Effects of lidocaine via the perforated outer cuff of dual-cuff endotracheal tube and remifentanil on the recovery profiles from general anesthesia of female patients undergoing thyroidectomy: an one-centre, double-blind, randomized study

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Research Article

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Abstract

Background: Cough caused by endotracheal tube (ETT) is ubiquitous and correlates with adverse outcomes. Remifentanil *via* target-controlled infusion (TCI) was one of cough prevention measures during recovery. In the pilot study, lidocaine *via* the perforated outer cuff of dual-cuff endotracheal tube also prevented cough to the ETT. We therefore compared these two preventions of cough during recovery after thyroidectomy in the one-centre, double-blind, randomized study in China from 09 / 10 / 2020 to 30 / 04 / 2021.

Methods: Ninety-eight female patients, aged 18–65 years, with an American Society of Anesthesiologists I and II, were scheduled to undergo thyroidectomy. The ETT contains an internal cuff covered by an outer cuff with holes as lidocaine delivery channel. Patients were randomized to receive either 4 ml saline solution (Group R, n = 49) or 4 ml 2% lidocaine in the outer cuff (Group L, n = 49) at the beginning of the skin suture. Remifentanil 2 ng/ ml in Group R was maintained until extubation, while remifentanil in Group L was maintained until the end of the skin suture. The primary outcome was cough during patient transfer, 1 min before extubation and extubation. The secondary outcomes were hemodynamics and other recovery profiles.

Results: The primary outcomes included remifentanil *vs.* lidocaine in the incidence of cough during patients transfer (0% *vs.*0%), 1 min before extubation (22% *vs.* 4%; $P = 0.015$), and extubation (61% *vs.*20%; $P = 0.000$). Compared with remifentanil, lidocaine more effectively decreased the rate of elevation of heart rate and hypoxemia at 5 min after extubation, spontaneous respiration recovery time, extubation time, duration of post-anesthesia care unit (PACU), and Richmond Agitation-Sedation Scale in agitated and Critical-Care Pain Observation Tool.

Conclusion: Lidocaine *via* the perforated outer cuff of the ETT significantly improved recovery profiles from general anesthesia compared to remifentanil in female patients after thyroidectomy.

Trial registration: Chinese Clinical Trial Registry (No. ChiCTR2000038653), registered on 27 / 09 / 2020.

Introduction

Cough is ubiquitous (76–80%) during recovery from general anesthesia with endotracheal tube[1, 2], which correlates with hypertension and tachycardia[3, 4], agitation[5] and postoperative hemorrhage[6]. The cough prevention during recovery is recommended for patients with suspected or confirmed coronavirus disease (COVID-19), which can reduce airborne material and droplets[7]. Cough prevention is imperative to reduce the incidence of difficult breathing associated with hemorrhage after thyroidectomy [8].

Remifentanil *via* target-controlled infusion (TCI)[9, 10] was one of the cough prevention measures during recovery. In addition, in order to adequately reduce the stimulation of tracheal mucosa contacted by the cuff of endotracheal tube, we modified dual-cuff endotracheal tube (ETT, Xi'an Shen Lan Bio-medical Engineering Co., Ltd, China) (Supplemental video 1) and found that topical lidocaine *via* the dual-cuff ETT could effectively prevent cough during recovery. In the pilot study, one patient was intubated with the dual-cuff ETT while sitting up in bed and signing her name (Supplemental video 2). This dual-cuff ETT (Fig. 1B) contains internal cuff covered by outer cuff. Small-bore channel incorporated within the wall of the endotracheal tube is the channel which delivers lidocaine to the perforated outer cuff with 16 small holes (Supplemental video 3). The benefit of modified dual-cuff ETT is that the tracheal mucosa contacted by outer cuff is under topical anesthesia by lidocaine *via* the perforated outer cuff without deflating the internal cuff, which is not restricted by the timing of lidocaine administration.

The one-centre, double-blind, randomized study was designed to evaluate the hypothesis that the cough prevention on the newly investigated topical lidocaine *via* the dual-cuff ETT before extubation would be higher than that of remifentanil during recovery after thyroidectomy. The cough during recovery was chose as the primary outcome for further study on the potential benefits of a modified dual-cuff ETT such as the prevention of cough during recovery for patients with suspected or confirmed COVID-19. The main secondary outcomes included hemodynamics, time related with recovery, hypoxemia and other recovery profiles.

