ORIGINAL ARTICLE

The effect of lidocaine on reducing the tracheal mucosal damage following tracheal intubation

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Background: The aim of this study was to investigate the efficacy of lidocaine solution in the cuff of the endotracheal tube in reducing mucosal damage following tracheal intubation. **Materials and Methods:** This was a randomized controlled trial study undertaken in the intensive care unit patients. Participants, who met all eligibility criteria, were randomly assigned to one of two groups of patients, according to whether lidocaine or air was used to fill the tracheal tube cuff. The tracheal mucosa at the site of cuff inflation was inspected by fiberoptic bronchoscopy and scored at the 24 h and 48 h after intubation. **Results:** In all, 51 patients (26 patients in the lidocaine group and 25 patients in the control group) completed the study. After 24 h, erythema and/or edema of tracheal mucosa were seen in 2 patients (7.7%) of lidocaine group and 6 patients (24%) of air group (P = 0.109). Binary logistic regression analysis showed that lidocaine has a significant protective effect against mucosal damage (odds ratio = 0.72, confidence interval = 0.60-0.87). **Conclusion:** The inflation of the tracheal tube cuff with lidocaine was superior to air in decreasing the incidence of mucosal damage in the 24 h and 48 h post intubation.

Key words: Intubation, lidocaine, mechanical ventilation, mucosal damage

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INTRODUCTION

Tracheal intubation is one of the most frequently performed procedures in the intensive care unit (ICU) and has an essential role in airway management in critically ill patients.[1-3] Hemodynamic instability, hypoxemia and acidosis in ICU patients indicate the need for maintaining a secure airway for these patients.[4] Poor physical conditions, emergent intubation, and medication in ICU bring the high risk of intubation complications as high as 54%.[5] On the other hand, high incidence of tracheal mucosal lesions is attributed to high cuff pressure compression.[6] The cuff is designed to provide an airway seal and reduces aspiration of orotracheal secretions.[7] Hyperinflation of the endotracheal cuff to pressures more than 25 cm H2O or greater is contributed to mucosal ischemia and subsequent destruction of the tracheal wall.[8] Mucosal ischemia is associated with inflammation, hemorrhage, and necrosis.[9] These circumferential lesions heal by fibrosis, leading to a progressive tracheal stenosis, which occurs in 1-4% of the patients after treatment at ICUs.[10]

Several interventions have been used to reduce the cuff pressure and decrease the incidence of associated adverse consequences. Providing the stable cuff pressure by filling the cuffs with anesthetic gas mixture[11] and tight control of cuff pressure was effective in minimizing the incidence and severity of tracheal mucosal damage.[12] In another study, inflating cuffs with either air or saline was examined in two groups. In saline group, cuff pressure remained stable during anesthesia and tracheal lesions were significantly lower at the time of extubation.[13]

The role of lidocaine in reducing the frequency of postoperative cough and sore throat was demonstrated in several studies.[14-16] Lidocaine is also thought to be useful in reducing injury to the tracheal mucosa with vasodilation mechanism.[17] Until now, there has not been any study regarding the effect lidocaine on mucosal damage considering bronchoscopy evaluation. Therefore, the aim of this study was to investigate the efficacy of lidocaine solution in the cuff of the endotracheal tube in reducing mucosal damage following tracheal intubation and compare it with the air.

MATERIALS AND METHODS

This was a double-blinded randomized controlled trial study that was undertaken in the ICU of University

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Hospital, Isfahan, Iran. The target population was hospitalized patients in the ICU, requiring tracheal intubation and mechanically ventilation for acute respiratory failure.

Eligibility criteria included age more than 18 years and less than 70 years, no history of hematologic, cardiovascular and pulmonary diseases, undergoing surgery rather than thoracic surgery, stable hemodynamic condition, no prior intubation in the last year, not pregnant, and not suspected as difficult intubation and the absence of any contraindication for performing bronchoscopy. Patients who were extubated earlier than 48 h were excluded. Other exclusion criteria were: Cuff pressure more than 25 mmHg, unstable hemodynamic condition during the study, persistent hypoxemia, coagulation abnormalities or bleeding during the study and death.

