



## COMPARISON OF INTRACUFF LIGNOCAINE AND AIR AND ITS RELATED COMPLICATIONS

**Dr. Gaurav Acharya\*, Dr Rashpal Singh Gill, Dr Prem Chandra Arya and Dr Kishore Kumar Arora**

Department of Anesthesiology, Mgm Medical College Indore. (M.P.) India.

**\*Correspondence for Author: Dr. Gaurav Acharya\***

Department of Anesthesiology, Mgm Medical College Indore. (M.P.) India.

Article Received on 13/02/2016

Article Revised on 04/03/2016

Article Accepted on 24/03/2016

### ABSTRACT

**Background:** The study was conducted to study the benefits of using alkalized lidocaine 40 mg for filling the cuff of an endotracheal tube (ETT) to prevent post-intubation sore throat. **Methods:** The current study was conducted to study the diffusion of alkalized lidocaine solution through the low-pressure, high-volume cuff of an ETT. A comparative study was conducted with 50 patients in each group, with lignocaine group which received an alkalized lidocaine to fill ETT cuff and control groups who received air to fill ETT cuff. **Results:** Our study revealed that the incidence of sore throat was much lower in lignocaine group as compared to air group. The study also revealed that there was a considerable decrease in the hemodynamic response in lignocaine group as compared to air Group and there were no complications like endotracheal tube cuff rupture and alkalized lignocaine toxicity. **Conclusions:** Alkalized intracuff lignocaine helps in reducing post extubation sore throat and also has decreased hemodynamic response to extubation when compared to intracuff air which offers no advantage. In addition alkalized lignocaine intracuff maintains a stable cuff pressure during oxygen nitrous anaesthesia thus, preventing the damages that occur due to increased cuff pressure during general anaesthesia.

**KEYWORDS:** lidocaine intracuff extubation.

### INTRODUCTION

Postoperative sore throat is the most common complaint after endotracheal intubation and is seen in up to 90% of intubated patients.<sup>[1]</sup> Sometimes it is categorized under tracheal tube (ETT)-induced emergence phenomenon along with laryngeal oedema and ischaemia. To overcome such associated complications it has been advised to replace N<sub>2</sub>O with air and monitoring of N<sub>2</sub>O concentration to minimize the expansion of air in ETT cuff.<sup>[2,3]</sup> Sometime the cuff is deflated or is filled with saline.<sup>[4,5]</sup> Both in vivo and in vitro studies have been conducted on cuffs filled with lignocaine.<sup>[6-10]</sup> In the past high doses of lignocaine (200-500 mg) have been used but they are associated with complications if the cuff ruptures.<sup>[8]</sup> Sodium bicarbonate is added to increase the diffusion of lignocaine at low doses (40 mg) through the cuff thereby preventing complications like sore throat, hemodynamic changes, restlessness, dysphonia and hoarseness.<sup>[11,12]</sup> This comparative study was conducted to study the effect of low dose of alkalized lignocaine and air in the ETT cuff.

### METHODS

After obtaining institutional ethics committee approval and written informed consent from the patients adult patients scheduled for surgery (ASA I or II) were allotted into two groups. Patients with difficult airway i.e. Mallam Patti grade III/IV, patients with history suggestive of

Gastro esophageal reflux, patients with history of laryngeal or tracheal surgery and history of asthma, cardiovascular disease, smoking, recent respiratory infection, patients who need nasogastric tube intraoperatively and where surgery lasting less than 40 min were excluded from the study. Subjects were allocated into two groups, Group(A) where the endotracheal tube cuff was filled with alkalized lignocaine 2 ml (40 mg) made alkalized with 1.4% sodium bicarbonate 3 ml (the sodium bicarbonate 8.4% is available, which is diluted six times) and Group (B) where the endotracheal tube cuff was filled with intracuff air according to computer generated randomization sheet.

