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ORIGINAL ARTICLE

Efficacy of endotracheal lidocaine administration with continuous infusion of remifentanil for attenuating tube-induced coughing during emergence from total intravenous anesthesia

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Abstract
Purpose Although attenuation of tube-induced coughing is necessary in specific types of surgery, the best method for such attenuation is still unclear. We studied the combined intervention of endotracheal lidocaine and intravenous remifentanil compared to intravenous remifentanil alone with respect to coughing during emergence from anesthesia.
Methods We examined 60 ASA 1–2 patients (age, 20–69 years) undergoing tympanoplasty under general anesthesia. Anesthesia was induced with propofol, remifentanil, and rocuronium. The trachea was intubated using a laryngotracheal instillation of topical anaesthetic (LITA) tracheal tube. Anesthesia was maintained with propofol and remifentanil (0.1–0.3 μg/kg/min). Propofol was discontinued and remifentanil (0.1 μg/kg/min) was continued at the end of the operation. Patients were randomly allocated to the lidocaine ($n = 30$) and control groups ($n = 30$). We administered 3 ml 4 % lidocaine via the LITA tube to patients in lidocaine group at the end of the operation. The trachea was extubated when the patient regained consciousness and followed orders. Coughing was evaluated using a 4-point scale by an observer who examined the video records at extubation.
Results Fewer patients in lidocaine group (8 of 30) than in control group (18 of 30, $p < 0.01$) coughed. Fewer patients in lidocaine group (2 of 30) than in control group (12 of 30, $p < 0.01$) had moderate or severe cough (scale 2 or 3).
Conclusions This study is consistent with the finding that endotracheal lidocaine administration and continuous infusion of remifentanil before extubation is useful to prevent coughing on emergence from anesthesia.

Keywords Anesthetics local, lidocaine · Anesthetic techniques, i.v. infusion · Analgesics opioid, remifentanil · Complications, extubation tracheal

Introduction

Tube-induced coughing is observed during emergence from anesthesia. In tympanoplasty, middle ear pressure may increase because of tube-induced coughing and severe head movement and thereby cause adverse effects for the patients. Use of a laryngeal mask or extubation under deep anesthesia may prevent tube-induced coughing [1]. However, these procedures might be associated with a risk of aspiration or coughing induced by saliva trickling into the trachea [2, 3]. Some previous studies have suggested that total intravenous anesthesia (TIVA) reduces tube-induced coughing [4]. Other recent studies have shown that continuous infusion of remifentanil is useful for attenuating tube-induced coughing [5]. On the other hand, some studies have shown that endotracheal lidocaine administration before extubation is beneficial for reducing coughing [6, 7]. However, to the best of our knowledge, there are no reports

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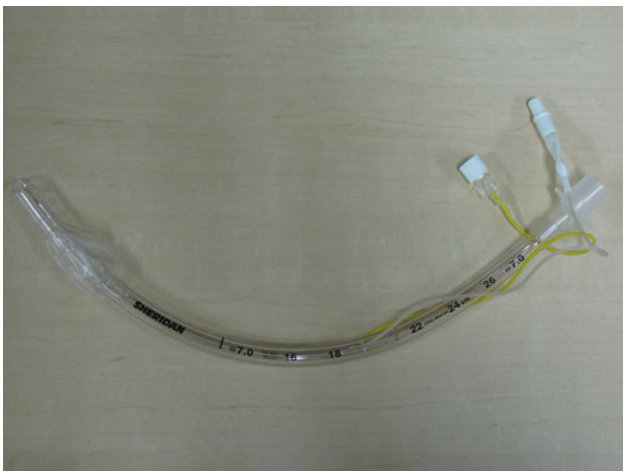

Fig. 1 The laryngotracheal instillation of topical anaesthetic (LITA) tube has two holes below the cuff and eight holes above the cuff for administration of 4 % lidocaine

on the efficacy of endotracheal lidocaine when remifentanil was intravenously administered for preventing coughing during emergence.