For a statistically significant level of 5%, a statistical power of 80%, ($P1 = 0.4$, $P2 = 0.1$) a sample size of 25 patients per group was required.

Between March 2012 and October 2012, participants, who met all eligibility criteria, were randomly assigned to one of two groups, according to whether lidocaine or air was used to fill the tracheal tube cuff. The randomization was performed by a ratio of 1:1, using Excel software random number generation. All patients were intubated with a standard 8.0 mm polyvinyl chloride oral cuffed Endo tracheal Tube [ETT] for men and 7.5 mm for women. The same anesthetist performed all tracheal intubations.

In the control group, after orotracheal intubation, the tracheal tube cuffs were inflated with air, up to a pressure of 25 mmHg.

Patients in the intervention group underwent intubation using a tracheal tube, which filled with 2% lidocaine (Caspian tamin, Pharmaceutical company, Rasht, Iran) associated to a volume that was sufficient to cause a cuff pressure of 25 mmHg the tracheal tube cuff pressures were measured using a control-inflator device after intubation, and then after 24 h and 48 h.

Data relating to oxygen saturation, systolic, and diastolic blood pressure, were obtained immediately after orotracheal intubation, and then 6, 12, 18, 24, 30, 36, 42, and 48 h after the intubation [Table 1].

All patients underwent fiberoptic bronchoscopy at 24 and 48 h after the study. Bronchoscopy examination was performed by an ICU specialist who was blind to the study group. The fiberscope was fed in the tracheal tube as the endoscope went below the end of the endotracheal tube, the cuff was deflated. The endotracheal tube and the endoscope were gently withdrawn concomitantly; the tracheal mucosa at the site of cuff inflation was inspected and scored according to the following scoring: 0 = normal, 1 = erythema and/or edema, 2 = erosion and/or hemorrhage on one side of tracheal wall, 3 = erosion and/or hemorrhage on both anterior and posterior tracheal walls.[18]

Table 1: Demographic and clinical characteristics of patients in two groups during the study

Variable	Lidocaine group mean (SD)/*n* (%)	Air group mean (SD)/*n* (%)	*P* value
Age (year)	49.02 (13.58)	45.13 (13.82)	0.313
Gender			
Female	10 (19.5)	4 (9.1)	0.072
Male	16 (31.3)	21 (40.1)	
Oxygen saturation (%)			
After intubation	95.08 (2.24)	95.40 (2.61)	>0.05
After 6 h	95.46 (1.58)	95.88 (1.97)	
After 12 h	95.42 (2.21)	93.64 (2.41)	
After 18 h	95.38 (1.94)	96.64 (2.03)	
After 24 h	95.81 (1.91)	96.04 (2.40)	
After 30 h	96.12 (1.63)	95.12 (1.82)	
After 36 h	96.58 (1.81)	96.64 (1.64)	
After 40 h	96.35 (2.20)	96.44 (2.12)	
After 42 h	96.38 (2.06)	96.44 (2.10)	
After 48 h	96.12 (2.07)	96.04 (2.24)	
Mean blood pressure (mmHg)			
After intubation	92.24 (15.03)	90.46 (12.02)	>0.05
After 6 h	93.76 (13.68)	91.23 (11.24)	
After 12 h	91.85 (12.86)	92.34 (13.66)	
After 18 h	92.87 (14.13)	90.22 (12.56)	
After 24 h	94.86 (14.39)	92.89 (13.78)	
After 30 h	95.67 (16.04)	93.67 (15.44)	
After 36 h	93.79 (13.71)	94.02 (14.22)	
After 40 h	94.87 (14.76)	93.65 (13.85)	
After 42 h	92.44 (12.62)	89.21 (13.26)	
After 48 h	93.13 (12.51)	91.27 (11.78)	
Hemoglobin (mg/dl)			
Female			
After intubation	10.61 (0.71)	11.97 (2.36)	>0.05
After 24 h	10.60 (0.59)	11.92 (2.41)	
After 48 h	10.50 (0.57)	11.92 (2.41)	
Male			
After intubation	11.06 (1.21)	11.39 (1.31)	>0.05
After 24 h	10.63 (0.78)	11.24 (1.23)	
After 48 h	10.37 (0.32)	10.97 (1.66)	

Demographic and clinical data of participants (age, gender, etiology of disease, medical history) were collected by a questionnaire.