Standard monitors were attached which included ECG, NIBP, SPO<sub>2</sub>; ETCO<sub>2</sub>. Study subjects were premedicated with Inj Glycopyrrolate 0.005mg/kg body weight, Inj Midazolam 0.05mg/kg body weight, Inj Fentanyl 2 microgram/kg body weight. Baseline hemodynamic parameters were noted. Patients were preoxygenated with 100% oxygen for 3 min. Patients induced with Inj propofol 2mg/kg body weight, Inj atracurium 0.5mg/kg body weight to facilitate tracheal intubation.

Tube size of 7.5mm was used in females and 8.5mm in males. For group (A) cuff of the ETT was inflated with alkalized lignocaine [contains approximately 2 ml(40mg) of lignocaine and (3ml) 1.4% NaHCO<sub>3</sub>] and in

group (B) patient, endotracheal tube was inflated with air as inflating agent and the cuff pressure set at 20 cm of water with a Rusch endotest cuff inflator. For group (B) the amount of air required to attain the set cuff pressure that is 20 cm of water measured and the same amount of alkalized lignocaine injected to inflate the cuff.

Cuff pressure was recorded throughout, ensuring a starting pressure 20 cm H<sub>2</sub>O, using manometers set for pressure measurements in a cuff. Anaesthesia was maintained with Nitrous: Oxygen (35:65), Inj Atracurium 1/4<sup>th</sup> the intubating dose depending upon the etco<sub>2</sub> changes. Lungs mechanically ventilated with tidal volume of 8-10ml/kg body weight. Pulse oximeter, Non invasive blood pressure, ECG and ETCO<sub>2</sub> monitored.

At the end of surgery, Nitrous oxide was discontinued and 100% oxygen was given. Patient taken on mapleson D circuit reversed with Inj Glycopyrrolate 0.005 mg/kg body weight and Inj Neostigmine 0.05 mg/kg body weight. Cuff pressure measured just before deflating the cuff and recorded, Extubation was performed after checking for spontaneous ventilation, ability to follow verbal commands (eye opening, tongue protrusion).

Immediately after extubation patient assessed for sore throat, heart rate, blood pressure, at 1 hour & 24 hrs.. Sore throat recorded as either occurred or not occurred by another anaesthesiologist who is not present at the time of intubation.

#### Statistical analysis

Appropriate statistical analysis was done with help of SPSS version 21. Demographic data and hemodynamic data was analyzed by using Unpaired Student t test and chi square test. The incidence of sore throat compared using the Test of proportions. Sample size was calculated by considering incidence of sore throat as 38% with type B error rate as  $\alpha = 0.05$  and type II error rate of  $\beta = 0.02$  with a power of 80%, and using formulae.

$$N = \frac{2(2\alpha + 2\beta)2p(1-p)}{(P1 - P2)^2}$$

A sample of 100 patients was taken out of which 50 will be in group (a) and 50 in group (b).

**Table 1: demographic data**

GROUPS	AGE IN YEARS (MEAN±SD)	WEIGHT IN KGS (MEAN±SD)
Group A	37.26±9.84	57.10±8.24
Group B	34.32±9.36	56.02±9.22
'p' value	0.129	0.539
GROUPS	MALE	FEMALE
GROUP A	30	20
GROUP B	30	20
GROUPS	ASA I	ASA II
GROUP A	18	32
GROUP B	12	38

#### RESULTS

The mean age in group A was 37.26±9.84 years and in group B was 34.32±9.36 years. The mean weight in group A was 57.10±8.24 kg and in group B was 56.02±9.22 kg and was comparable, with insignificant 'p' value. The distribution of sex was similar in both the groups with 30 males and 20 females. Distribution of patients according to ASA grade I & II was 18 & 32 respectively in group A and 12 & 38 respectively in group B with non-significant p value. The mean duration of anaesthesia in the group A was 162.70±78.35 and in group B was 141.10±62.70 which was comparable with an insignificant 'p' value (0.131).

In group A the mean cuff pressure at the end of surgery was 19.96±0.727. In group B the mean cuff pressure at the end of surgery was 38.58±8.129. The groups were incomparable and had a significant 'p' value (<0.000) Seven patients (14%) had sore throat after 1 hour in alkalized lignocaine group as compared to 18 patients (36%) in intracuff air group.