We hypothesized that a combination of endotracheal lidocaine administration and continuous infusion of remifentanil can attenuate tube-induced coughing better than remifentanil alone during emergence from anesthesia. We prospectively studied the efficacy of the combined intervention of endotracheal lidocaine and intravenous remifentanil with respect to coughing using laryngotracheal instillation of topical anesthetic (LITA) tracheal tube (Sheridan Catheter, Argyle, NY, USA) (Fig. 1).

Materials and methods

This study was registered with UMIN-CTR (UMIN000008087). We obtained institutional approval and written informed consent, and we examined 60 ASA 1–2 patients aged 20–69 years who underwent tympanoplasty under general anesthesia between April 2009 and May 2010. We excluded patients who had risk factors for mask ventilation or tracheal intubation difficulty; those with respiratory tract symptoms such as coughing, sore throat, rhinorrhea, asthma, or dyspnea; or those who had risk factors for perioperative aspiration of gastric contents such as stroke, disturbance of consciousness, or gastroesophageal reflux disease.

Patients were not premedicated. Anesthesia was induced with propofol (target organ concentration, 3–5 μg/ml), remifentanil (0.25–0.5 μg/kg/min), and rocuronium (0.6–1.0/mg/kg). The trachea was intubated using a laryngotracheal instillation of a LITA tracheal tube, which had two holes below the cuff and eight holes above the cuff for administration of the fluid. The cuff was inflated with air, and cuff pressure was maintained at 20 cm H_2O throughout the operation.

Anesthesia was maintained with propofol (target organ concentration, 2–5 μg/ml) and remifentanil (0.1–0.35 μg/kg/min). The target organ concentration of propofol was regulated using entropy monitoring (M-entropy module; Datex Ohmeda, Helsinki, Finland) to maintain the entropy state between 40 and 60. Patients were randomly allocated to the lidocaine group ($n = 30$) and the control group ($n = 30$) by the sealed envelope technique (Fig. 2). The randomization process was not blinded to the attending anesthesiologist. Flurbiprofen axetil 50 mg was intravenously administered 30 min before the end of the operation. At the end of the operation, propofol was discontinued, while remifentanil administration (0.1 μg/kg ideal body weight/min) was continued after endotracheal suction. At the same time, 3 ml 4 % lidocaine was administered via the LITA tube to the lidocaine group, whereas none was administered to the control group.

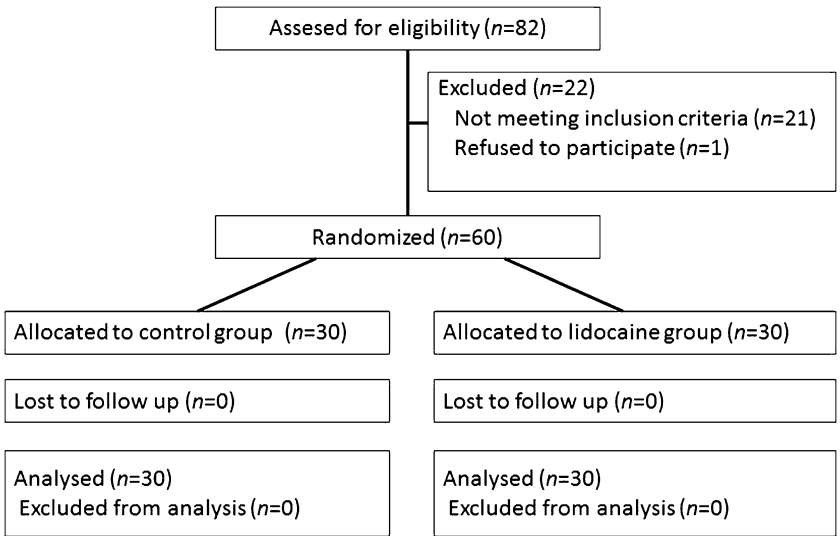

Fig. 2 CONSORT flow diagram showing the flow of participants through each stage of this randomized trial

Table 1 Evaluation score of coughing

0	No coughing
1	Mild coughing (a cough that does not make the patient's head move away from the bed)
2	Moderate coughing (repeated coughs, only one of which makes the patient's head move away from the bed)
3	Severe coughing (repeated coughs, at least two of which make the patient's head lift away from the bed)

Reversal agent (atropine, 1 mg; neostigmine, 2 mg) was administered if full recovery of neuromuscular function (train-of-four ratio >0.9) was not presented. When the patient regained consciousness and followed instructions given by the investigator such as shaking hands and opening mouth, remifentanil was discontinued. The investigator continued to observe the patient's spontaneous respiration and told the patient to breathe until sufficient spontaneous respiration (>10 times/min) was obtained. After the patient completely followed the investigator's order, the patient was extubated. The scene of the tracheal extubation was recorded using a video camera.