Statistical analysis

All descriptive statistics are presented as means and standard deviations (SD) for quantitative variables and as relative

frequencies and percentages for categorical variables. Student *t*-test and Chi-square test were conducted to compare the baseline characteristics of two groups. Repeated measure analysis of variance was used to examine any difference in the study outcomes (systolic and diastolic blood pressure, oxygen saturation and cuff pressure) between the intervention and the control groups over the evaluation period. The severity of tracheal mucosal damage was compared between two groups using Chi square analysis of variance.

Binary logistic regression analysis was applied to assess the predictors of mucosal damage. Considering the presences of mucosal lesions after 48 h as the dependent variable, the independent (predictor) variables were entered in the model, including the age of participants, gender and etiology of hospitalization in ICU. The level of significance was set at $P < 0.05$ and all tests were two-tailed. The analysis of data was performed by the predictive analytic software (SPSS version 18) for Windows.

Ethics

The design of the study was approved in Ethics committee of Vice Chancellor for Research, Isfahan University of Medical Sciences (project no. 391341). Legally authorized representatives were provided written informed consent and the confidentiality of all information was managed carefully by researchers.

RESULTS

Seventy-five patients acquired the inclusion criteria and were enrolled in the study. Seven patients were excluded due to extubation earlier than 48 h. Other reasons of exclusion include: Hemoglobin concentration less than 10 (n = 10), cardiac arrest (n = 4) and cuff pressure more than 25 mmHg (n = 3). In all, 51 patients (26 patients in the lidocaine group and 25 patients in the control [air] group) actually completed the study and were evaluated for the outcome [Figure 1].

