Intracuff buffered lidocaine versus saline or air – A comparative study for smooth extubation in patients with hyperactive airways undergoing eye surgery

Jaichandran VV, DA, ***Bhanulakshmi IM,*** DA, ***Jagadeesh V,*** MD
Department of Anaesthesiology, Sankara Nethralaya, Vision Research Foundation, Chennai, Tamil Nadu, India.
Thennarasu M, M.Sc Statistics, Department of Biostatistics, Sankara Nethralaya, Vision Research Foundation, Chennai, Tamil Nadu, India.

Correspondence to: Dr VV Jaichandran, e-mail: jaichand1971@yahoo.com

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ABSTRACT
Background: Increased cough and restlessness during emergence from general anaesthesia in patients undergoing ophthalmologic surgical procedures might result in increased intraocular pressure, ruptured sutures and suprachoroidal haemorrhage, which can be detrimental to the outcome of surgery. In hyperactive airway patients, as the cough receptors are in the hypersensitised stage, the patients tend to cough more frequently and violently during extubation. Hence, in such patients, we sought to determine the benefits of filling the endotracheal tube cuff with either buffered lidocaine, saline or air, so as to prevent endotracheal tube-induced coughing during emergence from general anaesthesia.

Methods: Seventy five patients either with a history of chronic smoking or recently treated upper respiratory tract infections were randomly assigned into three groups ($n = 25$), based on the type of endotracheal tube cuff inflation, as follows: Group A (air), Group B (6 ml normal saline) and Group C (6 ml 2% lidocaine + 0.5 ml 7.5% sodium bicarbonate). A second, blinded anaesthetist, graded the extubation as: Grade 0 (no cough), Grade 1 (cough < 15s) and Grade 2 (cough > 15s).

Results: Extubation was smooth in Group C compared with Groups B and A ($p < 0.0001$). Further, the incidence of sore throat was found to be lower in both liquid groups, B and C, compared with Group A at 1 h ($p < 0.0001$) and 24 h ($p < 0.01$) postoperatively.

Conclusions: Injecting buffered lidocaine into the endotracheal tube cuff, produces smooth extubation even in patients with hyperactive airways as the cough receptors in the tracheal mucosa gets blocked by the increased diffusion of uncharged base form of the drug across the hydrophobic polyvinyl chloride wall of the cuff.

Introduction

Emergence from general anaesthesia is often complicated by endotracheal tube (ETT) induced coughing.[1] In hyperactive airway patients, like chronic smokers and those with recently treated upper respiratory tract infections (URTIs), the receptors meant for cough reflex, the rapidly adapting stretch receptors (RARs), are in a hypersensitised stage.[2–8] Hence these patients tend to cough more frequently and violently during extubation. Restlessness and coughing can produce adverse effects like hypertension, tachycardia or tacharrhythmias, myocardial ischaemia, bronchospasm, and increased bleeding at the surgical site.[1,9,10] Apart from this, it can also have an adverse impact on the outcome of ophthalmological procedures, like penetrating keratoplasty, open globe repair, trabeculectomy, etc, owing to a rise in intraocular pressure, rupture of sutures and suprachoroidal haemorrhage.[10–14] It is of utmost importance that patients undergoing eye surgery emerge smoothly from general anaesthesia.[14]

On review of the literature, in most of the retrospective studies the incidence of suprachoroidal haemorrhage was found to be higher in patients undergoing eye surgery under general anaesthesia rather than under local anaesthesia.[12–14]

The cough receptors in the tracheal mucosa can be blocked topically by filling the ETT cuff with buffered lidocaine, as this helps in the diffusion of the uncharged base form of the drug across the hydrophobic polyvinyl chloride (PVC) wall of the ETT cuff.[1,10] From our previous *in vitro* study,[15] using high performance liquid chromatography, we found that by filling the ETT cuff with a mixture of 6 ml 2% lidocaine HCl + 0.5 ml $NaHCO_3$, the minimum concentration of lidocaine ($Cm = 155$ μg/ml) that is required for blocking the cough receptors was obtained at around 90 min.[16] With this background knowledge, we sought to determine the benefits of filling the ETT cuff with buffered lidocaine, saline or air to prevent ETT-induced coughing during extubation, in patients with hyperactive airways undergoing eye surgery under general anaesthesia.

