The effect of intracuff alkalinized 2% lidocaine on emergence coughing, sore throat, and hoarseness in smokers

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Summary

Objective: We evaluated whether endotracheal tube (ETT) intracuff alkalinized lidocaine was superior to saline in blunting emergence coughing, postoperative sore throat, and hoarseness in smokers. **Methods:** In our prospective, double-blind trial, we enrolled 50 smoking patients undergoing surgery under general anesthesia including nitrous oxide (N_2O). Patients were randomly allocated to receive either ETT intracuff 2% lidocaine plus 8.4% sodium bicarbonate (L group), or ETT intracuff 0.9% saline (S group). The ETT cuff was inflated to achieve a cuff pressure that prevented air leak during positive pressure ventilation. Incidence of emergence coughing, sore throat, and hoarseness were analyzed. The volume of inflation solution, the intracuff pressure, the duration of anesthesia, the time elapsed to extubation after discontinuation of anesthesia, and the volume of the inflation solution and the air withdrawn from the ETT cuff were also recorded. **Results:** Intracuff alkalinized 2% lidocaine was superior to saline in blunting emergence coughing ($p < 0.001$). The incidence of sore throat was significantly lower in the L group at the post-anesthesia care unit (PACU) ($p = 0.02$). However, at 24 hours after extubation, sore throat incidence was similar in both groups ($p = 0.07$). Incidence of hoarseness was similar in both groups. Intracuff pressure in the saline group increased with time while the intracuff pressure in the lidocaine group remained constant. **Conclusion:** The present study demonstrated that the intracuff alkalinized 2% lidocaine was superior to saline in decreasing the incidence of emergence coughing and sore throat during the postoperative period in smokers.

Keywords: Smoking; lidocaine; cough; hoarseness; nitrous oxide.

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Submitted on: 10/26/2011
Approved on: 12/05/2011

Financial Support:
FAPESP – Grant #2005/55458-5; CAPES

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Conflict of interest: None.

Introduction

Smoking remains one of the most common risk factors that predispose patients to perioperative complications[1-2]. Although smoking affects a variety of organs, such as heart, lung, immune and nervous systems, the respiratory system is the most often affected during the perioperative period[3]. General anesthesia and tracheal intubation may contribute in exacerbating these respiratory complications. The emergence period may require special attention, since it elicits undesirable and exacerbated airway reflexes.

Chronic smokers develop laryngeal epithelial inflammation, metaplasia, and dysplasia, which may impair laringeal integrity and function[3]. Erskine et al. evaluated airway reflexivity to chemical and mechanical stimulations. They observed an increase in sensitivity in chronic smoking patients, which was associated with a higher incidence of laryngospasm, airway obstruction, and decreased oxygen saturation[4]. It has been suggested that because smoking induces these chronic changes in the upper airway epithelium, there is a greater exposure of subepithelial airway receptors to stimuli[3]. Tracheal intubation results in stretch stimuli in the trachea caused by the tube and its cuff. Intravenous[5-7] and topical[7,8] lidocaine has been in use for many years in blunting the emergence adverse phenomenon after general anesthesia. Targeted delivery of lidocaine to the mucosa in contact with the tracheal tube (ETT) cuff can be used as a method for decreasing tracheal stimuli. When lidocaine is injected into the ETT cuff[9,10], it spreads through the semi-permeable membrane wall and induces anesthetic action in the trachea. This increases tolerance to the placement of tracheal[11] and tracheotomy[12] tubes. Hemodynamic alterations after tracheal extubation are thereby minimized, and the incidence of coughing is reduced[13,14]. However, a study using intracuff non-alkalinized 4% lidocaine in smokers who underwent short procedures (< 90 minutes) failed to demonstrate a decrease in emergence cough[15].

A reliable technique for improving endotracheal tube tolerance while providing smooth and fast extubation has not been established in smoking patients. We conducted a randomized double-blind clinical trial to study whether tracheal tube intracuff 2% alkalinized lidocaine was superior to saline in blunting emergence coughing, and postoperative sore throat and hoarseness in smokers who underwent tracheal intubation.

