Laryngotracheal Topicalization with Lidocaine Before Intubation Decreases the Incidence of Coughing on Emergence from General Anesthesia

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Coughing on emergence can result in a number of undesirable side effects, including hypertension, tachycardia, tachyarrhythmias, increased intracranial pressure, and increased intraocular pressure. The efficacy of endotracheal spraying with lidocaine at the time of intubation in preventing coughing on emergence is unknown. In a double-blind placebo-controlled study, we randomized 50 ASA physical status I and II patients presenting for elective gynecological surgery <2 h duration to receive either endotracheal lidocaine 160 mg or placebo before intubation. Both groups were comparable in terms of demographics and intraoperative conditions. The incidence of coughing before tracheal extubation was less frequent in the lidocaine group (26%) than in the placebo group (66%, $P < 0.01$), as was the incidence after tracheal extubation (4% versus 30%, $P = 0.022$). This study supports the use of endotracheal lidocaine before intubation in patients undergoing general anesthesia for surgery <2 h duration where coughing on emergence is undesirable.

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The incidence of coughing on emergence from general anesthesia in the presence of an endotracheal tube (ETT) has been estimated as ranging between 38% and 96% (1,2).

Coughing on emergence can result in a number of undesirable side effects including hypertension, tachycardia, tachyarrhythmias, increased intracranial pressure and increased intraocular pressure (3,4). Various methods have been applied to attenuate this response, including tracheal extubation while the patient is in a deep plane of anesthesia and IV administration of various drugs, such as lidocaine and short-acting opioids, before tracheal extubation (3,5,6). Concerns about the use of these techniques include delayed emergence from anesthesia, precipitation of airway obstruction, and aspiration in the presence of an unprotected airway.

Endotracheal spraying with lidocaine has been widely accepted as a useful method for obtunding the pressor response to intubation (7). The efficacy of spraying at the time of intubation in preventing coughing during emergence is unknown, and the technique has not been investigated. We conducted a double-blind placebo-controlled randomized trial to examine the efficacy of laryngotracheal spraying with lidocaine before tracheal intubation in preventing coughing on emergence from general anesthesia.

Methods

With university and institutional ethics approval and written informed consent from each subject, we enrolled ASA I and II adults undergoing elective gynecological surgery with a scheduled anesthesia duration between 30 and 120 min and a requirement for tracheal intubation. Patients were excluded from the study if they had an anticipated difficult tracheal intubation, had risk factors for perioperative aspiration of gastric contents, were cigarette smokers, or had a history of respiratory disease or recent respiratory tract infection.

After establishing IV access and routine monitors and IV access, patients were breathed with 100% oxygen. Anesthesia was induced with propofol 2–2.5 mg/kg (containing lidocaine 0.1 mg/mL) and fentanyl 1 μg/kg. Rocuronium 0.5 mg/kg was given to facilitate tracheal intubation. Approximately 2 min after administration, direct laryngoscopy was performed.

Using a randomly generated computer assignment, patients were allocated to receive either endotracheal

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normal saline (placebo group) or endotracheal lidocaine (study group). Both were administered using an LTA® 360 kit. The LTA kit is a disposable kit consisting of a sterile anatomically curved rigid plastic cannula fixed to a vial injector. The cannula has numerous perforations located circumferentially at various distances from the distal end of the cannula. To use the LTA, a prefilled vial labeled "study drug," containing either 4 mL of sterile 0.9% saline or 4 mL of sterile 4% aqueous lidocaine HCl (160 mg) solution, was attached to the injector by screwing it clockwise into the injector until fully seated. The tip of the cannula was inserted between the cords using the black guide mark located 10.8 cm from the tip of the cannula to avoid touching the carina with the distal tip. The vial was depressed rapidly into the injector to produce a circumferential jet-like instillation, bathing the walls of the larynx and trachea with lidocaine. The injectates for both groups were prepared by a third party immediately before use and were visibly indistinguishable to the administrator, who was blinded to the study allocation.