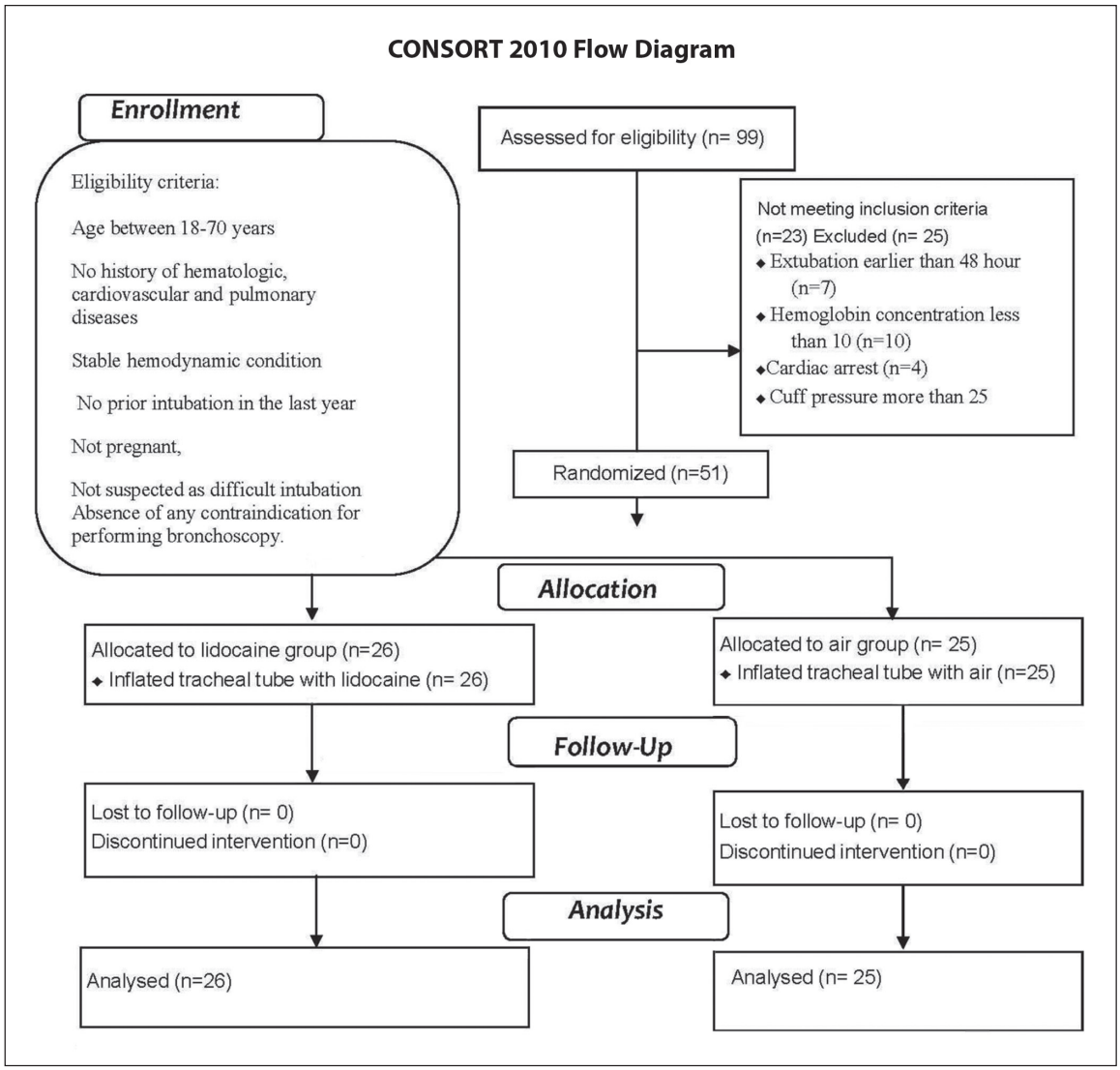

Figure 1: CONSORT trial flow diagram

The mean age of patients in the intervention group and control group was 49.0 years (SD = 13.5) and 45.1 (SD = 13.8), respectively ($P = 0.31$).

Of whom, 14 patients were female (27.5%) and 37 patients were men (72.5%) [Table 1]. Baseline clinical and demographic characteristics were balanced across treatment arms, indicating the success of randomization.

There were no differences in demographic data between the patients who attended and those who dropped out ($P > 0.05$).

The most common causes of ICU hospitalization were: Intracranial hemorrhage (12%) and multiple trauma (10%).

There was no statistically significant difference between two groups regarding the etiology of ICU hospitalization ($P = 0.15$). The mean arterial blood pressure was not statistically significant different between two groups ($P = 0.72$).

The cuff pressure remained stable in two groups (25 mmHg) and there were no gas leaks at the tracheal tube during the intubation. Consequently, oxygen saturation was not statistically significant different between lidocaine and air groups during the 48 h ($P = 0.134$).

After 24 h, erythema and/or edema of tracheal mucosa were seen in 2 patients (7.7%) in lidocaine group and 6 patients (24%) of air group. Severe lesions were not seen in both groups. There was no statistically significant difference between two groups regarding the bronchoscopy findings after 24 h ($P = 0.109$).

Bronchoscopy findings after 48 h indicated erythema and edema of tracheal mucosa in the same patients (2 patients (7.7%) in lidocaine group and 6 patients (24%) of air group). In one of the patients of air group, erosion and hemorrhage on the anterior wall of trachea was present ($P = 0.147$). No exposed cartilage in the cuff contact area was seen in any patient [Table 2].

Table 2: Frequency of tracheal mucosal damage after 24 h and 48 h

Bronchoscopy findings	Tracheal mucosal damage	Group study		*P* value
		Lidocaine *n* (%)	Air *n* (%)	
Bronchoscopy findings after 24 h	Grade I	24 (92.3)	19 (76)	0.109
	Grade II	2 (7.7)	6 (24)	
	Grade III	0	0	
	Grade IV	0	0	
Bronchoscopy findings after 48 h	Grade I	24 (92.3)	18 (72)	0.147
	Grade II	2 (7.7)	6 (24)	
	Grade III	0	1 (4)	
	Grade IV	0	0	

Binary logistic regression analysis showed that lidocaine has a significant protective effect against mucosal damage (odds ratio [OR] = 0.72, confidence interval [CI] = 0.60-0.87). Age of participants (OR = 1.02, CI = 0.95-1.08), gender (OR = 0.34, CI = 0.02-7.36) and etiology of hospitalization (OR = 1.06, CI = 0.92-1.22) were not significant predictors of tracheal mucosal damage.