Methods

After obtaining institutional ethics committee approval and the patients' written informed consent, 75 ASA grade I or II patients, aged 18–70 years, undergoing any ophthalmic surgery with a minimum duration of 90 min were enrolled for the study. We included patients either with a history of chronic smoking (> 10 cigarettes/day) for two years or more or those with recently treated (< 2 weeks interval) URTI to study the effect on hyperactive airways. Patients who were not intubated in the first attempt, patients on ACE inhibitors (having increased cough reflex sensitivity) and those in whom C_3F_8/SF_6 gases were used for settling the detached retina (use of N_2O has to be discontinued) were excluded from the study. The following routine anaesthetic protocol was followed in all the patients: glycopyrrolate 0.005 mg/kg IM and pentazocine 0.5 mg/kg IM were used for premedication. Routine monitoring included ECG, non-invasive arterial blood pressure (NIBP), pulse oximetry and capnography. Induction was achieved with propofol 1.5 mg/kg IV and intubation facilitated with vecuronium 0.1 mg/kg IV. Tracheal intubation was done with a high-volume, low-pressure ETT tube (Portex Ltd, UK). The sizes of the ETTs used were the following: for males 8.5 mm or 8.0 mm ID and for females 7.5 mm or 7.0 mm ID. The ETT cuff was lubricated with a water-soluble gel (K–Y jelly, Johnson and Johnson).

Intubated patients were subsequently randomly divided into three groups based on the ETT cuff filling as:
Group A: Air
Group B: 6 ml normal saline
Group C: 6 ml 2% lidocaine HCl + 0.5 ml 7.5% sodium bicarbonate

In all the patients the ETT cuff was filled depending upon the minimal occlusion volume (volume at which no palpable leak was felt over the trachea) of each patient and care was taken to ensure that the starting cuff pressure was approximately 25 cmH_2O, measured using a high volume, low-pressure cuff manometer (Portex, UK).

Anaesthesia was maintained with N_2O/O_2 (70/30%) and 0.6% isoflurane. Further neuromuscular block was maintained with intermittent boluses of vecuronium (one-quarter of the intubating dose at half-hourly intervals) and lungs were ventilated with an Ohmeda ventilator attached with closed circuit, to maintain normocarbia. After surgery isoflurane was discontinued, the circuit was flushed with O_2 to remove residual inhalational agent, and residual neuromuscular block was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). Mechanical ventilation was maintained until swallowing or spontaneous ventilation resumed, and then assisted manual ventilation was done. Final ETT cuff pressure was recorded before extubation.

The patient was extubated when the following criteria were met: (1) spontaneous ventilation; (2) ability to follow verbal commands (eye opening or hand grip) and (3) ability to demonstrate purposeful movements. Just before extubation a second anaesthetist blinded to the study group was called in to grade the extubation based on the occurrence of coughing following extubation as: Grade 0 – No cough; Grade 1 – Cough lasting for < 15 sec and Grade 2 – Cough lasting for > 15 sec. The incidence of sore throat at 1 h and 24 h postoperatively was noted by the second blinded anaesthetist. The degree of sore throat was assessed as: Score 0 – No pain; Score 1 – Tolerable (mild –moderate) and Score 2 – Intolerable pain (severe).
The $p < 0.05$, obtained by using Fischer's exact test for two proportions, was considered statistically significant. A pilot study of 30 patients, 10 in each group, was initially done. Based on the incidence of patients coughing > 15 sec (Group A 60% and Group C 12%), sample size (n = 23) was calculated with α equal to 0.05, and the power of the study was 90%.

