A Comparative Study to Study the Difference in Effect between Intracuff Saline, Lidocaine and Alkalinized 2% Lidocaine on Emergence Cough, Sore Throat and Hoarseness

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ABSTRACT

Introduction: 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. The study was conducted to study the benefits by filling the cuff of an endotracheal tube (ETT) with alkalinized lidocaine to prevent postoperative sore throat, cough and hoarseness of voice. The aim of this study was to evaluate the effect of intracuff saline, intracuff lidocaine and intracuff alkalinized 2% lidocaine on emergence coughing, postoperative sore throat, and hoarseness of voice.

Material and Methods: We performed a randomized controlled study on 180 patients of ASA I-II status divided into 3 groups of 60 each. ETT cuff was filled with saline, plain lignocaine and alkalinized lignocaine respectively in each group. The degree of coughing, sore throat 1hr and 24 hrs and hoarness of voice after 24hrs were assessed postoperatively.

Results: Demographic data and duration of anaesthesia were comparable among study groups ($p > 0.05$). In Alkalinized lidocaine group, the incidence of emergence coughing was significantly lower presented in only 4 patients (7%) having Grade II and 8 patients (13%) having Grade I out of 60 patients, which was considerably lower in alkalinized lidocaine group with a P value 0.000(≤ 0.01) than saline and plain lignocaine.

Conclusion: Inflation of the ETT cuff with alkalinized 2% lidocaine was superior than ETT cuff filled with plain lignocaine and saline in decreasing the incidence of emergence coughing and preventing sore throat and hoarseness during the postoperative period.

Keywords: Endotracheal Tube, Intracuff (Lignocaine, Alkalinized lignocaine, Saline), Cough, Sore Throat, Hoarseness

INTRODUCTION

Tracheal intubation results in stretch stimuli in the trachea caused by the tube and its cuff. Intravenous[1] and topical[2] lidocaine has been in use for many years in blunting the emergence adverse phenomenon after general anesthesia.

It appears that only the hydrophobic neutral form of L-HCl was able to diffuse across a membrane, while for charged alkalinized L-HCl only a permeation phenomenon occurred. Following the Henderson-Hasselbach equation (i.e., the ratio between ionized and nonionized species being a function of both the pK_a of the substance and the pH of the dissolving medium) the addition of $NaHCO_3$ to alkalinized L-HCl alkalinizes the L-HCl solution. This provides the corresponding hydrophobic base and allows the diffusion of this uncharged form through the hydrophobic PVC wall of the cuff more readily than the alkalinized L-HCl and allows for the best release profile observed with the lidocaine base.[3]

Coughing induced by an endotracheal tube can complicate emergence from general anesthesia. Irritant or stretch stimuli in the trachea caused by the tube and its cuff are the presumed mechanisms. Rapidly acting receptors are found throughout the trachea and are primarily superficial.[4] They are thought to be the irritant receptors involved in the cough reflex.[5] These nociceptive stimuli can be blocked by topically applied anesthetics.[6]

Coughing during emergence can result in hypertension, tachycardia, increased intraocular and intracranial pressure, myocardial ischemia, bronchospasm, and surgical bleeding. This can be of particular relevance in neurosurgical, ophthalmic, and vascular procedures. Maneuvers to reduce coughing include the administration of IV or topically applied local anesthetics.[1,2] The administration of IV narcotics or tracheal extubation in a deep plane of anesthesia are alternatives; however, in many cases they are undesirable. The benefit of topically applied drugs before tracheal intubation is limited to a short time post-application, as they are absorbed through the tracheobronchial mucosa.

Endotracheal tubes (ETs) allow pressure to be maintained in the airways during the inhalation phase of artificial breathing and prevent exhalation of regurgitated gastro-esophageal contents. However, the pressure of the ET cuff is transmitted to the tracheal mucosa. When elevated, may cause ischemia of the mucosal vessels followed by serious complications such as ciliary loss[8], inflammation, ulceration, hemorrhaging[7], tracheal stenosis[9] and tracheo-esophageal fistula.[10] Nitrous oxide (N_2O), a gaseous anesthetic used in daily anesthetic practice, easily diffuses inside ET cuffs, thereby raising their pressure.[9] Over inflation of the cuff and the consequent tracheal mucosa lesions result in sore throats, hoarseness and coughing, thus causing discomfort to patients after the removal of the intubation.

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How to cite this article: Sagar Jolly, Pravin Ubale. A Comparative study to study the difference in effect between intracuff saline, lidocaine and alkalinized 2% lidocaine on emergence cough, sore throat and hoarseness. International Journal of Contemporary Medical Research 2018;5(3):C1-C6.