At 24 hour the incidence of sore throat in alkalized lignocaine was 12% compared to 52% in intracuff air group. There was a significant statistical difference between the alkalized lignocaine group and intracuff air group. The 'p' value being 0.000 was highly significant.

The Pulse rate at 0min was 82.70±9.61 and 102.18±11.20 in group A and group B respectively and was comparable but statistically insignificant. Pulse rates at 30 minute, 60 minute, 90 minute and 120 minutes were 96.06±11.11, 95.02±8.83, 90.60±10.75 and 84.68±9.859 for group A and 82.06±9.34, 102.18±11.2, 101.86±11.25 and 95.02±10.65 respectively for group B which were statistically significant (p value < 0.05).

The mean arterial pressures at 0 min were comparable. The pressures were 105.76±102.72, 102.72±8.63, 99.38±8.27 and 97.009±7.045 at 30 minute, 60 minute, 90 minute and 120 minutes in group A. Similarly the pressures in group B were 114.88±9.68, 109.12±9.11, 104.98±7.52 and 102.06±6.25 respectively. These values were incomparable and highly significant statistically.

	Group a	Group b	'p' value
Age in years	37.26±9.84	34.32±9.36	0.129
Weight in kgs	57.10±8.24	56.02±9.22	0.539
Male	30	30	
Female	20	20	
Asa i	18	12	
Asa ii	32	38	
Duration in minutes	162.70±78.35	141.10±62.70	0.131

Table 2 comparison of cuff pressure

CUFF PRESSURE (START)	20.00±0.00	20.00±0.00	
CUFF PRESSURE (END)	19.96±0.727	38.58±8.129	<0.000

Table 3 Cough in 1 hour

GROUP	Yes	No	Total
Group A	7	43	50
Group B	18	32	50
Total	25	75	100

\*  $\chi^2 = 6.453$        $df = 1$   $p = 0.011$

Table 4 Cough in 24 hours

GROUP	Yes	No	Total
Group A	10	40	50
Group B	22	28	50
Total	32	68	100

\*  $\chi^2 = 18.382$   $df = 1$   $p = 0.000$

Table 5 Comparison of Pulse Rate(per minute)

GROUPS	0min	30min	60min	90min	120min
	MEAN±SD	MEAN±SD	MEAN±SD	MEAN±SD	MEAN±SD
Group A	82.70±9.61	96.06±11.11	95.02±8.83	90.60±10.75	84.68±9.859
Group B	102.18±11.20	82.06±9.34	102.18±11.2	101.86±11.25	95.02±10.65
'p' value	0.080	0.000	0.001	0.000	0.000

Table 6 Comparison of Mean Arterial Pressure(mm of Hg)

GROUPS	0min	30min	60min	90min	120min
	MEAN±SD	MEAN±SD	MEAN±SD	MEAN±SD	MEAN±SD
Group A	97.60±7.43	105.76±9.98	102.72±8.63	99.38±8.27	97.00±7.045
Group B	97.16±8.58	114.88±9.68	109.12±9.11	104.98±7.52	102±6.25
'p' value	0.785	0.000	0.000	0.0001	0.000

## DISCUSSION

Extubation of the trachea in a patient undergoing general anaesthesia is associated with its own problems and complications, which can be detrimental to the patient and unpleasant to the attendant anaesthesiologist. Sore throat during emergence in a lighter plane of anaesthesia can result in hypertension, tachycardia, and myocardial ischemia, raised intraocular and intracranial pressures. These features are particularly undesirable in patients undergoing neurosurgical or ophthalmic procedures or those who are at an increased risk of adverse cardiovascular events.<sup>[13-15]</sup>

Numerous methods of attenuating cough reflex during tracheal extubation have been advocated such as use of

narcotics, extubation in a deeper plane of anaesthesia, and use of IV alkalized lignocaine.

In one of the early studies, **Sconzo and colleagues**<sup>[16]</sup> demonstrated that air diffuses across the cuff of endotracheal tubes. This finding applied by **Waka Hirota**<sup>[8]</sup> showed that when endotracheal tube cuffs were inflated with alkalized lignocaine, concentrations of alkalized lignocaine in a water bath would reach 8 and 17  $\mu\text{gml}^{-1}$  after 30 and 60 minutes of cuff inflation respectively. Alkalized lignocaine concentration of 100 $\mu\text{M}$  is required to produce a 50% reduction in  $\text{Na}^+$ -channel activity. This data suggests that a minimum period of 2 hours would be required for attaining these concentrations.