During the same laryngoscopy, after laryngotracheal topicalization, the trachea was immediately intubated using an unlubricated 7.5-mm internal diameter high volume/low pressure ETT (Mallinckrodt Inc., St. Louis, MO) and the cuff was inflated with a volume of air 2 mL more than that required to prevent a leak with positive pressure ventilation. The lungs were mechanically ventilated using a tidal volume of 8–10 mL/kg and the respiratory rate was adjusted to maintain normocarbia. Anesthesia was maintained using desflurane in oxygen and 70% nitrous oxide. Supplementary analgesia (IV morphine 0.1–0.2 mg/kg or fentanyl 1 μg/kg) was administered at the discretion of the anesthesiologist. Neuromuscular blockade was maintained using increments of rocuronium 0.15 mg/kg as required.

At the end of the case, the oropharynx was suctioned, desflurane was stopped, and the patient was administered 100% oxygen. Return of neuromuscular function was confirmed using train-of-four peripheral nerve stimulation. Residual neuromuscular block was reversed using neostigmine and glycopyrrolate. Patients were then placed in the recovery position, mechanical ventilation was discontinued, and ventilation was assisted until spontaneous ventilation resumed. The trachea was extubated when patients demonstrated the ability to follow verbal commands or demonstrated purposeful movement in addition to resumption of regular spontaneous respiration. A blinded observer noted the presence or absence of cough during emergence before and after extubation and before transfer to the postanesthetic care unit. Cough was recorded as either "yes" or "no." If cough was present, it was graded using a three-category scale (Table 1).

Table 1. Three-Category Scale for Scoring Cough on Emergence

Severity	Definition
Mild	Single cough
Moderate	More then one episode of unsustained (≤5 s) coughing
Severe	Sustained (>5 s) bout(s) of coughing

The sample size was calculated based on an estimated incidence of coughing of 76.5% shown in a previous study (8). A 50% relative risk reduction was felt to be of clinical significance. Using an $\alpha \leq 0.05$ and a power = 0.8, 25 patients per group, or 50 patients, would be needed. Dichotomous data were summarized as proportions and percentages and were compared between groups using χ^2 test or Fisher's exact test. Continuous data were summarized as means and standard deviations and were compared between groups using Student's *t*-test. A P value <0.05 was considered statistically significant.

Results

Fifty-four patients were enrolled in this study. Four patients were excluded: two patients had unanticipated difficult intubations requiring multiple laryngoscopies before successful tracheal intubation, one patient removed the ETT, and one patient received an intraoperative opioid infusion, which violated the study protocol. Five patients (one in placebo group, four in lidocaine group) received anesthetics between 120 and 140 min in duration. These individuals were included. Thus, the data from 50 patients were analyzed.

There were no significant differences between the groups in terms of age, weight, or height. They were also similar in terms of duration of anesthesia, amount of opioid analgesia administered, and number of patients administered opioid analgesia 30 min before extubation (Table 2). Fewer patients in the lidocaine group (6 of 23, 26%) coughed before tracheal extubation compared with patients in the placebo group (19 of 27, 70%; $P < 0.01$; Fig. 1). Similarly, fewer patients in the lidocaine group (1 of 23, 4.3%) coughed after extubation compared with patients in the placebo group (8 of 27, 30%; $P = 0.022$; Fig. 1).

Discussion

The results of this study show a decrease in the incidence of coughing observed in patients emerging from general anesthesia after laryngotracheal spraying at the time of intubation with lidocaine compared with placebo.