Methods

The study was approved by the Research and Ethics Committee of Faculdade de Medicina de Botucatu. Written informed consent was obtained from each patient. Fifty patients scheduled for elective gynecological, orthopedic, or plastic surgery were enrolled in this prospective, randomized double-blind study. All patients were over 18 years of age, of either gender, with ASA physical status I or II, and their Mallampatti classification was equal to 1. All patients were smokers for a period longer than five years, consuming at least five cigarettes a day, and did not interrupt the habit before the surgical procedure. Patients undergoing laryngeal surgery, with tracheotomy, laryngeal disease, or asthma were excluded from the study. Anticipated difficult intubation, more than one attempt for intubation, need for nasogastric tube, history of respiratory tract infection, and contraindication for use of nitrous oxide (N_2O) were also exclusion criteria.

This is a posttest-only design research study to evaluate the efficacy of intracuff alkalinized 2% lidocaine in reducing the incidence of cough during emergence from general anesthesia and tracheal morbidity in smokers. Tracheal morbidity was defined as postoperative hoarseness or sore throat. Patients were randomly allocated to receive either ETT intracuff alkalinized 2% lidocaine (L group) or ETT intracuff 0.9% saline (S group). Before induction, the anesthesia provider was given a 20 mL syringe filled with 0.9% saline or with 2% lidocaine mixed with 8.4% sodium bicarbonate, in a 19:1 mL proportion. At the time of intubation, the experimental group (L) received intracuff lidocaine and the control group (S) received intracuff saline in a volume sufficient to establish a cuff pressure that would prevent the air from leaking during positive pressure ventilation. The anesthesia provider was blinded to lidocaine or saline administration, since all solutions were colorless in a volume of 20 mL. A staff nurse, not otherwise involved in the study, prepared the solutions. The application of local anesthetic by any other means was prohibited. The ETT cuffs were lubricated with 4 mL of water-soluble gel (KY Gel®, Johnson & Johnson – France) before tracheal intubation in both groups.

Intraoperative procedures

Patients were premedicated with oral midazolan (7.5 mg) one hour before anesthesia induction. Monitoring included electrocardiogram, pulse oximetry, capnography, and non-invasive blood pressure (NIBP). Both groups received a standardized balanced anesthesia management, including isoflurane and continuous infusion of sufentanil. Neuromuscular blockade was ensured throughout surgery, using neuromuscular monitoring, with continuous infusion of rocuronium. The intubation was based on the response to ulnar stimulation, performed when the 4th stimulus/1st stimulus ratio was equal to zero. A standard 8.0 mm ID polyvinyl chloride oral cuffed ETT was used in males and a 7.5 mm ID was used in females. Continuous intracuff pressure was monitored with a pressure monitor that included a pressure transducer (Portal Monitor DX 2020, Dixtal - Manaus, Brazil) connected to a three-way stopcock. The ETT pilot balloon and the 20 mL syringe

with lidocaine or saline were attached to the other two-way stopcocks. After inflation of the cuff, the three-way stopcock was closed to atmosphere and the initial pressure reading was taken with patient under ventilation with 100% oxygen. The volume of the inflation solution was noted (T0). N_2O was then initiated and the patient was ventilated with 60% N_2O in oxygen throughout the surgical procedure. At the end of the surgical procedure, the neuromuscular block (NMB) was reversed with neostigmine and atropine. The tracheal tube was removed when the following signs of complete NMB reversion occurred: spontaneous ventilation, response to ulnar stimulation such that the 4th stimulus/1st stimulus ratio was greater than 0.9, and response to verbal commands (eye opening or hand squeezing).

Data recorded

The volume of inflation solution, the intracuff pressure, the duration of anesthesia, the time elapsed to extubation after the discontinuation of anesthesia, and the volume of the inflation solution and air withdrawn from the ETT cuff were recorded.

The coughing was assessed as present or absent in all patients. Coughing was considered absent when no coughing or coughing only while removing the ETT cuff occurred. It was considered present when the patient coughed while breathing regularly or irregularly with the ETT in place. An anesthesiologist who did not know to which group (L or S) the patient belonged evaluated the incidence of emergence coughing (yes/no), sore throat, and hoarseness. Sore throat and hoarseness were evaluated at the time of release from the post-anesthesia care unit (PACU) and 24 hours after extubation.

Lidocaine concentration

Four peripheral blood samples were taken during the anesthetic-surgical procedure (10, 60, and 120 minutes after tracheal intubation, and at the end of anesthesia). Samples were placed in tubes containing sodium ethylenediaminetraacetic acid (EDTA) for high performance liquid chromatographic (HPLC) analysis of serum lidocaine concentrations.