Materials And Methods

Ethics and registration

Ethical approval

for this study (Ethical Committee IRB: ZF2020-130.2-01) was provided by the Ethical Committee of Guangdong Provincial Hospital of Traditional Chinese Medicine, Guangzhou City, Guangdong Province, People's Republic of China (Chairperson Prof. Jun Liu) on 28 / 08 /

2020. Written informed consent was obtained from each patient before study participation. The full trial protocol was registered before patient enrollment in the Chinese Clinical Trial Registry (ref: ChiCTR2000038653) on 27 / 09 / 2020 and adheres to the Consolidated Standards of Reporting Trials guidelines[11] and the Declaration of Helsinki.

In vitro experiment

In order to achieve the even distribution of lidocaine around the cuff, we modified a dual-cuff endotracheal tube and conducted a dyeing experiment *in vitro*. We evenly punctured small holes through the outer cuff as dye liquid delivery channel. As the tracheal diameter ranges between 8.9–17 mm in women[12], a tube with an internal diameter of 14 mm was used to simulate the trachea and graph paper was placed on the internal surface of the tube to record the outcome of the experiment. The dual-cuff ETT was placed into the 14 mm tube lined with graph paper and the internal cuff pressure was maintained at 25 cmH_2O. To optimize the number of holes and the volume of dye liquid, we assessed the difference between 8 and 16 holes by using 1–4 ml dye liquid used to simulate lidocaine; this experiment was performed in triplicate. The dye liquid was fully transferred from the outer cuff by injecting 20 ml air into the outer cuff. This optimum combination was subsequently used *in vivo* experiment.

In vivo experiment

1) Study Design

This one-centre, double-blind, randomized study was conducted at the Department of Anesthesiology, Guangdong Provincial Hospital of Traditional Chinese Medicine in Guangzhou, China, from 09 / 10 / 2020 to 30 / 04 / 2021.

2) Patients

All 98 ASA I–II females, aged 18–65 years, with a height of 140–180 cm and weight of 40–85 kg, planned for elective thyroidectomy due to unilateral thyroid neoplasm (T1 /T2 N0 M0 in Tumor-Node -Metastasis System/American Joint Committee on Cancer). The exclusion criteria included patients using the NIM standard reinforced EMG endotracheal tube, signs of a difficult airway, perioperative aspiration, psychosis, acute respiratory tract infection lasting less than 2 weeks, smoking lasting less than 48 h, allergic reaction to lidocaine, beta-adrenergic receptor line, and serious cardiovascular, pulmonary, hepatic, or renal disease.

3) Randomization

Patients were randomly allocated in a 1:1 ratio to either 4 ml 2%lidocaine in the outer cuff (Group L) or predicted effect-site concentration (Ce) of TCI remifentanil 2.0 ng/ ml (Group R), according to a computer-generated centralized random table with no block size and stratification factors. A unique randomization number was took out from the sequentially numbered containers on the morning of surgery. The first anesthetist generated the random allocation sequence, enrolled participants, and assigned participants to interventions.

4) Blind evaluation

Three anesthetists and 3 anesthetist nurses participated in this study to conduct a blinded evaluation. The first anesthetist was the only one with knowledge of the group. The other anesthetists, anesthetist nurses, and patients were blinded to the groups. The first anesthetist completed the following tasks at the beginning of skin suture: shielding the TCI pump from other anesthetists, control of the TCI pump, and handling 4 ml 2% lidocaine or 4 ml saline solution to the second anesthetist who was blinded to the actual treatments. The second anesthetist completed the intraoperative and postoperative care, except for the control of the TCI pump. The third anesthetist and 3 anesthetist nurses recorded variables in the post-anesthesia care unit (PACU).

5) Intraoperative and Postoperative Care

Basic monitoring was performed at 3 min intervals. All patients received induction medication including propofol 1.5 mg/ kg, cisatracurium 0.2 mg/ kg, predicted effect-site concentration of TCI remifentanil (Ce 3.5 ng/ ml) and sufentanil 0.4 ug/ kg to facilitate tracheal intubation. Remifentanil was administered as a TCI pump (targeted effect-site TCI, Minto model and CONCERT-III, Guangxi VERYARK Technology Co., Ltd, China). All patients received a 7.0 mm modified dual-cuff ETT, and the internal cuff pressure was maintained at 20–30 cmH_2O. Maintenance with sevoflurane (1.2–2.5%) and TCI remifentanil (Ce 2–5 ng/ ml) kept the mean arterial pressure (MAP) and heart rate (HR) within 20% of baseline (values at one day before surgery). Nasopharyngeal temperature was maintained at 36–37 ℃. The tidal volume and ventilatory frequency were adjusted using end-tidal carbon dioxide ($ETCO_2$) at 34–45 mmHg.