The toxicity of local anesthetics must be considered regardless of the route of the administration. In this regard, our concerns were twofold, the risks of systemic absorption and the consequences of cuff damage with subsequent leakage of 2% lidocaine or saline into the bronchial tree. Although 40 mg/mL lidocaine (4%) was used, the mean volume used per endotracheal tube was  $6.1 \text{ mL} \pm 0.9 \text{ mL}$  (SD) ( $244 \text{ mg} \pm 36 \text{ mg}$ ). This is considerably less than the amount of lidocaine used in a study by Sutherland and colleagues,<sup>17</sup> in which a fixed dose of 370 mg of lidocaine was used in 21 adult patients to topically anaesthetize the airway for fiberoptic bronchoscopy and no incidence of toxic plasma concentrations of lidocaine was recorded.

Another study by **Efthimiou**<sup>[18]</sup> with 41 patients undergoing fiberoptic bronchoscopy, using average doses of 9.3 mg/kg of lidocaine, recorded only two patients in which plasma levels exceeded the toxic levels ( $5.0 \mu\text{g/mL}$ ) and no complications were observed. All tube cuffs were intact post extubation.

The basis of our study was that lignocaine inserted into the endotracheal cuff might cause anaesthesia of the trachea by diffusing across the polyvinyl chloride membrane of which the cuff is composed. Anaesthesia should be confined to the mucosa in contact with the cuff, thus overcoming the difficulties experienced by **Gonzalez and others**.<sup>[19]</sup> In addition, the protective cough reflexes above the tube cuff and of the vocal cords should remain intact.

Previously done studies by **Carl Fagan and colleagues** have compared the incidence of sore throat and hemodynamic changes between intracuff alkalized lignocaine, intracuff saline and intracuff air and concluded that incidence of sore throat is significantly lower in intracuff alkalized lignocaine group<sup>20</sup>. In one study done by **Soltani and colleagues**<sup>[21]</sup> compared the incidence of sore throat and sore throat after general anaesthesia in six different groups which included spraying of the distal end of ETT cuff with 10% alkalized lignocaine, spraying of 10% to laryngopharyngeal structures, application of 2% alkalized lignocaine jelly to cuff of the tube, intravenous alkalized lignocaine at the end of surgery, Intracuff alkalized lignocaine and application of normal saline to the cuff end of the tube. They concluded that IV lignocaine, intracuff alkalized lignocaine considerably decreases the incidence of sore throat post extubation.

Since alkalized lignocaine is most commonly and widely used as a lubricant and as an agent to decrease the emergence phenomena. We compared intracuff alkalized lignocaine which can be easily administered without any special equipment needed. We monitored the cuff pressure changes with air used as an inflating agent when air was applied against intracuff alkalized lignocaine, which was not done in some of the previous

studies. We also recorded the hemodynamic parameters in both the groups and studied the effect of the technique on the hemodynamic parameters.

There was no statistical difference between the 2 groups with regard to age, sex and weight. The mean duration of anaesthesia in the group A was  $162.70 \pm 78.35$  and in group B was  $141.10 \pm 62.70$  which were comparable and an insignificant 'p' value (0.131). Some of the previous studies stated that the average duration required for diffusion of alkalized lignocaine to attain desirable concentration was 120 min.<sup>[8]</sup> This criterion was meeting in our study as the average duration of anaesthesia was 150 minutes.