Statistical analysis

Power analysis suggested that 25 patients in each group would allow for detection of a 35% decrease in the incidence of coughing and sore throat for a type I error of 0.05, a type II error of 0.20, and a power equal to 0.80.

For anthropometrical variables and duration of the anesthesia, the Student *t* test was used. The incidence of coughing, sore throat, and hoarseness were compared by the chi-square test for multiple variables. Values were considered significant when $p < 0.05$.

Results

All 50 patients enrolled in the study completed it. With respect to gender, 74% of the patients were female and 26% were male, with no statistical difference within the groups ($p = 0.33$). The groups were similar with respect to patient characteristics, as well as in the duration of anesthesia ($p > 0.05$) (Table 1). The mean time elapsed from discontinuation of the anesthesia to extubation was longer for the S group when compared with the L group, but no statistically significant difference was noted ($p = 0.052$) (Table 1).

Intracuff pressure and volumes

It can be seen in Table 2 that the initial pressure (T0) (cm H_2O) required to "seal" the trachea and avoid air leak during positive pressure ventilation was higher in the L group when compared with the S group (17.8 ± 2.1 vs. 15.9 ± 1.3, respectively; $p < 0.05$). However, the intracuff pressure in the S group increased with time, while in the L group it remained constant. Although initially lower, the intracuff pressure in the S group is statistically higher than the pressure in the L group at the end of the study (T final) (20.4 ± 9.1 vs. 16.3 ± 5.7, respectively; $p < 0.05$) (Table 2). In both groups, the intracuff pressure was maintained below the critical tracheal perfusion pressure of 25 cm H_2O[15].

The initial volume needed to inflate the ETT cuff was similar in both groups (S group = 7.21 ± 2.1 and L group = 6.9 ± 2.6) ($p = 0.77$). There was a decrease in the volume of the solution withdrawn from the cuff at the end of the study, with no statistically significant difference between the groups (3% and 10% decrease in S group and L group, respectively; $p = 0.55$).

Table 1 – Anthropometric variables of the patients, duration of anesthesia, and time elapsed from discontinuation of anesthesia to extubation. Data shown as mean ± standard deviation

Variable	Group		p-value
	Saline	Lidocaine	
Weight (kg)	67.3 ± 12.0	69.3 ± 15.0	0.61
Height (cm)	162.8 ± 7.8	163.7 ± 10.5	0.72
Duration of anesthesia (min)	223.6 ± 99.3	206.6 ± 63.1	0.47
Time elapsed from discontinuation of anesthesia to extubation (min)	14.1 ± 11.6	9.2 ± 4.2	0.05

Table 2 – Intracuff pressure (cm H_2O) throughout the anesthesia procedure

Time points (minutes after tracheal intubation)	Group	
	Saline	Lidocaine
T 0	15.9 ± 1.3	17.8 ± 2.1#
T 30	16.8 ± 6.4	17.2 ± 7.0
T 60	17.1 ± 6.7	17.9 ± 6.5
T 90	18.2 ± 8.4	17.5 ± 7.2
T 120	19.1 ± 9.0	16.3 ± 6.8
T_{end} of anesthesia	20.4 ± 9.1*	16.3 ± 5.7

Data shown as mean ± standard deviation. #p = 0.04 for the difference between groups in the same time point; *p = 0.04 for the difference between time points in the same group.

Coughing

The incidence of coughing at emergence of general anesthesia was considerably lower in the L group ($p < 0.001$), when compared with the S group, demonstrating a beneficial effect of the alkalinized lidocaine in suppressing the irritation stimuli of the ETT cuff on the tracheal mucosa when compared with the ETT cuff inflation with saline (Figure 1).