Table 2. Patient Demographics

Variable	Placebo (n = 27)	Lidocaine (n = 23)
Age (yr)	44 ± 13	49 ± 14
Body Mass Index (kg/m^2)	29 ± 6	27 ± 9
ASA I	17 (63%)	14 (61%)
ASA II	10 (37%)	9 (39%)
Case duration (min)	85 ± 20	85 ± 30
Total Morphine (mg)	7.3 ± 5.2	7.5 ± 5
Morphine <30 mins before extubation	8 (30%)	6 (26%)
Total Fentanyl (μg)	170 ± 62	167 ± 49
Fentanyl <30 mins before extubation	5 (19%)	3 (12%)
Pts given both opioids 30 min before extubation	1 (3.7%)	1 (4.3%)

Discrete data are expressed as absolute numbers and percentages; continuous data are expressed as means ± SD.

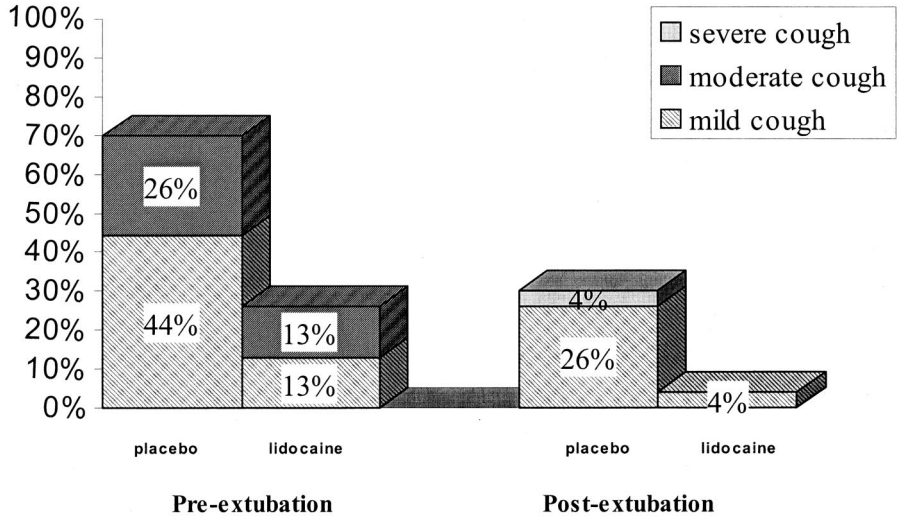

Figure 1. Bar chart showing distribution of patients with coughing on emergence from general anesthesia.

In addition to topical administration of lidocaine, administration of IV lidocaine before tracheal extubation has been shown to prevent coughing on emergence from general anesthesia (9,10). As with topical administration, the precise mechanism for this effect is unclear. It may be that the primary sites of action for the two methods of administration are different, i.e., that topical administration is peripherally mediated and IV administration is centrally mediated. Gonzalez et al. (2) compared topical and IV administration of lidocaine 100 mg before tracheal extubation using a LITA tube™ (Sheridan Catheter Corp., Argyle, NY), a modified ETT, to spray the mucosa both proximal to and distal to the inflated cuff before tracheal extubation and found that laryngotracheal spraying was associated with a significantly reduced incidence of coughing compared to placebo or IV administration. The difference in efficacy may be the result of different sites of action. Yukioka et al. (11) examined the effects of IV lidocaine administration on cough suppression and reported that complete cough suppression on tracheal intubation using IV lidocaine 2 mg/kg 1 minute before intubation required serum lidocaine levels >3 μg/mL. Nishino et al. (9), in their study on IV lidocaine and airway reflexes in anesthetized patients, also reported that suppression of cough reflex occurred at plasma concentrations >3 μg/mL. These studies show that cough suppression using IV lidocaine requires a minimal serum concentration for effect.

Diachun et al. (12) used a LITA to administer 2 mg/kg of 4% lidocaine before tracheal extubation and also showed cough suppression on emergence but with peak serum levels <1.63 μg/mL (mean, 0.43 μg/mL). A local effect on the laryngotrachea by spraying the mucosa would not be dependent on serum concentrations nor would they reflect efficacy.