At the beginning of the skin suture, sevoflurane was maintained at 1.4–1.5 an end-tidal concentration and remifentanil was maintained at 2 ng/ ml. At the same time, ketorolac 0.5 mg/ kg was administered to relieve pain and tropisetron 4.48 mg was administered to prevent nausea and vomiting. Neostigmine (50 ug/kg) and atropine (15 μg/kg) were administered to reverse the neuromuscular block to confirm a train-of-four response greater than 90%. Patients with ETT were randomized to receive either 4 ml 2% lidocaine in the outer cuff (Group L) or 4 ml saline solution (placebo) in the outer cuff (Group R), followed by 20 ml air into the outer cuff at the beginning of skin suture (each time the internal cuff pressure was less than 30 cmH_2O). Remifentanil in group R was maintained at 2 ng/ ml and turned off at tracheal extubation. Remifentanil in group L and sevoflurane in the two groups were turned off at the end of the skin suture (the end of surgery).

Patients with ETT were transferred to the post-anesthesia care unit (PACU) after confirmation of stable hemodynamics. During the transfer of patients (the phase from operating table to PACU), remifentanil 2.0 ng/ ml by TCI was maintained for Group R, whereas remifentanil was stopped in Group L. It took 4 min during the phase from the end of surgery to the beginning of transfer and 2 min during patient transfer. The shielded TCI pump from all the patients was taken to the PACU. Recovery profiles were recorded in the PACU by video after obtaining the patients' consent. Manual ventilation was provided until the patient breathed spontaneously. Mild hypercapnia (end-tidal carbon dioxide, $ETCO_2$ 45–55 mmHg) was permitted to promote spontaneous respiration. Continuous verbal stimuli were used to prompt the patients to open their eyes without any other stimuli. After opening their eyes, the patients were asked to breathe deeply and nod their head. Extubation was completed when adequate breath on command ($ETCO_2$ < 50 mmHg and ventilatory frequency > 12 beats/min), nodding and handshake on command, and spontaneous deglutition were achieved.

6) Primary Outcomes

The primary outcome was the incidence of cough during the recovery period. A cough was defined as any evidence of irritation from a tube in the trachea[13]. Cough was recorded while patients transfer (the phase from the operating table to the PACU), 1 min before extubation and extubation.

7) Secondary Outcomes

Five time points were defined as follows: T0, one day before surgery (baseline); T1, end of surgery; T2, 1 min before extubation; T3, 5 min after extubation; and T4, 20 min after extubation. The secondary outcomes were the following variables: MAP and HR at the above five time points, elevation of blood pressure and heart rate at T2, T3 and T4 (MAP and HR increase by 30% from their respective values at baseline), eye opening time (time period from the end of surgery to first eye opening on command), consciousness recovery time (time period from the end of surgery to nodding on command), spontaneous respiration recovery time (time period from the end of surgery to $ETCO_2$ ≤ 55 mmHg and ventilatory frequency ≥ 10 beats/ min), extubation time (time period from the end of surgery to extubation), duration of PACU stay (the time period from the end of surgery to leaving from PACU), the Richmond Agitation-Sedation Scale (RASS) [14] at T2, and the Critical-Care Pain Observation Tool (CPOT) [15] at T2.

In addition, the secondary outcomes were a composite of the following variables: hypoxemia at T3 and T4 (less than 95% of Spo_2), sedation grading system (SGS) [16] at T3, postoperative pain at T4 (more than 5 points on the visual analog scale), residual sedation at T4 (less than Grade 2 on the SGS), nausea and vomiting at T4 (need for drug), and pharyngalgia at T4 (swallowing with more than 3 points on the visual analog scale).

8) Sample size calculation

The incidence of cough was 76% during recovery from general anesthesia[1]. Based on the assumption that TCI remifentanil Ce 2.0 ng/ ml could suppress cough by 90%[17] and 4 ml of 2% lidocaine used with the dual-cuff endotracheal tube could suppress cough by 50% [16, 18], 49 patients in each group would be required for 80% power at a two-sided α of 0.05, with 20% lost to follow-up.

9) Statistical Analysis

All values are expressed as mean ± standard deviation or number (proportion). Continuous variables with normal distribution were assessed with *a t*-test or repeated measures analysis of variance with Bonferroni correction. Continuous variables with non-normal distributions were assessed using the Mann-Whitney U-test. Categorical data were assessed using the $\chi 2$ test or Fisher's exact test. SPSS Statistics 20 (SPSS Inc., Chicago, IL, USA) was used to assess the data. Statistical significance was set at $P < 0.05$.