Our data confirmed the increased cuff pressure and cuff volume after air inflation with N<sub>2</sub>O and oxygen anaesthesia.<sup>[5,22]</sup> It has been reported that the over inflation occurring during general anaesthesia was attributable to an increase in temperature and most importantly, because of more rapid N<sub>2</sub>O diffusion into the cuff than out from the cuff.<sup>[21,22]</sup> This over inflation of the ETT cuff has been associated with damage to the pharyngeal mucosa and recurrent laryngeal nerve palsy<sup>1</sup> The lack of hyper pressure is probably one advantage of liquid filling of ETT cuffs.<sup>[23,24]</sup> In our study we monitored the endotracheal cuff pressure keeping the endotracheal cuff pressure at 20 cm H<sub>2</sub>O in both the groups after intubation. In Group A the mean cuff pressure at the end of surgery was  $19.96 \pm 0.727$  and showed no significant rise in cuff pressure. In Group B the mean cuff pressure at the end of surgery was  $38.58 \pm 8.129$  showed significant rise in cuff pressure. The groups were incomparable and had a significant 'p' value ( $<0.000$ ). Thus, confirming the data with previous studies.

The incidence of sore throat and sore throat on emergence from general anaesthesia in the presence of ETT has been estimated to range from 38% to 96%.<sup>[9,19]</sup> **Selvaraj and Dhanpal**<sup>[25]</sup> found the incidence of postoperative cough and hoarseness to be higher in the lidocaine jelly group than in the control group.<sup>[26]</sup> Klemola UM studied the effect of laryngeal spray with alkalized lignocaine and alkalized lignocaine jelly application on 95 patients. The incidence of sore throat when both the techniques used was 95%, when alkalized lignocaine jelly alone used was 85% and in the control group it was 62%. Thus, stating that the use of alkalized lignocaine jelly was associated with a high incidence of post extubation sore throat and hoarseness.

In our study the incidence of sore throat was recorded in four different intervals. It was recorded as having occurred or not. The severity or grade of sore throat was not recorded since categorization is very subjective. Seven patients (14%) had sore throat at 1 hour in alkalized lignocaine group as compared to 18 patients (36%) in intracuff air group. At 24 hour the incidence of sore throat in alkalized lignocaine was 14% much

higher than that noted at 1 hour in alkalized lignocaine group as compared to 52% in intracuff air group thus showing a considerable decrease in the incidence of sore throat. There was a significant statistical difference between the alkalized lignocaine group and intracuff air group. The `p` value being 0.003 (<0.001) is highly significant. These results were comparable to the previous studies done.

In the study done by **Estebe JP and others**<sup>[27]</sup> on 60 patient intracuff alkalized lignocaine was compared with intracuff saline and intracuff air. The results stated that there was a trend of reduced hypertension and tachycardia in the intracuff air group and alkalized lignocaine group.<sup>[28]</sup> In another study done by the same author were alkalized lignocaine was compared with gel lubricants concluded that there was no significant changes in the arterial blood pressure and heart rate.

**Lais Helena**<sup>[29]</sup> (2012) found that the dose [lidocaine 6.9±2.6 mL (138±52mg)] 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.

Hemodynamic parameters were measured immediately after extubation at 0 minute, 30 minute, 60 minute, 90 minutes and 120 minutes in both the groups. The mean pulse rates at 0 min were 82.70±9.61, 102.18±11.20 for alkalized lignocaine and intracuff air group. It was statistically insignificant with `p` value 0.000. Following extubation the maximum increase was noted immediately after extubation and at 30 minute then it gradually decreased. The comparisons between the two groups were significant and had significant `p` values.

The mean arterial pressures were also measured at the same intervals as the heart rate. The mean arterial pressures at 0 min were comparable. The peak values were obtained immediately after extubation and 30 minute thereafter. These values were incomparable and highly significant statistically. The pressures settled after 90 minute tending to fall back to baseline values. The statistical data was analyzed with unpaired student t test and test of proportions with `p` value less than 0.05 being significant, <0.01 being highly significant and <0.001 being very highly significant.

Our hemodynamic data was not comparable with the

earlier studies done by Carl Fagan and colleagues and Estebe JP others which stated that there was no statistical difference in the hemodynamic parameters in their study.<sup>[9,27]</sup>

These results varied as the sample size was much larger 100 patients in our study as compared to 63 in their study. The extubation criteria were also different in both the studies which could have had an impact on the hemodynamic parameters.

