI: 4.7-18.3)	0.02

Table 3 Incidence of postoperative adverse outcomes in 24 h

Adverse events:	Topical group: n (%)	IV group: n (%)	p-value
Sore throat (NRS > 3)	6 (8.1) (95% CI: 33.8-55.9)	5 (6.8) (95% CI: 2.9-14.9)	>0.99
Hoarseness	0	4 (5.4) (95% CI: 2.1-13.1)	0.12
Dysphagia	0	2 (2.7) (95% CI: 0.7-9.3)	0.49

4. Discussion

The present study shows that cough reduction with topical spraying 10% lidocaine on the true vocal cords and the ETT was similar in effectiveness to a 1.5 mg/kg intravenous injection of 2% lidocaine. The severity of cough was observed that no statistically significant difference in severity grade of 0 to 2 between both groups; whereas, the incidence of the patient with intense cough severity grade of 3 in the topical group was significantly less than the intravenous group. Although the combination of lidocaine application between spraying on true vocal cord and spraying on ETT has not been mentioned before, the efficiency of this modified topical technique was satisfactory to reduce cough as systemic intravenous administration. Regarding intravenous lidocaine injection, Saltoni et al[15] reported that this administration route allowed great efficiency for reducing cough during extubation; however, the chances of systemic complications (i.e. bradycardia, local anesthetic systemic toxicity, and hypotension from high rapid absorption) occurring via systemic injection are higher than our topical application technique. Therefore, this modified topical lidocaine technique may be an alternative approach to reduce cough during extubation.

Regarding the side effects of the topical group, we found no significant difference POST between topical and IV group after modified spraying lidocaine at the true vocal cord and spraying four puffs on the ETT cuff. There was moderate POST (NRS > 3) of 8.1% in the topical group which is similar to D´Aragon et al.[18] that reported the moderate POST of 7.1% in the spray-cuff group. Most patients had experience with mild POST (NRS ≤ 3) and spontaneous improvement within 24 h that seems low meaningful impact on clinical practice as the previously mentioned study.[18]

Other side effects of applying 10% lidocaine including hoarseness and dysphagia were not significantly different between the groups ($p > 0.05$). However, hoarseness and dysphagia were less likely to occur in the group treated with the modified technique, suggesting meaningful and beneficial clinical outcomes from this approach.

There were no significant differences between the two groups regarding the hemodynamic response from baseline to after extubation, including heart rate, systolic blood pressure, diastolic blood pressure, and oxygenation saturation. However, heart rate and blood pressure trended higher with systemic injection than with the modified technique in the first five min. Thus, this modified local lidocaine application technique may be a supportive factor to stabilize the hemodynamic response after extubation; however, this issue still needs further study.

5. Limitations

The limitation of our study is that there was no record of the frequency of coughing. This issue may be the evidence support that modified topical spraying or systemic injection of lidocaine application is more effective for reducing cough during extubation. Moreover, the frequency of coughing may have influenced the POST result. Another limitation is the different timing of lidocaine applications that maybe affect our results. Although we attempt to exclude the surgery with the anticipated operative time more than 120 min according to D´Aragon et al.[18] They observed that the efficacy of lidocaine spray reduced coughing in surgeries of less than two h. Therefore, further study should be developed for closing the knowledge gap.

6. Conclusion

The combination of 10% lidocaine spray on the laryngeal inlet and the cuff of the ETT shows similar efficacy in reducing coughing during extubation compared with systemic intravenous injection of 2% lidocaine. Furthermore, the benefits of the combination method allow reducing the incidence of grade 3 cough severity, no dysphagia or hoarseness events, and no local anesthetic toxicity.

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8. Conflicts of interest

All authors have no personal, financial, or institutional interest in any of the materials and devices described in this article. The authors identified no conflict of interest.

9. Authors' contributions

CT and PK participated in manuscript preparation, including its conception.

CT, PK, TW, PS participated in data collection and/or processing.

CT, PK, TW participated in drafting the article.

CT and PK participated in critically revising the article. All authors read and approved the final version of the manuscript before submission.

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