Lidocaine inhibits neuronal transmission by its action in stabilizing the neuronal membrane. The central nervous system (CNS) manifestations of this may be excitatory and/or depressant, and the antitussive effect of IV lidocaine might be a result of this. However, at the doses required for this antitussive effect, there may also be other CNS effects. In studies on dogs, Himes et al. (13) were able to demonstrate a decrease of up to 28% in the minimum alveolar concentration of halothane with blood lidocaine levels between 3 and 10 μg/mL. Gonzales et al. (2) showed a significantly longer time to

tracheal extubation in the group administered IV lidocaine compared with those administered topical lidocaine or placebo. This may also be attributable to a depressant effect of lidocaine on the CNS.

The efficacy of IV lidocaine in suppressing cough appears to be short lived. Yukioka et al. (11) administered IV lidocaine 1, 3, 5, 7, 10, and 15 minutes before endotracheal intubation and found that the incidence of cough increased gradually from zero percent at 1 minute to 53% at 15 minutes. The effect was consistent with a decrease in serum lidocaine concentrations measured at the respective times.

After endotracheal administration of lidocaine we were able to show efficacy for up to 2 hours. This may be attributable in part to absorption characteristics after endotracheal administration. Prengel et al. (14) measured lidocaine levels after endotracheal and endobronchial administration. After endotracheal administration of lidocaine 2 mg/kg, they observed a biphasic pattern with a peak in blood concentrations occurring immediately after administration and a second peak between 5 and 34 minutes later. Most of the absorption occurred in the second delayed absorption phase, resulting in mean plasma levels of 1.4 μg/mL after 20 minutes. Significantly, however, mean levels of 0.47 μg/mL were detected at 120 minutes. Although the derived mean absorption time for the second phase was 23.9 minutes, there was large interindividual variation (range, 5.4–94 minutes). These levels may reflect slow absorption from the respiratory mucosa. Lidocaine, as a weak basic and lipophilic drug, binds avidly to the respiratory mucosa. The absorption characteristics of the mucosa, epithelial thickness, number of membrane pores, and tissue pH also serve to delay absorption. This intrapulmonary "depot effect" may contribute to the longer than expected effect of lidocaine.

As patients emerge from general anesthesia, the stimulating effect of positive pressure ventilation on the mechanosensitive receptors of the trachea and larger bronchi may provoke coughing (15). To account for this, we assessed and recorded separately coughing occurring before and after tracheal extubation. When assessing the effect of lidocaine on coughing on emergence, the antitussive effect of opiates administered during the case is also a confounding factor (5). In our study, both groups were comparable in terms of the amounts given and times administered.

We did not measure plasma levels of lidocaine at the time of tracheal extubation. As we have discussed, suppression of cough on emergence by spraying the larynotrachea is probably mediated through a peripheral effect and serum levels of limited value. If there were a correlation between patients who coughed and serum lidocaine concentrations at the time, the concentrations would most likely be small and a correlation difficult to show.

We did not measure the end-tidal desflurane concentration at the time of tracheal extubation. It may have been informative to see whether there was a difference in end-tidal concentration of desflurane at the time of tracheal extubation between patients who coughed and those who did not. Fagan et al. (1) looked at this in their study examining the efficacy of intracuff lidocaine in the prevention of cough on emergence. Although they found a decreased incidence in coughing on emergence in the intracuff lidocaine group, they were unable to find any difference in the end-tidal isoflurane concentration between the groups at the time of tracheal extubation.

Our study was conducted in a single large tertiary referral center. As anesthesiologists are not routinely assigned to the same weekly lists, we were unable to limit the number of anesthesiologists involved in the study. Although a standard protocol was followed, variations in individual anesthesiologist's techniques and practices could have led to different incidences of coughing. Also, it was not feasible to use the same observer for each patient; thus, interobserver variability cannot be excluded.

In conclusion, we were able to show that spraying the larynotrachea with lidocaine, compared with placebo, before tracheal intubation decreases the incidence of coughing on emergence from general anesthesia in nonsmokers where anesthesia time was <2 hours.

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