#### LIMITATIONS OF THIS STUDY

Measurement of plasma alkalized lignocaine levels was not done in our study. There was no practical way of assessing the amount of alkalized lignocaine that diffused across the cuff.

#### SUMMARY

The present study compares the effects of Intracuff Alkalized lignocaine with Intracuff Air for prevention of post operative sore throat.

The study included 100 ASA grade 1 and 2 patients between the age group of 18 to 50 years divided into two groups consisting of 50 patients each after randomization by a computer generated randomization table.

**Group A** – Intracuff alkalized lignocaine group.

**Group B** – Intracuff air group.

Air was used intracuff to inflate the cuff and keep the cuff pressure at 20 cm of H<sub>2</sub>O. Sore throat and hemodynamic parameters were recorded post extubation for a period by an anaesthesiologist who was not present at the time of intubation.

Our study revealed that the incidence of sore throat was much lower in group A as compared to group B. The study also revealed that there was a considerable decrease in the hemodynamic response in group A as compared to Group B and there were no complications like endotracheal tube cuff rupture and alkalized lignocaine toxicity.

#### CONCLUSION

Alkalized intracuff lignocaine helps in reducing post extubation sore throat and also has decreased hemodynamic response to extubation when compared to intracuff air which offers no advantage.

In addition alkalized lignocaine intracuff maintains a stable cuff pressure during oxygen nitrous anaesthesia thus, preventing the damages that occur due to increased cuff pressure during general anaesthesia.

#### REFERENCES

1. Lev R, Rosen P. Prophylactic lidocaine use preintubation: a review. *J Emerg Med.*, 1994; 4: 499±506.
2. Tu HN, Saidi N, Lieutaud T, Bensaid S, Menival V,