Results

In vitro **experiment**

Figure 1A showed the results of the dyeing experiment. There was no interaction in holes (8 and 16 holes) and dye liquid volume (1, 2, 3, and 4 ml) (P = 0.064). There was statistically significant difference in pairwise comparison on the area of 16 holes and 8 holes (P = 0.021, 796.67mm^2 *vs. 584.17* mm^2). There was statistically significant difference in pairwise comparisons on the area of 4ml and 1ml (P = 0.000, 937.67mm^2 *vs.* 477.50mm^2), 4ml and 2ml (P = 0.010, 937.67mm^2 *vs.* 634.83mm^2), and 4ml and 3ml (P = 0.033, 937.67mm^2 *vs.* 711.67mm^2). On the basis of this results, 16 holes and 4 ml dye liquid were the optimal combination.

In vivo **experiment**

Patients

We assessed 416 patients, of which 98 were enrolled in this study. All 98 patients completed the study [group L (n = 49); group R (n = 49)] (CONSORT Flow Diagram). The patient characteristics were similar between the two groups (Table 1).

Table 1
Characteristics of Patients Randomized between the Two Groups

Characteristic	Group R (n = 49)	Group L (n = 49)	Difference (95% CI)	Odds ratio (95% CI)	*P*
Age (year)	46.8 ± 11.24	46.8 ± 11.24	4.3 (-0.21–8.82)		0.052[a]
ASA physical status (□/□)	41(84%)/8(16%)	40(82%)/9(18%)		1.153 (0.405–3.286)	1[b]
Height (cm)	158.2 ± 5.07	158.9 ± 5.23	-0.7 (-2.72–1.41)		0.532[c]
Weight (kg)	56.8 ± 8.80	56.1 ± 9.93	0.7 (-3.03–4.49)		0.531[a]
Duration of surgery (min)	88.1 ± 23.05	84.7 ± 20.98	3.4 (-5.24–12.5)		0.659[a]
Duration of anaesthesia (min)	126.1 ± 25.53	126.1 ± 25.53	3.5 (-6.30–13.47)		0.642[a]

Data are expressed as mean ± SDs or number of patients (%). ASA, American Society of Anesthesiologists; R, TCI of remifentanil; L, topical lidocaine *via* the perforated outer cuff; CI, confidence interval. [a] Mann-Whitney U-test. [b]Fisher's exact test. [c]*t*-test.

Primary Outcomes

There was no cough during the patient transfer. The incidence of cough during T2 was significantly higher in group R than in group L (22% *vs.* 4%, P = 0.015). The incidence of cough during extubation was also significantly higher in group R than in group L (61% *vs.* 20%, P = 0.000) (Table 2).

Table 2
Primary Outcomes and Its profiles

Time	Cough	Group R (n = 49)	Group L (n = 49)	Odds ratio (95% CI)	*P*
Patients transfer	Cough occurrence	0 (0%)	0 (0%)		
1 min before tracheal extubation	Cough occurrence	11 (22.45%)	2 (4.08%)	0.15 (0.03–0.70)	0.015[b]
Tracheal extubation	Cough occurrence	30 (61.22%)	10 (20.41%)	0.16 (0.07–0.40)	□0.001[b]

Data are expressed as number of patients (%). R, TCI of remifentanil; L, topical lidocaine *via* the perforated outer cuff; CI, confidence interval; transferring patients, the phase from operating table to the post-anesthesia care unit. [b]Fisher's exact test.

Secondary Outcomes

The secondary outcomes are shown in Table 3. The groups did not differ significantly in MAP or HR (Fig. 2). The incidence of elevated blood pressure was similar between groups. The occurrence of heart rate elevation at T2 and T4 was also similar between the groups, but the elevation of heart rate at T3 ($P = 0.0028$) was significantly lower in group L than in group R. The time related with recovery on remifentanil *vs.* lidocaine was as follows: eye opening time ($P = 0.460$, 8.3 min *vs.* 7.7 min), consciousness recovery time ($P = 0.346$, 9.8 min *vs.* 8.4 min), spontaneous respiration recovery time ($P = 0.000$, 14.8 min *vs.* 9.7 min), extubation time ($P = 0.009$, 16.7 min *vs.* 12.8 min) and duration of PACU stay ($P = 0.001$, 55.4 min *vs.* 46.4 min). The RASS in the agitated range was significantly lower in group L than in group R ($P = 0.012$), but there was no significant difference in the alert, clam, and sedation ranges. CPOT was significantly higher in group R than in group L ($P = 0.003$). The occurrence of hypoxemia at T3 was significantly lower in group L than in group R ($P = 0.000$), but there was no significant difference at T4. The groups did not differ significantly in grade 2/Grade 3 sedation at T3, postoperative moderate pain, nausea and vomiting, and pharyngalgia at T4. No residual sedation was observed at T4 in either group.

