

Effects of intracuff dexamethasone on post-extubation reactions

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Background: The most common complications after tracheal intubation during general anesthesia are sore throat, hoarseness, and laryngospasm which can cause severe discomfort to patients. Several methods have been suggested to prevent these complications. In this study, the effects of intracuff dexamethasone, lidocaine, and normal saline in reducing post-extubation reactions were compared. **Methods:** This double-blind clinical trial was performed on 180 men of ASA (American Society of Anesthesiologists) class I or II who underwent general anesthesia for elective inguinal herniation surgery in Imam Reza Hospital, Tehran, Iran during 2008-2010. Depending on the kind of drug used to fill the endotracheal tube (ETT) cuff, patients were randomly allocated into normal saline, lidocaine, and dexamethasone groups. Post-extubation reactions were then evaluated in all groups. **Results:** The groups were demographically comparable. There were no significant differences between the three groups regarding post-extubation sore throat, hoarseness, or laryngospasm ($p > 0.05$). However, a significant difference in cough existed between the three groups ($p = 0.02$). Moreover, the groups were not significantly different in terms of patient satisfaction after 24 hours ($p = 0.062$). Prolongation of spontaneous ventilation time and time to extubation were observed in the three groups. No significant differences were detected between the three groups regarding hemodynamic variables. **Conclusion:** The three drugs were not significantly different in attenuating post-extubation reactions such as hoarseness, sore throat, and laryngospasm. However, lidocaine was more effective on cough incidence while dexamethasone had better efficacy in reducing cough severity. In addition, all three drugs could satisfy patients after 24 hours. ETT tolerance was more in the lidocaine group than the other two groups.

Key words: Dexamethasone, Post-Extubation Symptom, Lidocaine, Normal Saline, Tracheal Tube Cuff

INTRODUCTION

Using cuffed endotracheal tubes (ETT) is a standard for general anesthesia. However, tracheal tube cuff pressure would cause a range of complications in tracheal mucosa. The problems include loss of mucosal cilia, ulceration, hemorrhage, tracheal stenosis and tracheoesophageal fistula. More often, patients complain of symptoms like sore throat, hoarseness and dysphagia in the immediate post-extubation period.^[1] In fact, sore throat and hoarseness have been reported by up to 50% of patients in the first few hours after extubation.^[2]

Coughing induced by an ETT can complicate emergence from general anesthesia, thus resulting in potentially dangerous hyperdynamic responses in the postoperative period. Such responses include hypertension, tachycardia, dysrhythmia, increased intraocular pressure, increased intracranial pressure, wound dehiscence, and bronchospasm. It has been well documented that coughing and its sequelae can be harmful for patients.^[3,4] Many factors, such as cuff pressure, gastric tube insertion, type of surgery, gender, head and neck positions, ETT size, trauma to pharyngolaryngeal mucosa

caused by laryngoscopy and oral suctioning are known to contribute to these symptoms.^[5,6]

Intracuff pressure increases when nitrous oxide is used in general anesthesia and this pressure may cause postoperative sore throat.^[7] Nitrous oxide diffuses inside an air filled cuff faster than nitrogen can escape from it, this leads to increase in both volume and pressure inside an air filled cuff.¹ Filling an ETT cuff with a liquid instead of air can prevent rising pressure inside the cuff.^[8,9]

Intravenous (IV) lidocaine is frequently used during anesthesia just before intubation and in the presence of ETT to suppress coughing or as an antiarrhythmic agent.^[10] On the other hand, dexamethasone is a potent corticosteroid with analgesic, anti-inflammatory, and antiemetic properties. Preoperative IV dexamethasone has been reported to reduce the incidence of postoperative pain and swelling following oral surgeries.^[11,12]

An effective method to reduce reactions to emergence from anesthesia may attenuate postoperative morbidity and improve patient outcome after

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surgery.^[3] Therefore, this study compared three methods of filling tracheal tube cuff with normal saline, lidocaine, and dexamethasone to evaluate the efficacy of dexamethasone on post-extubation reactions.

METHODS

The current double-blind clinical trial compared the incidence of postoperative sore throat, cough, hoarseness and laryngospasm after general anesthesia when intracuff dexamethasone, lidocaine and normal saline were used.