Results
Demographic data of the three groups of patients are shown in Table I. There were no statistically significant differences in age, weight, gender and total surgical duration among the groups.

The final ETT cuff pressure measured in Group A was significantly higher compared with that in Groups B and C, $p < 0.0001$. There was no statistical significant increase in final ETT cuff pressure compared with initial cuff pressure in both the liquid groups, B and C (see Table II).

Sixty-eight per cent of patients in Group C were extubated smoothly, whereas only 16% and 20% of patients in Group A and B respectively had smooth extubation, $p < 0.0001$ (see Figure 1). One patient in Group A had laryngospasm during extubation, which was managed by ventilating with O_2 using the bag and mask technique.

Discussion
During anaesthesia with N_2O the cuff pressure increases with time as N_2O diffuses into it more rapidly than it diffuses out, because of the partial pressure gradient across the PVC membrane.[10,17–19] When the cuff pressure exceeds the capillary perfusion pressure (30–40 mmHg) tracheal mucosal erosion occurs, resulting in sore throat postoperatively,[18–21] as evidenced in our study. By replacing air with liquid (saline/buffered lidocaine), cuff hyperinflation problems can be avoided.[10,17–19]

Rapidly adapting stretch receptors in the tracheal mucosa are believed to be the irritant receptors meant for cough.[9] These receptors are highly sensitive to mechanical stimuli like touch, displacement and stretch.[22–24] Tracheal intubation with ETT, cuff inflation and the resulting hyperinflation in turn stimulate these receptors, thus producing cough in normal patients during extubation[23,25] (ETT-induced cough). In chronic smokers and those with recently treated URTI the threshold stimulation for cough receptors is reduced.[2–6]

Long-term smoking causes neutrophilic infiltrates in vulnerable smokers that sensitise the cough-sensitive nerves by the release of sensory neuropeptides and direct stimulation of the nerves/receptors.[26] Empey et al report cough threshold values

Table I: Demographic data

	Groups		
	A	B	C
	(n = 25)	(n = 25)	(n = 25)
Age (years)	30.12 ± 11.96	34.96 ± 15.84	31.52 ± 12.38
Sex (M/F)	20/5	21/4	20/5
Body weight (kg)	55.80 ± 12.32	54.92 ± 10.36	58.24 ± 9.78
Number of smokers	16	15	16
Treated URTIs	9	10	9
Duration of surgery (min)	137.80 ± 40.88	140.40 ± 36.86	143.80 ± 38.17

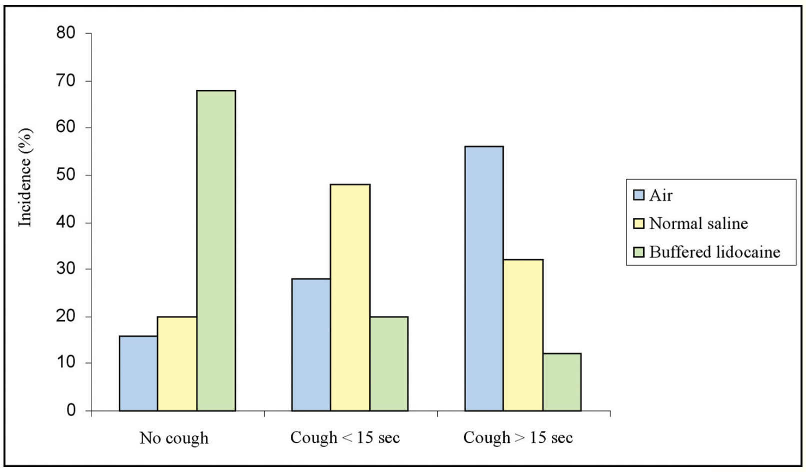
Values are expressed in Mean ± SD. URTIs: Upper respiratory tract infection

Table II: ETT cuff pressures measured at the start and at the end of the surgery

Parameter	A	B	C
Initial cuff pressure (cm H_2O)	24.92 ± 2.89	22.20 ± 2.36	22.52 ± 2.42
Final cuff pressure (cm H_2O)	56.68 ± 10.59*	23.88 ± 2.36†	23.64 ± 2.67†

Results are expressed in Mean ± SD
*$p < 0.0001$, †$p > 0.05$. Final ETT cuff pressure compared with initial cuff pressure.