Table 3
Secondary Outcomes and Its Components

Components	Group R (n = 49)	Group L (n = 49)	Difference (95% CI)	Odds ratio (95% CI)	*P*
Elevation of blood pressure at T2	3 (6.12%)	3 (6.12%)		1.00(0.19–5.22)	1[b]
Elevation of blood pressure at T3	2 (4.08%)	1 (2.04%)		2.04(0.18–23.29)	1[b]
Elevation of blood pressure at T4	2 (4.08%)	2 (4.08%)		1.00(0.14–7.40)	1[b]
Elevation of heart rate at T2	13 (26.53%)	5 (10.20%)		3.18(1.04–9.75)	0.066[b]
Elevation of heart rate at T3	16 (32.65%)	6 (12.25%)		3.48(1.23–9.85)	0.028[b]
Elevation of heart rate at T4	6 (12.25%)	7 (14.29%)		0.84(0.26–2.70)	1[b]
Time related to recovery					
Eye opening time (min)	8.3 ± 4.22	7.7 ± 3.05	0.6 (-0.93–2.03)		0.460[c]
Consciousness recovery time (min)	9.8 ± 4.87	8.4 ± 3.15	1.4 (-0.25–3.04)		0.346[a]
Spontaneous respiration recovery time (min)	14.8 ± 7.64	9.7 ± 3.90	5.1 (2.67–7.29)		□0.001[a]
Extubation time (min)	16.7 ± 7.84	12.8 ± 5.26	3.9 (1.28–6.63)		0.009[a]
Duration of PACU stay (min)	55.4 ± 15.71	46.4 ± 11.05	9 (3.55–14.45)		0.001[c]
RASS at T2					
□0 agitated range	8 (16.33%)	1 (2.04%)		0.09 (0.01–0.79)	0.012[b]
0 alert and clam	26 (53.06%)	35 (71.43%)		2.21 (0.96–5.10)	0.095[b]
□0 sedation range	15 (30.61%)	13 (26.53%)		0.64 (0.26–1.58)	0.367[b]

Data are expressed as mean ± SDs or number of patients (%).. Elevation of blood pressure, increase by 30% from mean arterial pressure at one day before surgery (T0); Elevation of heart rate, increase by 30% from heart rate at T0; PACU, post-anesthesia care unit; RASS, The Richmond Agitation-Sedation Scale; CPOT, Critical-Care Pain Observation Tool; Hypoxemia, Spo_2 less than 95%; Grade of sedation: Grade 0: deeply sedated and unresponsive; Grade 1: sedated but responsive to light glabellar tap; Grade 2: sedated but responsive to normal voice; Grade 3: awake and responding. Postoperative pain, more than 5 points on the visual analog scale (VAS); residual sedation, less than Grade 2; nausea and vomiting, need for drug; pharyngalgia, swallowing with more than 3 points on the VAS. CI, confidence interval; R, TCI of remifentanil; L, topical lidocaine *via* the perforated outer cuff; CI, confidence interval; T2, 1 min before tracheal extubation; T3, 5 min after tracheal extubation; T4, 20 min after tracheal extubation. [a] Mann-Whitney U-test. [b]Fisher's exact test. [c]*t*-test.

Components	Group R (n = 49)	Group L (n = 49)		Difference (95% CI)	Odds ratio (95% CI)	*P*
CPOT at T2	1.04 ± 1.74		0.33 ± 1.14	0.71(0.12–1.31)		0.003[a]
Hypoxemia occurrence at T3	28 (57.14%)		7(14.29%)		8 (3.00–21.32)	0.001[b]
Hypoxemia occurrence at T4	6 (12.24%)		1 (2.04%)		0.15 (0.02–1.29)	0.111[b]
Grade of sedation at T3 (Grade 2/ Grade 3)	13(27%)/36(73%)	13(27%)/36(73%)	13(27%)/36(73%)	13(27%)/36(73%)	1 (0.41–2.45)	1[b]
Postoperative pain at T4	1 (2.04%)		1 (2.04%)		1 (0.61–16.45)	1[b]
Residual sedation at T4	0 (0%)		0 (0%)			
Nausea and vomiting at T4	4 (8.16%)		1 (2.04%)		0.23 (0.03–2.18)	0.362[b]
Pharyngalgia at T4	15 (30.61%)		7 (14.29%)		0.38 (0.14–1.03)	0.89[b]