Diffusion of lidocaine across the endotracheal tube (ETT) cuff may enable the cuff to serve as a reservoir for local anesthetic and subsequent anesthesia of underlying tracheal mucosa, by blocking the cough receptors or rapidly adapting stretch receptors (RARs).[10] Only the non-ionized base form of the drug diffuses across the hydrophobic polyvinyl chloride walls of the ETT cuff.[3,10] Increasing the pH of the solution can predictably increase the percentage of the non-ionized fraction of the drug. Addition of bicarbonate resulted in a 63-fold increase in the diffusion of lidocaine across the ETT cuff[11], allowing to use lower lower doses of lidocaine (without exceeding the toxic limits).

In the proportions used in Navarro et al[12] (19 ml of 2% lidocaine to 1 ml of 8.4% sodium bicarbonate) the pH of the solution changed from 6.92(lidocaine Chlorohydrate) to 7.43 (Alkalinized lidocaine), thereby increasing the non-ionized fraction. Increasing the alkalinity of the local anesthetic using sodium bicarbonate also dramatically increases its diffusion through the ET cuff. This allows the possibility of reducing the dosage of local anesthetic.

Hence we studied whether tracheal tube intracuff 2% alkalinized lidocaine was superior to intracuff saline and intracuff lignocaine in blunting emergence coughing, and post-operative sore throat and hoarseness, who underwent tracheal intubation.

MATERIAL AND METHODS

This was prospective randomized control study conducted in tertiary care teaching public hospital after obtaining ethical permission and well informed written consent from the patients. The study was conducted over a period of one and a half years from September 2014 to March 2016. We enrolled patients aged 18 to 65 years with American Society of Anesthesiologists (ASA) physical status 1-2, Mallampatti classification equal to 1 posted for surgeries under general anaesthesia with minimum surgical duration of 90 to 120 minutes. We excluded patients with laryngeal disease/ surgery/ tracheotomised, ASA III and IV, difficult intubation, or failed extubation. Study protocol was given to respective operation theatre incharge of anaesthesia along with randomization codes. He/She divided the group to which the patient belongs according to randomized computer-generated numbers. A total of 180 patients were included in the study. The identity and consent of the patient were confirmed prior to induction of anaesthesia.

Sample Size: Sample size was calculated for the study taking into consideration the prevalence of emergence coughing, sore throat, and hoarseness in study group. Sample size was found to be 11 patients per group for coughing, 32 patients per group for sore throat at PACU, 58 patients per group for sore throat 24 hours after extubation and 50 patients per group for hoarseness of voice 24 hours after extubation for a type I error of 005 and a type II error of 0.02 with a power equal to 80% and confidence interval of 95%. Thus the total sample size was 60 patients in each group.

A standard protocol has been followed for all the patients. A detailed history and examination was taken and the procedure to be done had been explained to the patient and a written informed consent was obtained for the general anaesthesia to be given. Monitoring in the form of Electrocardiogram, Pulse oximeter, Non-invasive Blood pressure was instituted. All the patients were given general anaesthesia by following standard protocol i.e. Premedication to be done with I.V. Glycopyrrolate 0.004mg/kg body weight, I.V. Ondansetron 0.08mg/kg body weight, I.V. midazolam 0.03 mg/kg body weight and I.V. fentanyl 2 micrograms/kg body weight. Patient pre-oxygenated for 3 minutes of tidal ventilations on 100% oxygen. Patient induced with I.V. Thiopentone 5mg/kg body weight, I.V. Vecuronium 0.1 mg/kg to facilitate intubation and muscle relaxation.

Endotracheal tubes with high residual volume, low-pressure cuff, with an inner diameter of 7.0 mm for female and 8.5 mm for male were used to intubate all patients.

In Saline group – ETT cuff was filled with of 0.9% saline that will prevent air leak during positive pressure ventilation.

In Lidocaine group – ETT cuff was filled with 2% lidocaine that will prevent air leak during positive pressure ventilation.

In ALK Lidocaine group – ETT cuff was filled with 2% lidocaine mixed with 7.5% sodium bicarbonate, in a 19:1 mL proportion that will prevent air leak during positive pressure ventilation.

Continuous intracuff pressure was monitored with a hand held aneroid pressure monitor connected to the 3-way stopcock. The ETT pilot balloon and the 20 mL syringe with saline, lidocaine or alkalinized lidocaine were attached to the stopcock. 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 glycopyrrolate.