Figure 1: Incidence of patients with smooth extubation: cough lasting less than 15 sec and more than 15 sec



The incidence of sore throat was significantly higher in Group A than in Groups B and C, both at 1 h, $p < 0.0001$, and 24 h, $p < 0.01$, post operatively (see Figures 2 and 3).

Figure 2: Incidence of patients with sore throat at 1 h postoperative time interval

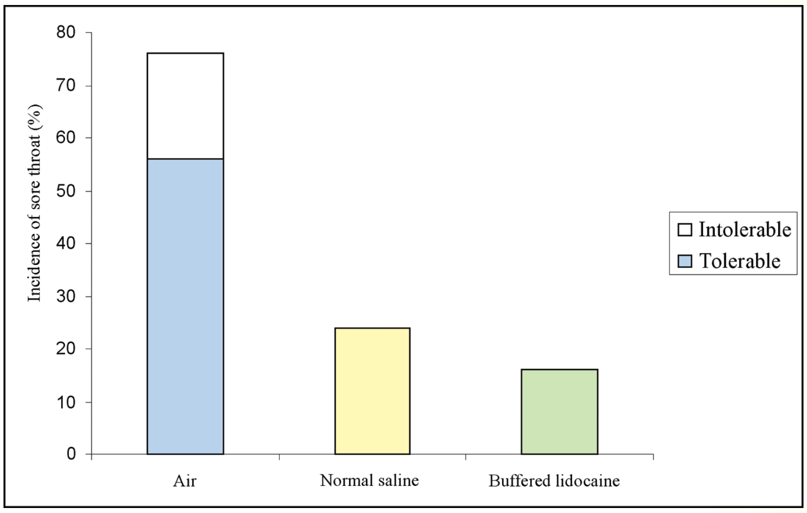
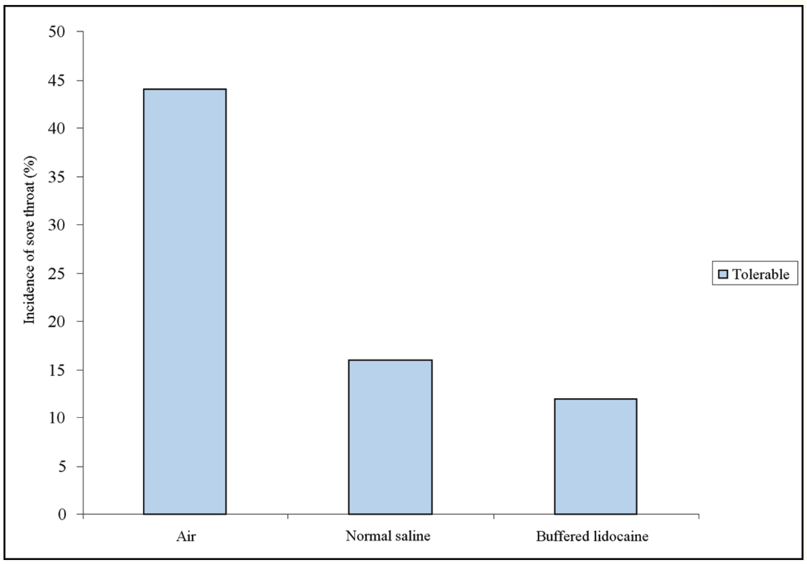


Figure 3: Incidence of patients with sore throat at 24 h postoperative time interval



to be significantly low for up to two weeks following URTIs.[4] Hence smokers tend to cough more frequently and violently during emergence from general anaesthesia. Stimulation of these receptors also results in the release of substance P (which causes mucosal vasodilatation, plasma exudation and airway mucus secretion), calcitonin gene-related peptide (causes mucosal vasodilatation) and neurokinin A (causes bronchoconstriction).