Data are expressed as mean ± SDs or number of patients (%).. Elevation of blood pressure, increase by 30% from mean arterial pressure at one day before surgery (T0); Elevation of heart rate, increase by 30% from heart rate at T0; PACU, post-anesthesia care unit; RASS, The Richmond Agitation-Sedation Scale; CPOT, Critical-Care Pain Observation Tool; Hypoxemia, Spo_2 less than 95%; Grade of sedation: Grade 0: deeply sedated and unresponsive; Grade 1: sedated but responsive to light glabellar tap; Grade 2: sedated but responsive to normal voice; Grade 3: awake and responding. Postoperative pain, more than 5 points on the visual analog scale (VAS); residual sedation, less than Grade 2; nausea and vomiting, need for drug; pharyngalgia, swallowing with more than 3 points on the VAS. CI, confidence interval; R, TCI of remifentanil; L, topical lidocaine *via* the perforated outer cuff; CI, confidence interval; T2, 1 min before tracheal extubation; T3, 5 min after tracheal extubation; T4, 20 min after tracheal extubation. [a] Mann-Whitney U-test. [b]Fisher's exact test. [c]*t*-test.

Discussion

Compared with remifentanil, lidocaine *via* the perforated outer cuff more effectively decreased the incidence of cough during recovery, the rate of elevation of heart rate, spontaneous respiration recovery time, extubation time, duration of PACU stay, RASS in agitated, CPOT, and hypoxemia at T3. The other recovery profiles did not differ between the two groups.

A meta-analysis [19] compared treatments for cough suppression during recovery from general anesthesia. Lidocaine is the least effective compared to dexmedetomidine, remifentanil, and fentanyl[19]. In addition, the extubation time was delayed by lidocaine *via* intracuff compared with remifentanil[19]. However, the results of this study were not inconsistent with the rank of treatments suppressing cough, as lidocaine *administered via* the topical route had a better antitussive effect and shortened extubation time compared to remifentanil.

The high efficiency of lidocaine in this study was possibly due to the use of topical anesthesia compared with remifentanil. Remifentanil takes effect by delivering opioids to the central nervous system[20], whereas lidocaine topical anesthesia on the tracheal mucosa is peripherally mediated[21]. Tracheal topical lidocaine includes the tracheal tube, intracuff, and topical distribution on the glottis or *via* both the upper and lower endotracheal tube cuffs onto the tracheal mucosa [19]. The lower efficacy of lidocaine administration compared to that used in this study is possibly due to the following reasons. Lidocaine *administered via* the tracheal tube before intubation for surgeries lasting < 2 h was undesirable in suppressing cough during recovery [21]. However, the duration of general anesthesia in this study was > 2 h. The cough-suppressing effect of alkalinized lidocaine intracuff is dependent on the time necessary for the alkalinized lidocaine to permeate across the cuff membrane [22]. The dual-cuff ETT avoids this issue, as the holes in the outer cuff allow lidocaine to rapidly distribute around the cuff of the dual-cuff ETT. Lidocaine *via* a laryngotracheal instillation of topical anesthesia (LITA) tube is distributed on the glottis or both the upper and lower cuff before extubation[23] [13], which results in cough suppression in only 75% [13]

of patients on recovery. The above data was lower than result of this study. The tube cuff is a mechanical barrier that hinders the distribution of topical lidocaine anesthesia to the tracheal mucosa [13]. The outer cuff of the modified dual-cuff ETT can break the mechanical barrier and does not deflate the cuff to administer lidocaine topical anesthesia onto the tracheal mucosa. The tracheal mucosa is under topical anesthesia with lidocaine via the perforated outer cuff of the ETT, which reduces stimulation of the tracheal mucosa. All of these factors could potentially explain the lower RASS and CPOT recorded in Group L in this study.

In this study, lidocaine resulted in better recovery profiles for respiratory complications and the duration of PACU stay. In contrast, remifentanil increased hypoxemia occurrence (57.14%) at T3, spontaneous respiration recovery time, and extubation time. This is consistent with Beloeil 's study[24], which described hypoxemia in 61% of the patients treated with remifentanil. Compared with remifentanil, the lower respiratory complications in patients treated with lidocaine in this study could be remifentanil-free during recovery from general anesthesia.

Compared to remifentanil, intravenous (IV) lidocaine increased residual sedation [16]. Lidocaine serum concentration was greater than 3 μg/ ml with 2 mg/kg I.V. lidocaine[25]. However, 2 mg/kg of 4% lidocaine topical distribution was used by Diachun [13] before extubation, which resulted in peak serum levels < 1.633 μg/ ml. Since lidocaine doses in this study were lower than those used in Lee et al.'s study[16], this may explain why lidocaine used in this study, compared with remifentanil TCI, did not increase residual sedation.