The institutional ethics committee approved this study (No. 1026; IRCT number: 201105095536N3) and written informed consents were obtained from all participants. A total number of 180 ASA (American Society of Anesthesiologists) I and II men, aged 20 to 50 years, scheduled for elective inguinal surgery in Imam Reza Hospital during 2008-2010, were recruited for the study. The exclusion criteria were body weight 20% more than the ideal body weight, impaired kidney or liver functions, a history of bronchial asthma and chronic obstructive pulmonary disease, a history of smoking, respiratory tract infection during the past 6 weeks, hypertension, taking angiotensin converting enzyme inhibitors, operation time of less than 1 or more than 2 hours, hypersensitivity to local anesthetics, using corticosteroids and analgesics before surgery, factors predictive of difficult intubation (number of tracheal intubation attempts), and the need for a nasogastric tube.^[4,6]

Depending on the kind of drug used to fill the ETT cuff, 60 patients were assigned to each group using the sealed envelope method. The same investigator filled the ETT cuffs, but did not participate in any other parts of the study (i.e. anesthesia, intubation, and extubation). In previous studies, the ETT cuffs were prefilled with lidocaine for 90 minutes prior to intubation to saturate the cuff membrane.^[13] This procedure might be due to the thin polyvinyl chloride membrane constituting the tube cuff which allows simple diffusion of lidocaine. In addition, the diffusion coefficient and the material thickness can be assumed to be standard across a specific range of endotracheal tubes. The limiting factors would thus be lidocaine concentration and time. In vitro studies examining this diffusion process have reported an increased transfer of lidocaine after 60 minutes using the 4% formulation.^[14] In another study, prefilling of the tube cuff with lidocaine for a fixed duration before the test period resulted in a

slightly increased diffusion across the cuff.^[4] Hence, we felt that prefilling the cuffs was impractical on a busy operating schedule because of the unpredictability of anesthesia induction time for each patient.

Therefore, cuffs in the first to third groups were filled with normal saline, dexamethasone, and 2% lidocaine, respectively. The trachea was intubated with a Soft Seal® cuffed sterile polyvinyl chloride ETT with a standard high volume-low pressure (HVLV) cuff (Supa Medical Devices, Tehran, Iran). After evaluating patient's airway, suitable tracheal tube size was calculated as $(age + 16)/4$. The tracheal tube cuff was injected with fluid at a peak airway pressure of 20 cm H₂O until no leakage could be heard. All patients were monitored with standard monitoring tools including noninvasive blood pressure, electrocardiogram, and pulse oximetry. General anesthesia was induced with 3µg/kg IV fentanyl and (1%) 2-3 mg/kg propofol. Tracheal intubation was performed 2-3 minutes after anesthesia while neuromuscular blockade with 0.5 mg/kg IV atracurium was used to facilitate the procedure. Anesthesia was maintained with 5 mg/kg/h propofol, O₂ 50%, and N₂O 50%.

In order to give the drugs sufficient time to diffuse after intubation, patients whose surgery took less than one hour were excluded. During surgery, cuff pressure was kept at 20 cm H₂O through connection to a water column.

The extubation protocol was the same in all groups. Therefore, when all extubation criteria, i.e. full reversal of neuromuscular block, spontaneous ventilation, ability to follow verbal commands, eye opening or handgrip, were met, tracheal extubation was performed immediately after suctioning at the discretion of the anesthetist in charge of the patient. Time to extubation (time from the beginning until the end of extubation) and spontaneous ventilation time (time between beginning spontaneous breathing and extubation) were recorded.

An independent, blinded observer (an anesthesiologist uninvolved with the case) assessed the patient during emergence and 24 hours after surgery for hemodynamic indices, including heart rate and blood pressure, and incidence of post-extubation sore throat, cough, laryngospasm and hoarseness. A combination of the results from the two different moments was used. Sore throat was graded on a four-point scale on which 0-3 corresponded none, mild (scratchy throat), moderate

(similar to that noted in cold), and severe (more severe than in cold) sore throat. Hoarseness was similarly graded on a four-point scale on which 0-3 represented none, noted by the patient, obvious to the observer, and aphonia, respectively. Laryngospasm was also graded as 0 (none), 1 (mild), 2 (moderate), and 3 (severe).

Statistical analyses were performed on a computer using SPSS¹⁸. Quantitative variables were compared using one way analysis of variance (ANOVA) and Tukey's post hoc test whenever appropriate. The Kruskal-Wallis test was used for qualitative (ranking) variables. Data was presented as mean \pm SD or number (%) and p values $<$ 0.05 were considered as statistically significant.

RESULTS

A total number of 180 men were recruited to the study. There were no statistically significant differences among the three groups regarding surgical, anesthetic, and baseline characteristics (Table 1). No problems with tracheal intubation or cuff inflation occurred. No significant differences were observed between the three groups in frequency of post-extubation sore throat ($p = 0.085$), hoarseness ($p = 0.191$), or laryngospasm ($p = 0.998$). The effects of dexamethasone in controlling symptoms such as sore throat, hoarseness, and laryngospasm after surgery are thus the same as the other two drugs.