- Duvaldestin P. Nitrous oxide increases endotracheal cuff pressure and the incidence of tracheal lesions in anesthetized patients. *Anesth Analg*, 1999; 89: 187±90.
3. Karasawa F, Ohshima T, Takamatsu I, et al. The effect on intracuff pressure of various nitrous oxide concentrations used for inflating an endotracheal tube cuff. *Anesth Analg*, 2000; 91: 708-13.
  4. Karasawa F, Matsuoka N, Kodama M, Okuda T, Mori T, Kawatani Y. Repeated deflation of gas-barrier cuff to stabilize cuff pressure during nitrous oxide anesthesia. *Anesth Analg*, 2002; 95: 243-8.
  5. Bennett MH, Isert PR, Cumming RG. Postoperative sore throat and hoarseness following tracheal intubation using air or saline to inflate the cuff: a randomized controlled trial. *Anaesth Intensive Care*, 2000; 28: 408-13.
  6. Sconzo JM, Moscicki JC, Difazio CA. In vitro diffusion of lidocaine across endotracheal tube cuffs. *Reg Anesth*, 1990; 15: 37-40.
  7. Navarro RM, Baughman VL. Lidocaine in the endotracheal tube cuff reduces postoperative sore throat. *J Clin Anesth*, 1997; 9: 394-7.
  8. Hirota W, Kobayashi W, Igarashi K, et al. Lidocaine added to a tracheostomy tube cuff reduces tube discomfort. *Can J Anesth*, 2000; 47: 412-4
  9. Fagan C, Frizelle HP, Laffey J, Hannon V, Carey M. The effects of intracuff lidocaine on endotracheal-tube-induced emergence phenomena after general anesthesia. *Anesth Analg*, 2000; 91: 201±5.
  10. Altintas F, Bozkurt P, Kaya G, Akkan G. Lidocaine 10% in the endotracheal tube cuff: blood concentrations, haemodynamic and clinical effects. *Eur J Anaesthesiol*, 2000; 17: 436-42.
  11. Dollo G, Estebe JP, Le Corre P, Chevanne F, Ecoffey C, Le Verge R. Endotracheal tube cuffs filled with lidocaine as a drug delivery system: in vitro and in vivo investigations. *Eur J Pharm Sci.*, 2001; 13: 319-23.
  12. Estebe JP, Dollo G, Le Corre P, Le Naoures A, Le Verge R, Ecoffey C. Alkalinization of intracuff lidocaine improves endotracheal tube-induced emergence phenomena. *Anesth Analg*, 2002; 94: 227-30.
  13. Paulissian R, Salem MR, Joseph NJ, Braverman B, Cohen HC, Crystal GJ. Haemodynamic responses to endotracheal extubation after coronary artery bypass grafting. *Anesth Analg*, 1991; 73(1): 10-15.
  14. Slogoff S, Keats AS. Does perioperative myocardial ischemia lead to postoperative myocardial infarction? *Anesthesiology*, 1985; 62: 107-14.
  15. Fujji Y, Toyoka H, Tanaka H. Cardiovascular responses to tracheal extubation or LMA removal in normotensive and hypertensive patients. *Can J Anaesth*, 1997; 44: 1082-4.
  16. Sconzo JM, Moscicki JC, DiFazio CA. In vitro diffusion of lidocaine across endotracheal tube cuffs. *Reg Anesth*, 1990; 15: 37-40.
  17. Sutherland AD, Santamaria JD, Nana A. Patient comfort and plasma lignocaine concentrations during fiberoptic bronchoscopy. *Anaesth Intensive Care*, 1985; 13: 370-4.
  18. Efthimiou J, Higenbottam T, Holt D, Cochrane GM. Plasma concentrations of lignocaine during fiberoptic bronchoscopy. *Thorax*, 1982; 37: 68-71.
  19. Gonzalez RM, Bjerke RJ, Drobycki T, Wolf HS, James MG, Michael JJ. Prevention of endotracheal tube induced coughing during emergence from general anesthesia. *Anesth Analg*, 1994; 79: 792-5.
  20. Bidwai AV, Stanley TH. Blood pressure and pulse rate responses to extubation with and without prior topical tracheal anaesthesia. *Can Anaesth. Soc. J.*, 1978; 25(5): 416-8.
  21. Hasan Ali Soltani, Omid Aghadavoudi. The effect of different lidocaine application methods on postoperative cough and sore throat. *J Clin Anesth*, 2004; 14(1): 15-8.
  22. Dullenkopf A, Gerber AC, Wiess M. Nitrous oxide diffusion into tracheal tube cuffs: Comparison of five different tracheal tube cuffs. *Acta Anaesthesiol Scand*, 2004; 48: 1180-4.
  23. Combes X, Schauvliege F, Peyrouset O. Intracuff pressure and tracheal morbidity: Influence of filling with saline during nitrous oxide anesthesia. *Anesthesiology*, 2001; 95: 1120-4.
  24. Ahmad NL, Norsidah AM. Change in endotracheal tube cuff pressure during nitrous oxide anaesthesia: A comparison between air and distilled water cuff inflation. *Anaesth Intensive Care*, 2001; 29: 510-4.
  25. Klemola UM, Saarnivaara L, Yrjola H. Post-operative sore throat: Effect of lignocaine jelly and spray with endotracheal intubation. *Eur J Anaesthesiol*, 1988; 5(6): 391-9.
  26. Selvaraj T, Dhanpal R. Evaluation of the application of topical steroids on the endotracheal tube in decreasing postoperative sore throat. *J Anaesthesiol Clin Pharmacol*, 2002; 18: 167-70.
  27. Estebe JP, Marc Gentili, Corre PL, Dollo G, Le Naoures A, Chevanne F, Ecoffey C. Alkalinization of intracuff lidocaine: Efficacy and safety. *Anesth Analg*, 2005; 10: 1536-41.
  28. Estebe JP, Delahaye S, Corre PL, Le Naoures A, Chevanne F, Ecoffey C. Alkalinization of intracuff lidocaine and use of gel lubrication protect against tracheal tube induced emergence phenomena. *Br J Anaesth*, 2004; 92: 361-6.
  29. Lais Helena Camacho Navarro, Rodrigo Moreira E Lima, Andressa Simoes Aguiar, Jose Reinaldo Cerqueira Braz Jeffrey. The effect of intracuff alkalinized 2% lidocaine on emergence coughing, sore throat and hoarseness in smokers. *Rev Assoc Med Bras*, 2012; 58(2): 248-253.