Limitations and generalisability

This study had several limitations. First, only women were included in the study because women have a higher incidence of thyroid cancer[26] and the incidence of cough differs significantly according to sex [27]. Second, the internal cuff carries the risk of air leakage. The internal cuff must be checked for leakage prior to intubation. Third, the injection of lidocaine, saline solution, or 20 ml air *via* the outer cuff could induce cough. Sufficient depth of anesthesia minimizes the risk through effect-site TCI remifentanil 2.0 ng/ ml and sevoflurane 1.4–1.5%. Fourth, NIM tubes were fairly standard in practice elsewhere, which may make this new modified dual-cuff ETT less useful in clinical practice for all patients undergoing thyroidectomy. However, cough during recovery was chosen as the primary outcome for further study on the potential benefits of the dual-cuff ETT, such as reducing airborne material and droplets during recovery for patients with suspected or confirmed COVID-19 [7]or other cough-related adverse events.

Conclusion

In conclusion, lidocaine administered via the perforated outer cuff of the ETT significantly improved recovery profiles from general anesthesia compared with remifentanil in female patients after thyroidectomy.

Abbreviations

ETT
endotracheal tube
OD
odds ratio
CI
confidence interval
COVID-19
coronavirus disease
TCI
target-controlled infusion
ASA
American Society of Anesthesiologists
R
remifentanil
L
lidocaine
Ce
effect-site concentration
PACU

post-anesthesia care unit
MAP
mean arterial pressure
HR
heart rate
$ETCO_2$
end-tidal carbon dioxide
RASS
Richmond Agitation-Sedation Scale
CPOT
Critical-Care Pain Observation Tool
SGS
Sedation Grading System
LITA
laryngotracheal instillation of topical anesthesia
I.V.
intravenous injection

Declarations

Ethics approval and consent to participate

Ethical approval for this study (Ethical Committee IRB: ZF2020-130.2-01) was provided by the Ethical Committee ofGuangdong Provincial Hospital of Traditional Chinese Medicine, Guangzhou City, Guangdong Province, People's Republic of China (Chairperson Prof. Jun Liu) on 28 / 08 / 2020. Written informed consent was obtained from each patient before study participation. The full trial protocol was registered before patient enrollment in the Chinese Clinical Trial Registry (ref: ChiCTR2000038653) on 27 / 09 / 2020 and adheres to the Consolidated Standards of Reporting Trials guidelines[11] and the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from the participants for publishing the videos.

Availability of data and materials

The data used and analyzed in this study available from the corresponding author.

Competing interests

The authors declare no conflicts of interest.

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Author's contributions

PL and DL helped to design the study, conduct the study, analyze the data and approved final manuscript. LW helped to design the study and conduct the study. FY, SF, ZT helped to conduct the study. BY, LY,YS, XL and QY helped to design the study.GZ helped to design the study, analyze the data, write the final manuscript and handle this manuscript.