However, the three groups were significantly different in terms of cough ($p = 0.02$). In other words, while lidocaine was more effective on post-extubation incidence of cough, dexamethasone affected post-extubation cough severity more than the other 2 drugs (Table 2). Moreover, there were prolongations of spontaneous

ventilation time and time to extubation (increase in endotracheal tolerance) in the lidocaine group compared to dexamethasone and normal saline groups, respectively (Table 1).

However, no significant differences were recorded in arterial blood pressure and heart rate between the groups (Table 2). There was no significant difference between the three groups regarding patient satisfaction after 24 hours (Table 3).

Discussion

Common measures to prevent post-extubation reactions include using ETTs with low intracuff pressure, and smaller-sized or steroid coated ETTs, applying topical lidocaine, and inhalation of steroids.^[5]

In this study, dexamethasone was injected into the tracheal tube cuff. In order to eliminate the confounding factors of age and sex observed in previous studies,^[15] all our participants were men, underwent a similar procedure (i.e. hernia), and were in the same age range.

Our results showed no significant differences between the three groups regarding the frequency of post-extubation sore throat, hoarseness, and laryngospasm (Table 2). It can thus be concluded that dexamethasone and the two other drugs similarly affect sore throat, hoarseness, and laryngospasm. On the other hand, while lidocaine's preventive effect on cough incidence was more than the other two drugs, dexamethasone seemed to better prevent cough severity (Table 2). Therefore, it is not surprising that patient satisfaction after 24 hours was not significantly different between the three groups (Table 3).

Table 1. Surgical and anesthetic characteristics of patients in the three groups

	Dexamethasone	Lidocaine	Normal Saline	p
Age (years)	40.96 \pm 11.25	37.35 \pm 11.28	40.77 \pm 11.6	0.142
Weight (kg)	78.69 \pm 4.11	80.90 \pm 5.92	79.27 \pm 5.36	0.087
Duration of intubation (sec)	12 \pm 3	10 \pm 6	11 \pm 7	0.10
Duration of surgery (min)	65 \pm 8	67 \pm 5	66 \pm 7	0.121
Time to extubation (min)	19 \pm 4 [#]	21 \pm 6 ⁺	11 \pm 2 [#]	0.039 [*] 0.042 [#] 0.61 ⁺
Spontaneous ventilation time (min)	11 \pm 5 [#]	14 \pm 3 ⁺	7 \pm 4 [#]	0.034 [*] 0.045 [#] 0.067 ⁺

All values are expressed as mean \pm SD.

^{*} Comparison between lidocaine and normal saline

[#] Comparison between dexamethasone and normal saline

⁺ Comparison between dexamethasone and lidocaine

Table 2. Comparison of post-extubation variables and severity of cough between the three groups

	Lidocaine	Dexamethasone	Normal saline	p
SAP (mmHg)*	134 ± 10	140 ± 14	146 ± 57	0.073
DAP (mmHg)*	70 ± 9	75 ± 6	84 ± 11	0.061
HR (bpm)*	80 ± 13	92 ± 21	93 ± 10	0.086
Cough*	0.12 ± 0.323	0.29 ± 0.457	0.34 ± 0.478	0.024
Sore throat*	0.8 ± 0.269	0.19 ± 0.398	0.23 ± 0.426	0.085
Hoarseness*	0.02 ± 0.139	0.08 ± 0.269	0.11 ± 0.312	0.191
Laryngospasm*	0.02 ± 0.139	0.02 ± 0.139	0.02 ± 0.134	0.998
Mild Cough**	6 (50%)	19 (65.512%)	16 (47.051%)	
Moderate Cough**	4 (33.333%)	10 (34.481%)	10 (29.413%)	0.034
Severe Cough**	2 (16.666%)	0	8 (23.524%)	

* One-way ANOVA; ** Kruskal-Wallis test

Severity of cough: Mild (1-2); Moderate (3-4); and Severe (5 or greater).

SAP: Systolic arterial blood pressure; DAP: Diastolic arterial blood pressure; HR: Heart rate

Values are expressed as mean ± SD or number (%).