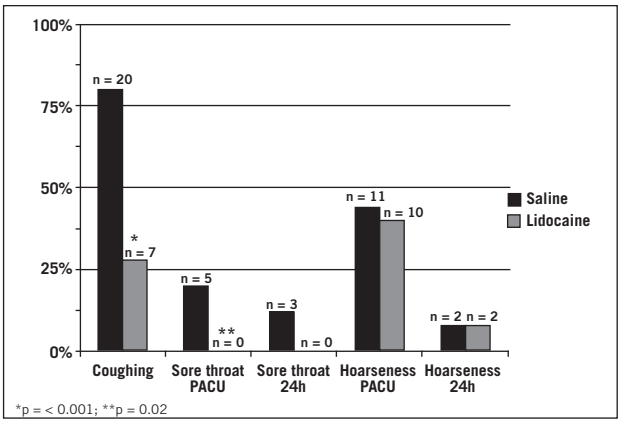

Figure 1 – Incidence of emergence coughing and tracheal morbidity present in the post-anesthesia care unit (PACU) and 24 hours after extubation. There were 25 patients in both groups. Saline = control group (0.9% saline - S group); lidocaine = treated group (alkalinized 2% lidocaine - L group).

Sore throat and hoarseness

The incidence of sore throat was significantly lower in the L group than in the S group at the time of release from the PACU ($p = 0.02$). The incidence of sore throat at 24 hours after extubation, however, was similar in both groups ($p = 0.07$). It is remarkable, and unexpected, that not a single patient in the L group had sore throat in the postoperative period (Figure 1).

The incidence of hoarseness in the postoperative evaluation revealed no statistically significant differences within the two groups in the PACU, as well as at 24 hours after extubation ($p = 0.77$ and $p = 1.0$, respectively) (Figure 1).

Plasma lidocaine assessment

The serum concentration of lidocaine in the L group did not vary significantly throughout the study. It was readily detectable 10 minutes after the inflation of the cuff with the local anesthetic, and remained constant throughout the study period ($T_{10} = 1.52 \pm 0.33$; $T_{60} = 1.60 \pm 0.71$; T120 = 1.60 ± 0.84; T_{end} of anesthesia = 1.87 ± 0.82) ($p > 0.05$).

Discussion

The major findings of the present study included a decrease in the incidence of coughing at the emergence from the general anesthesia, and of sore throat during the postoperative period in smokers, when the ETT cuff was inflated with alkalinized 2% lidocaine. Furthermore, intracuff lidocaine prevented a significant rise in the ETT intracuff pressure.

This study was limited to smokers because this group has underlying airway irritability. Strategies to attenuate the emergence phenomenon include extubation in a deeper plane of anesthesia, use of narcotics[16], and use of lidocaine[11,12,14]. Although many studies have been performed, a reliable technique for improving ETT tolerance has not been established for smokers. A study using nebulized lidocaine prior to the induction of anesthesia demonstrated a significant decrease in procedure-related complications in smoking patients[17]. Altintas et al. demonstrated lower incidence of bucking at the time of extubation with the use of intracuff lidocaine[13]. When lidocaine is used to inflate the ETT cuff, a higher tolerance for both tracheal[11-14] and tracheotomy tubing[12] is well demonstrated. However, a recent study failed to demonstrate the effectiveness of intracuff non-alkalinized 4% lidocaine in reducing coughing during emergence from general anesthesia in smokers[14] who underwent anesthesia lasting less than 90 minutes. The main reason for this lack of effect may be due to a lower drug diffusion rate through the cuff because of the low drug pH, since lidocaine was not alkalinized.

In this study, the incidence of coughing was demonstrably lower in the L group when compared with the S group.

In the proportions used in this study (19 mL of lidocaine: 1 mL of bicarbonate), a solution pH modification from 6.92 (lidocaine chlorohydrate) to 7.43 (alkalinized lidocaine) was obtained. This most likely provided for quicker diffusion of lidocaine through the cuff membrane, which allowed for the measurement of a similar significant lidocaine concentration in the analysis of the patients' blood samples just 10 minutes after inflation. The continuous metabolism of lidocaine by the liver may explain the constant serum concentration of the drug found in this study.

During general anesthesia, the use of intravenous lidocaine has been employed with the intent of suppressing cough reflex. To effectively suppress coughing, a high lidocaine serum concentration[18], around 3 mg/mL[1], is required. Such serum concentration may be achieved with an intravenous injection of 1-2 mg/kg[1] of the drug[19]. Lidocaine administered intravenously, however, can produce sedation and prolong the process of awakening from anesthesia[20]. In this study, the patients did not experience any prolongation in the awakening from anesthesia time due to the use of intracuff lidocaine. In fact, the time elapsed since the discontinuation of the anesthetic drugs until the extubation was shorter in the L group. This may be due to a smoother emergence period experienced by the patients with intracuff lidocaine, while in the S group the high incidence of coughing during emergence delayed the extubation.