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Figures

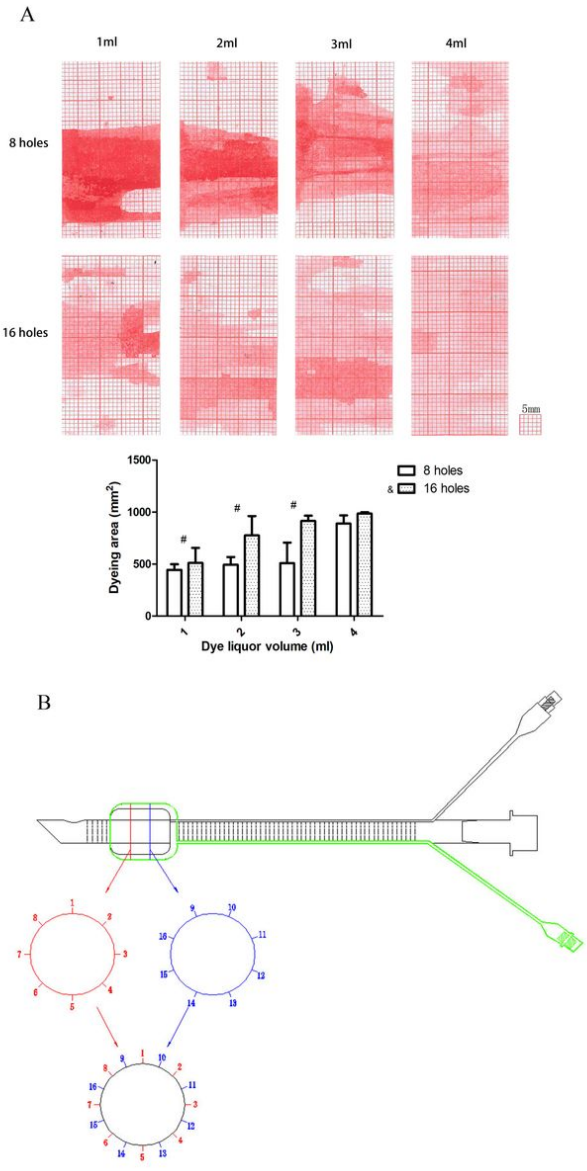

Figure 1

Dyeing areas (red areas) in different dye liquid volume and number of holes (A). The experiment was performed in triplicate for each combination. Graph paper (25mm^2 per unit) represents the area of simulative trachea contacted by the perforated outer cuff of the dual-cuff endotracheal tube. The optimal scheme to achieve the even distribution of dye liquid around the endotracheal tube cuff is 16 holes

and 4 ml dye liquid. $^{\#}P$<0.05 *vs.* 4ml dye liquor volume. $^{\&}P$<0.05 *vs.* 8 holes. The structure of a modified dual-cuff endotracheal tube (B). This modified dual-cuff endotracheal tube contains internal cuff covered by outer cuff. The function of internal cuff (black cuff) is the same as that of cuff in traditional endotracheal tube. Small-bore channel incorporated within the wall of the endotracheal tube is the channel which delivers lidocaine to the out cuff (green area). The out cuff contains 16 small holes (1mm in diameter of one hole), which are evenly arranged in two rows (8 holes per each row). The first row of holes (red area) and the second row of holes (blue area) are respectively arranged at one third and two thirds of the outer cuff contacted internal cuff (number represents the distribution of small holes in the out cuff). Topical lidocaine is accomplished via the small holes of perforated outer cuff.

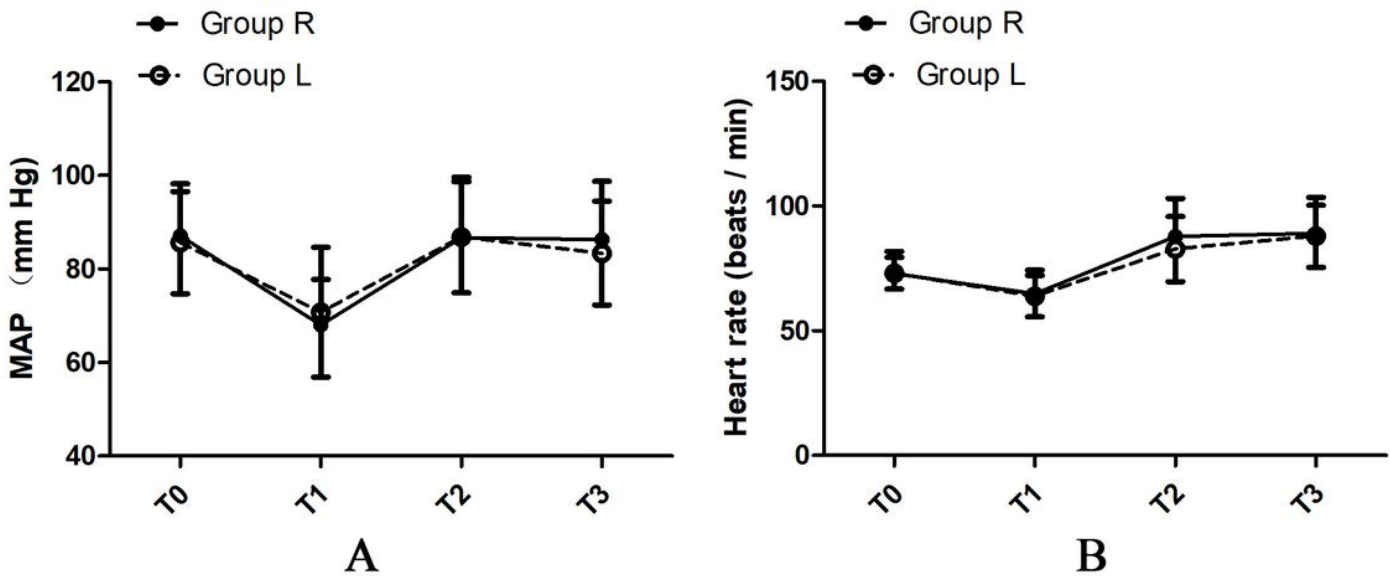

Figure 2

Hemodynamic changes during emergence from general anaesthesia. Data are expressed as mean (standard deviation). MAP is shown in Figure A and heart rate is shown in Figure B. R, remifentanil; L, topical lidocaine *via* the perforated outer cuff; MAP, mean arterial pressure; T0, one day before surgery; T1, the end of surgery; T2, 1 min before extubation; T3, 5 min after

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