After all 60 operations were finished, an observer who was not in charge of the patient's anesthesia evaluated the degree of coughing using a 4-point scale (0 = none, 1 = mild, 2 = moderate, and 3 = severe) (Table 1) with the video records of the extubation that were edited so that the observer could not know to which group the patient belonged.

Previous study has shown that 57.7 % of patients experienced coughing after TIVA [4]. Sample size calculation was based on the data and the expectation that endotracheal lidocaine administration might reduce the coughing to 25 %. Thus, 30 patients were required in each group ($\alpha = 0.05$ and $\beta = 0.2$).

Our primary outcome was the number of subjects who experienced coughing during emergence from anesthesia. All data were analyzed using GraphPad Prism 5 (GraphPad Software, La Jolla, CA, USA). The data obtained were compared by using Fisher's exact test, χ^2 test, Mann–Whitney *U* test, and Student's *t* test.

Results

No significant differences were observed between the two groups in sex ratio, age, history of smoking, length of interval from end of the operation to extubation, and hemodynamic changes (Table 2).

Fewer patients in the lidocaine group (8 of 30, 26.7 %) than the control group (18 of 30, 60.0 %) coughed (the difference between two proportions was 33.3 %, 95 % confidence interval = 8.3–58.4 %, $p < 0.01$). Fewer patients in the lidocaine group (2 of 30, 6.7 %) than the control group (12 of 30, 40.0 %) had moderate or severe coughing (scale 2 or 3) (the difference between the two proportions was 33.3 %, 95 % confidence interval = 12.0–54.7 %, $p < 0.01$) (Table 3).

None of the patients experienced adverse effects such as bronchospasm, laryngospasm, decrease of oxygen saturation (SpO_2), and postoperative respiratory diseases.

Table 2 Characteristics of the patients

	Lidocaine group ($n = 30$)	Control group ($n = 30$)
Sex (M/F)	11/19	16/14
Age (years)	50.1 (20–69)	53.9 (21–69)
Weight (kg)	62.4 (10.2)	59.8 (7.3)
Height (cm)	159.5 (11.8)	162.3 (9.5)
Smoker/non-smoker	5/25	8/22
Duration of surgery (min)	124 (52)	126 (54)
Time interval from the end of operation to extubation (min)	9.8 (1.0)	10.7 (1.3)
Intraoperative systolic blood pressure (mmHg)		
Before induction of anesthesia	139.2 (26.3)	142.3 (22.0)
At end of surgery	104.9 (10.6)	103.6 (10.4)
Immediately before extubation	111.9 (15.8)	118.9 (18.2)
At 5 min after extubation	117.7 (15.7)	121.2 (15.4)
Intraoperative heart rate (beat/min)		
Before induction of anesthesia	70.5 (15.7)	67.8 (16.2)
At end of surgery	57.3 (6.4)	58.5 (9.2)
Immediately before extubation	63.1 (9.7)	71.1 (18.2)
At 5 min after extubation	66.4 (10.8)	69.3 (13.9)

Data are expressed as mean (SD or range) or number. No significant differences were observed between the lidocaine group and control group

Table 3 Number of patients who experienced coughing in each grade

Grade	Lidocaine group ($n = 30$)	Control group ($n = 30$)	*p* value
Cough(−)			
0	22 (73.3 %)	12 (40 %)	<0.01
Cough(+)			
1	6 (20 %)	6 (20 %)	
2	2 (6.7 %)	9 (30 %)	
3	0 (0 %)	3 (10 %)	
2 + 3	2 (6.7 %)	12 (40 %)	<0.01