The pressure in the ETT pilot balloon, an indirect measure of the pressure exerted by the cuff on the tracheal mucosa, is not routinely determined by the anesthesiologist[21,22]. Several methods have been proposed to minimize the elevation of cuff pressure during N_2O anesthesia. These include the use of an ETT with regulatory pressure valves[23], the inflation of the cuff with a mixture of N_2O/O_2 in proportions identical to those used in the anesthesia[24], the use of a tracheal tube with a cuff impermeable to N_2O[25], and filling the cuff with 0.9% saline[26]. A reliable and alternative method of reducing high cuff pressure is filling the cuff with lidocaine. Others have used lidocaine in the form of chlorohydrate to fill the cuff in concentrations of 2%, 4% and 10% (200-500 mg)[8-10,13]. Lidocaine alkalinization[12] increases the rate of diffusion through the cuff wall, allowing a reduction of the lidocaine dose while achieving the same results. The ETT cuff served as a reservoir to release local anesthetic to the subjacent tracheal tissues[10,12]. Our results demonstrate that intracuff lidocaine prevents a significant rise in the cuff pressure during N_2O anesthesia, secondary to continuous drug diffusion. On the other hand, there was a time-dependent increase in the cuff pressure in the S group. The reason for the rise in intracuff pressure is likely due to the increased gas by absorption of N_2O[27]. Gas was also removed from the cuffs filled with lidocaine. The increased cuff gas in the L group at extubation was counter-balanced by a decrease in the liquid volume due to diffusion of alkalinized lidocaine through the cuff wall. This balance maintained adequate cuff pressure and protected the airway against air leak or aspiration of gastric content.

Cuff lubrication with lidocaine gel or spray has been associated with increased morbidity during emergence from anesthesia due to adherence of the ETT to the tracheal mucosa[28], and may promote cuff rupture[29]. Contrarily, cuff lubrication with a water soluble gel in association with alkalinized lidocaine increases tracheal tube tolerance and reduces the incidence of postoperative sore throat[28]. It has been suggested that sore throat is caused by the activation of tracheal pain receptors[20]. The proposal of a continuous application of local anesthetic to block these nociceptive receptors would therefore seem logical, in an attempt to reduce the incidence of sore throat. After tracheal extubation, sore throat has been reported in 15% to 80%[13,30] of cases. In our study, the incidence of sore throat was 20% and 12% in the S group at the time of discharge from the PACU and at 24h after extubation, respectively. In the L group, no patient presented with sore throat. This highly positive result was unexpected and may be related with the combination of three different techniques recognized as protective against sore throat: use of low ETT cuff pressure, use of intracuff alkalinized lidocaine, and use of water-soluble lubricant. However, despite all techniques applied for preventing tracheal morbidity, the incidence of hoarseness was similar in both groups, suggesting that this symptom is unlikely related to the cuff pressure or to the cuff inflation solution.

The toxicity of local anesthetic must be considered. The mean volume of lidocaine used in the study was 6.9 ± 2.6 mL (138 ± 52 mg). This dose is lower than the toxic systemic level. If a cuff rupture occurs, a relatively high dose of lidocaine can be delivered into the trachea and bronchium leading to toxicity. However, lidocaine induced cuff rupture has never been reported either *in vivo* or *in vitro*. In this study, all patients were extubated without any complications, and no evidence of cuff damage was observed. Bicarbonate is another drug that can lead to tracheal wall damage if a cuff rupture occurs. The small dose used in the present study (1 mL of 8.4% bicarbonate in 20 mL of solution) was enough to increase the pH of the lidocaine solution, and facilitate its diffusion, but is unlikely to produce damage on the trachea if any cuff damage occurs.

Conclusion

The present study demonstrated that the inflation of the ETT cuff with alkalinized 2% lidocaine was superior to saline in decreasing the incidence of emergence coughing and preventing sore throat during the postoperative

period in smokers. The low cuff pressure and the lubrication of the ETT cuff may have helped to reduce coughing and sore throat incidence, but these were used in both groups. We recommend considering the use of an ETT cuff filled with alkalinized lidocaine in smokers undergoing general anesthesia.

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