Activation of RARs is believed to constrict airways. However this view does not have a substantial basis and has been challenged.[22] The sample size used in the present study may be too small to detect a significant difference in the incidence of laryngospasm between the groups during extubation – a rather uncommon finding.

Preventing ETT-induced cough is of utmost importance in patients undergoing eye surgery. Cough can increase the intraocular pressure up to 50 mmHg.[27] The Valsalva effect produced by coughing can lead to vessel wall rupture due to a sudden increase in venous pressure, resulting in suprachoroidal haemorrhage (SCH),[28] a serious complication following eye surgery. Cases of delayed non-expulsive type of SCH have been reported after trabeculectomy following straining and bucking at the time of extubation.[13]

Intravenous and prior topical administration of lidocaine has been used to help reduce cough during emergence from general anaesthesia. Intravenous lidocaine (IVL) is known to suppress cough through its central nervous system depressant effect (cough centre in the medulla)[29] and hence it requires a minimal serum concentration (> 3 μg/ml) to be effective.[30] IVL produces delayed emergence from anaesthesia.[31] Moreover, the efficacy of IVL in suppressing cough is of short duration (5–20 min).[30]

Topical administration of lidocaine is known to produce its irritant effect long before its cough suppressant effect appears.[1,9] Other disadvantages encountered with this technique are that it requires a specially designed instrument for its application and the tracheal mucosa in direct contact with the ETT cuff wall is effectively shielded from exposure to lidocaine applied by this technique.[31]

Injecting lidocaine alone into the ETT cuff causes a low diffusion rate across the cuff (1% released during a 6 h period).[19,32] Higher doses of lidocaine (200–500 mg) are required to produce a clinical effect. Hence this had no advantages over saline, and could be dangerous if the cuff ruptures.[19,32] By filling the ETT cuff with buffered lidocaine, diffusion of the uncharged base form of the drug occurred across the hydrophobic PVC walls of the ETT cuff.[1,10,19] 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.[29] Thus the tracheal mucosa in direct contact with the ETT cuff wall can be anaesthetised locally with a longer than expected effect of lidocaine and with intact supraglottic reflexes, preventing aspiration in these patients.[25,29]

Buffering not only helped in increasing the diffusion of the drug in our study but also allowed us to use lower doses of lidocaine (without exceeding the toxic limits). From our previous *in vitro* study,[15] using high performance liquid chromatography, we found that by filling the ETT cuff with a mixture of 6 ml 2% lidocaine HCl + 0.5 ml $NaHCO_3$ the minimum concentration of lidocaine (Cm = 155 μg/ml) that is required for blocking the cough receptors[16] was obtained at the end of 90 min across the cuff walls. Hence in this *in vivo* study we used the above lidocaine buffered mixture for filling the ETT cuff in patients undergoing surgery with a minimum duration of 90 min.

This technique can also be used for patients requiring postoperative ventilatory support, as previous studies have documented that ETT tolerance is improved significantly by filling the ETT cuff with buffered lidocaine.[19,32] They might require lesser doses of narcotics for tube tolerance. Tracheostomised patients who have to keep the tube in for a long time and whose discomfort seems to arise mainly from the inflated cuff could benefit from use of this technique, as diffusion was found to occur across the tracheostomy tube cuff also.[33]

The limitations to our study were the inability to include children, and surgical procedures lasting less than 90 min duration, since the minimum concentration of lidocaine that is required for activation of the cough receptors was obtained in our *in vitro* study at around a 90 min interval.

Conclusions

Injecting buffered lidocaine into the ETT cuff not only reduces the incidence of sore throat but also enables improved ETT tolerance and helps in producing smooth extubation in patients with hyperactive airways. **SAJAA**

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