Data are shown as number (percentage). Significant differences were observed between the two groups in grade 0 and grade 2 + 3

Discussion

Our results demonstrated that combining endotracheal lidocaine and intravenous remifentanil was more useful than remifentanil alone for preventing coughing during emergence. Previous studies indicate that continuous infusion of remifentanil during emergence from anesthesia is useful for attenuating tube-induced coughing and improving hemodynamic response. On the other hand, some other studies have shown that endotracheal, intravenous, or intracuff lidocaine is useful to suppress tube-induced coughing [6, 8–13]. A recent study by Lee et al. [14] showed that target control infusion of remifentanil reduced responsiveness to the tracheal tube during emergence from anesthesia more effectively than intravenous lidocaine in female patients undergoing thyroid surgery. Although Song and coworkers reported the effectiveness of the combination of remifentanil, topical lidocaine, and midazolam for conscious sedation during fiberoptic intubation, the efficacy of endotracheal lidocaine administration with continuous infusion of remifentanil during emergence in TIVA was not clarified before we began this study [15]. We concluded that endotracheal lidocaine administration at the end of tympanoplasty was useful for preventing tube-induced coughing under continuous infusion of remifentanil during emergence from TIVA. In addition, no adverse events were observed in our study, although our method of preventing tube-induced coughing might increase risk of aspiration or respiratory depression.

The rate of patients who experienced coughing in our study was higher than that in previous studies in which remifentanil was continued during emergence from general anaesthesia. Lee et al. [16] reported that 95 % of effective target site concentration of remifentanil to suppress coughing at emergence from anesthesia was 2.14 ng/ml. In another report, Nho et al. [5] reported that the frequency of moderate or severe coughing during extubation was 0 % (0/20) at target site concentration of remifentanil of 1.5 ng/ml. However, in our study, 60 % of patients in the control group experienced tube-induced coughing at extubation although we continued remifentanil at the target site concentration of 2.5 ng/ml. In addition, moderate or severe coughing was observed in 40 % of patients in the control group. This difference might be caused by different patient backgrounds such as age, sex, the type of operation, and the investigator's technique during extubation. Furthermore, the different results might occur because we strictly evaluated coughing by observing head movement using video records.

A previous study [17] suggests that remifentanil infused in the presence of an infusion of propofol resulted in apnea with increasing duration at remifentanil infusion speeds of 0.5–2.5 ng/ml/min. The result leads to our presumption that high-dose remifentanil during extubation might lead to adverse effects such as respiratory depression and hypoxia. However, in our study, no patients experienced desaturation and adverse respiratory depression. We propose that endotracheal lidocaine could reduce the remifentanil requirement to prevent coughing and lead to postoperative safety management.

Lidocaine has a sedative effect under general anaesthesia. Himes and coworkers [18] showed plasma lidocaine concentration between 3 and 6 μg/ml decreased anesthetic requirements. However, no significant difference was observed in the time to extubation between the two groups in our study. Diachun et al. [19] showed that serum lidocaine concentration after endotracheal administration of 2 ml 4 % lidocaine was less than 1.63 μg/ml (mean, 0.43 μg/ml). Similarly, the serum lidocaine concentration in our study might not be high enough to affect the level of consciousness in the lidocaine group, and topical administration of lidocaine mainly acted on peripheral areas.

In a past study, Andrzejowski and Francis [20] studied the efficacy of 5 ml 2 % lidocaine administered via a LITA tube for preventing coughing during emergence from total intravenous anesthesia compared with the saline group. There was no significant difference between the groups in the degree of coughing in contrast to our study. We consider that 3 ml 4 % lidocaine and combined technique with continuous infusion of remifentanil might lead to our results.

Our study has some limitations. We could not know whether the incidence of coughing affected the long-term outcome of auditory function because we did not follow the patient's data after they were discharged from hospital. Second, our patients ranged from 20 to 70 years in age. We should not apply our result to patients more than 70 years old because older patients are more susceptible to opioids.

In conclusion, endotracheal lidocaine administration with continuous infusion of remifentanil before extubation is useful for preventing coughing on emergence from anesthesia.

Conflict of interest None.

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