The volume of inflation solution(ml), the intracuff pressure (cm H_20), the duration of anaesthesia(min). The following outcomes were studied.

Emergence Coughing

The coughing was assessed following extubation as-

- Grade 0: No Cough
- Grade I: Cough lasting for < 15 seconds
- Grade II: Cough lasting for > 15 seconds

Sore throat: 1 hr and 24 hr post-operative

- Score 0: No sore throat at any time since the operation
- Score 1: The patient answered in the affirmative when asked about sore throat (minimal sore throat)
- Score 2: The patient complains of sore throat on his/her own (moderate sore throat)
- Score 3: The patient is in obvious distress (severe sore throat)

Hoarseness: 24 hrs post - extubation

- Score 0: No complaint of hoarseness at any time since the operation

- Score 1: Minimal change in quality of speech. Patient answers in the affirmative only when enquired about (minimal hoarseness)
- Score 2: Moderate change in quality of speech of which the patient complains on his/her own (moderate hoarseness)
- Score 3: Gross change in the quality of voice perceived by the observer (severe hoarseness)

STATISTICAL ANALYSIS

After data collection, data entry was done in Excel. Data analysis was done with the help of SPSS Software 20 and Sigma plot Ver. 11. Quantitative data was presented with the help of Mean, Standard Deviation, Median and comparison between study groups was done with the help of one-way ANOVA test as per results of Normality test. Qualitative data was presented with the help of frequency and percentage table, association among study group was assessed with the help of Chi-Square test as per requirement of table. P value less than 0.05 was taken as significant level.

RESULTS

The age of the patients in our study was above 18 years old in study population. Mean age in saline group was 40.98 ± 10.05 years, in lidocaine it was 44.62 ± 11.77 years and in alkalinized lidocaine group it was 41.07 ± 9.65. The mean weight in saline group was 63.18 ± 6.74 kg, in lidocaine it was 64.52 ± 6.07 kg and in alkalinized lidocaine group it was 66.40 ± 5.28 kg. The 3 groups were comparable on the basis of age and weight with P > 0.05(Chi-square test).

The distribution of sex in our study was a total of 32 male (53%) patients and 28 female patients (47%) in Saline group, 35 male(58%) patients and 25 female(42%) in lidocaine group and 32 male**.** The ASA grade in Saline group was 32 patients (32%) ASA I and 28 patients (35%) ASA II, in lidocaine group 32 patients (32%) were ASA grade I and 28 patients (35%) were ASA II and in alkalinized lidocaine group 36 patients (36%) ASA I and 24 patients(30%) were belonging to ASA II. Both Sex and ASA grade in the 3 groups were statistically insignificant(P>0.05), thus were comparable on the basis of ASA grade.

The distribution of duration of anaesthesia between the 3 groups was statistically insignificant making the 3 groups comparable**.** (P>0.05)

The incidence of emergence coughing is depicted in (table 1). In Alkalinized lidocaine group, the incidence of emergence coughing was significantly lower presented in only 4 patients (7%) having Grade II and 8 patients (13%) having Grade I out of 60 patients, which was considerably lower in alkalinized lidocaine group with a P value 0.000(≤ 0.01). Whereas 25 patients (42%) and 8 patients (13%) were having grade II cough in saline and lidocaine group respectively, and 15 patients (25%) and 12 patients (20%) were having grade I

Group		Coughing			
		Grade 0	Grade I	Grade II	Total
Saline	Count	20	15	25	60
	Percent	33%	25%	42%	100%
Lidocaine	Count	40	12	8	60
	Percent	67%	20%	13%	100%
ALK Lidocaine	Count	48	8	4	60
	Percent	80%	13%	7%	100%
Total	Count	108	35	37	180
	Percent	60%	19%	21%	100%
Chi-Square Tests	Value	df	P value	Association	
Pearson Chi-Square	33.832[a]	4	0.000	Significant	

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 11.67; A p-value (**≤ 0.05**) indicates strong evidence against the null hypothesis.