In agreement with our results, Park et al. showed that prophylactic use of 0.2 mg/kg of dexamethasone significantly decreased the incidence and severity of sore throat and hoarseness 1 and 24 hours after tracheal extubation of a double-lumen endobronchial tube.^[16] Similarly, Sumathi et al. used another type of corticosteroids, such as betamethasone gel, to reduce post-extubation reactions. They showed that widespread application of betamethasone gel on the tracheal tube decreased the incidence and severity of postoperative sore throat, cough, and hoarseness of voice.^[17]

Unlike Sumathi et al.,^[17] Stride concluded that water-soluble 1% hydrocortisone cream was ineffective for reducing the incidence of postoperative sore throat.^[18] The difference in the findings of these 2 studies might have resulted from the length of the ETT lubricated with steroid gel. While Stride lubricated the ETT only to the 5-cm mark, Sumathi et al. lubricated the tube to the 15-cm mark. Thus, the more widespread application of steroid gel to the tube caused more gel to come in contact with the posterior pharyngeal wall, vocal cords, and trachea. However, Stride confined gel contact only to the tip and cuff of the tracheal tube. Intracuff dexamethasone delivers the drug in smaller doses and not in direct contact with the patient's air-

way compared with widespread lubrication of the tube with betamethasone which may increase the drug dose in contact with the mucosa of the oropharynx, larynx, and trachea, resulting in higher systemic absorption and a possible aggravation of local subtle infection, especially in pregnant patients.

Moreover, although Sumathi et al. did not perform intraoperative cuff pressure monitoring, we constantly monitored cuff pressure throughout the study.

The potential mechanism of intracuff dexamethasone is presumably based on its anti-inflammatory activity, which includes inhibition of leukocyte migration, maintenance of cell membrane integrity, attenuation of lysosome release, and reduction of fibroblast proliferation.^[16]

In another study, Singh et al. reported that use of saline or 2% lidocaine as a liquid media for filling the ETT cuff reduced postoperative sore throat and thereby tracheal morbidity.¹ Likewise, Wetzel et al. injected 4% lidocaine into the ETT cuff to reduce post-extubation reactions.^[3] Fagan et al. suggested that inflating the ETT cuff with lidocaine rather than air can reduce the incidence of post-extubation cough.^[4]

Table 3. Comparison of patient satisfaction after 24 hours between the three groups according Kruskal-Wallis test (p = 0.062)

	Patient satisfaction		
	Low	Medium	High
Lidocaine	15 (25%)	15 (25%)	30 (50%)
Dexamethasone	15 (25%)	17 (28.3%)	28 (46.6%)
Normal saline	17 (28.3%)	17 (28.3%)	26 (43.3%)

Values are shown as number of patients (%).

A systematic review included more than 1200 patients from 15 randomized high quality studies which evaluated the effectiveness of intracuff lidocaine to prevent post-extubation sore throat. Overall, 672 patients received topical or systemic lidocaine therapy and 560 patients were allocated to the control group. The results indicated both the topical and systemic lidocaine therapy to significantly reduce the risk of postoperative sore throat.^[19]

In all of these studies, the tracheal tube cuff acted as a reservoir of lidocaine and released the drug across the cuff membrane which numbed the tracheal mucosa. However, lidocaine release from the cuff membrane depends on time, dose, and pH. Alkalinized lidocaine is thus used for quicker and more efficient diffusion of lidocaine through the cuff membrane.^[4, 20-22]

In this study, lidocaine had more preventive effect on cough incidence due to the fact that it suppressed both the mechanical- and chemical-induced airway reflexes, including the cough reflex.^[23] Dexamethasone had more preventive effect on cough severity since it has been used as a mast cell stabilizer. It has been reported that dexamethasone enhances the activation of neutral endopeptidase which reverses the increased airway reactivity of airway epithelial cells. Furthermore, corticosteroids have been suggested to increase beta adrenergic receptors on lung cells.^[24]

ETT tolerance, associated with less cough (Table 2) and prolongation of spontaneous ventilation time and time to extubation (Table 1), was higher in the lidocaine group than dexamethasone and normal saline groups. In other words, improved ETT tolerance allowed for earlier reduction of anesthesia and spontaneous ventilation at the end of surgery. However, differences in recovery room stay were not observed in our study. Such results have presumably been caused by local effects of lidocaine rather than its systemic effects since high levels of plasma lidocaine ($> 3 \mu\text{g/mL}$) at intubation time have been reported to be obtained after IV administration of 2 mg/kg of the drug.^[25]

To conclude, using dexamethasone for filling the ETT cuff to reduce post-extubation reactions was as effective as lidocaine, but more effective than normal saline. Therefore, the drug is recommended to be considered in clinical practice to improve a patient's tolerance to anesthesia and intensive care especially in the case of cardiovascular disease, intracranial and intraocular hyperpressure, or pulmonary hyperreactivity.

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