DISCUSSION

The aim of this study was to study the efficacy of intra-cuff lidocaine solution in reducing postoperative mucosal damage of trachea. The tracheal mucosal damage was more frequent in the control group in comparison to the lidocaine group (24% vs. 7.7%). Although this difference was not statistically significant, logistic regression analysis showed that being in the lidocaine group has a significant protective effect against mucosal damage.

However, in our study, most patients did not experience tracheal damage, which may be due to tight control of cuff pressure during the study. Sajedi and Maaroffi confirmed that tight control of cuff pressure can minimize the incidence and severity of tracheal mucosal damage at the site of cuff inflation.[12]

The tracheal mucosa is extremely fragile. Previous studies showed that even a mild pulling of a cotton swab along it causes loss of epithelium.[19] Tracheal intubation and respiratory movements may cause mucosal damage and abrasion of tracheal epithelium following intubation especially in patients with poor general status.[20]

Esteller-Moré *et al*. examined the incidence of laryngotracheal injuries following intubation and/or tracheotomy in ICU. Endoscopic exploration of the upper airway 6-12 months after extubation revealed laryngotracheal injuries in 11% of the patients.[21] In the ICU care, the cuff pressure could not be decreased due to the risk of aspiration. Hence, the only way to reduce the tracheal mucosal damage is shortening the period in which patient is intubated. In our study, we examined another idea to reduce the mucosal damage by vasodilatory effect of lidocaine.

Our study showed that lidocaine is effective in reducing the incidence of intubation-induced mucosal damage. Lidocaine is the most widely used drug for local anesthesia.[22] This drug can diffuse across the cuff in a time- and concentration-dependent manner and influence the local tracheal receptors to induce local anesthesia and ultimately reduce the tube discomfort.[23] In addition to having analgesic effects, it is also may cause vasodilation by blocking sodium channels at clinically relevant doses.[24] This vasodilatory effect of lidocaine is also mediated by the release of nitric oxide from

vascular endothelium.[25] The protective effect of lidocaine against mucosal damage in our study may be due to the vasodilation mechanism of this drug. The vasodilator effects of lidocaine are believed to be due mainly to the sodium channel blocking in vasoconstrictor sympathetic nerves inhibiting the production and propagation of action potentials.[26] Furthermore, peripheral microcirculation is through the release of nitric oxide, which nitric oxide release also contributes to the vasoactivity of this drug.[25]

Intra cuff lidocaine has other beneficial effects. Several randomized controlled trial studies showed that filling the cuff with lidocaine could prevent postoperative sore throat resulting from intubation.[15,27-29] Furthermore, the effectiveness of lidocaine in reducing cough and incidence of cardiac arrhythmia was reported.[30-32] Lidocaine can diminish hemodynamic response after tracheal intubation by several mechanisms: Inhibiting sodium influx in the neuronal cell membrane and inhibiting signal conduction,[33] decreasing the sensitivity to the heart muscle to electrical pulses,[34] direct cardiac depression and peripheral vasodilatation properties.[35]

The toxicity of local anesthetic must be considered. In the event of a cuff rupture, 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*.[36]

The major strength of this study was the use of a randomized controlled design, which enhanced its generalizability. Our study was limited because of the small sample size that prevents more elaborate subgroup analysis. Furthermore, this study was not powered enough to detect a significant difference between two groups regarding the bronchoscopy findings. Performing bronchoscopy after 48 h and 1 week later may reveal more frequent tracheal mucosal damage. Further large clinical trial studies are also needed to evaluate the effectiveness of lidocaine in reducing the mucosal damage after intubation.

In conclusion, the present study demonstrated that the inflation of the tracheal tube cuff with lidocaine was superior to air in decreasing the incidence of mucosal damage in the 24 h and 48 h post intubation. Further large clinical trial studies are warranted to evaluate the effectiveness of lidocaine in reducing the mucosal damage after intubation.

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