Table-1: Association Between the 3 groups on the basis of Emergence coughing:

		Sore_throat_1hr_extubation				
Group		Score 0	Score 1	Score 2	Score 3	Total
saline	Count	21	21	14	4	60
	Percent	35%	35%	23%	7%	100%
lidocaine	Count	44	11	5	0	60
	Percent	73%	18%	9%	0%	100%
ALK lidocaine	Count	52	6	2	0	60
	Percent	87%	10%	3%	0%	100%
Total	Count	117	38	21	4	180
	Percent	65%	21%	12%	2%	100%
Chi-Square Test	Value	df	P value	Association		
Pearson Chi-Square	37.256[a]	6	0.000	Significant		

6 cells (50.0%) have expected count less than 5. The minimum expected count is .67

Table-2: Association Between the 3 groups on the basis of Sore Throat 1hr Post-Extubation

		Sore throat at 24 hr extubation				
Group		**Score 0**	**Score 1**	**Score 2**	**Score 3**	**Total**
Saline	Count	32	15	11	2	60
	Percent	53%	25%	19%	3%	100%
Lidoacaine	Count	53	5	2	0	60
	Percent	88%	9%	3%	0%	100%
ALK lidocaine	Count	57	2	1	0	60
	Percent	95%	4%	1%	0%	100%
Total	Count	142	22	14	2	180
	Percent	79%	12%	8%	1%	100%

Chi-Square Tests	Value	Df	P value	Association
Pearson Chi-Square	37.256[a]	6	0.000	Significant
a. 6 cells (50.0%) have expected count less than 5. The minimum expected count is .67				

Table-3: Association Between the 3 groups on the basis of Sore Throat 24 hr Post-Extubation

		Hoarseness at 24hr extubation				
Group		**Score 0**	**Score 1**	**Score 2**	**Score 3**	**Total**
Saline	Count	40	11	6	3	60
	Percent	67%	19%	10%	5%	100%
Lidocaine	Count	49	7	3	1	60
	Percent	82%	11%	5%	2%	100%
ALK lidocaine	Count	55	4	1	0	60
	Percent	92%	6%	2%	0%	100%
Total	Count	144	22	10	4	180
	Percent	80%	12%	6%	2%	100%

Chi-Square Tests	Value	df	P Value	Association
Pearson Chi-Square	13.039[a]	6	0.042	Significant
a. 6 cells (50.0%) have expected count less than 5. The minimum expected count is 1.33				

Table-4: Association Between the 3 groups on the basis of Hoarseness 24 hr Post-extubation

cough in the respective groups.

The incidence of Sore throat at 1hr post-extubation is depicted in (table 2). In Alkalinized lidocaine group, the incidence of sore throat 1 hr post-extubation was significantly lower presented in only 6 patients (10%) having Score 1, 2 patients (3%) Score 2 and 0 patients (0%) Score 3 out of 60 patients, which was considerably lower in alkalinized lidocaine group with a P value 0.000(≤ 0.01).

Whereas, 21 patients (35%) and 11 patients (18%) were having Score 1 in saline and lidocaine group respectively, 14 patients (23%) and 5 patients (9%) were having Score 2, 4 patients(7%) and 0 patients(0%) were having Score 3 in the respective groups.

The incidence of Sore throat at 24hr post-extubation is depicted in (table 3). In Alkalinized lidocaine group, The incidence of Sore throat at 24hr post-extubation was significantly lower presented in only 2 patients (4%) having Score 1, 1 patient (1%) Score 2 and 0 patients (0%) Score 3 out of 60 patients, which was considerably lower in alkalinized lidocaine group with a P value 0.000(≤ 0.01).

Whereas, 15 patients (25%) and 5 patients (9%) were having Score 1 in saline and lidocaine group respectively, 11 patients (19%) and 2 patients (3%) were having Score 2, 2 patients (3%) and 0 patients(0%) were having Score 3 in the respective groups.

The incidence of Hoarseness at 24hr post-extubation is depicted in (table 4). In Alkalinized lidocaine group, the incidence of Hoarseness at 24hr post-extubation was significantly lower presented in only 4 patients (6%) having Score 1, 1 patient (2%) Score 2 and 0 patients (0%) Score 3 out of 60 patients, which was considerably lower in alkalinized lidocaine group with a P value 0.042 (≤ 0.05).

Whereas, 11 patients (19%) and 7 patients (11%) were having Score 1 in saline and lidocaine group respectively, 6 patients (10%) and 3 patients (5%) were having Score 2, 3 patients (5%) and 1 patients (2%) were having Score 3 in the respective groups.

DISCUSSION

The highest incidence of sore throat and other airway related symptoms tends to occur in patients who have undergone tracheal intubation. It has been clearly demonstrated that the use of a smaller tracheal tube reduces the incidence of sore throat, presumably because of decreased pressure at the tube–mucosal interface.

Strategies to attenuate the emergence phenomenon include extubation in a deeper plane of anesthesia, use of narcotics, and use of lidocaine. A study using nebulized lidocaine prior to the induction of anesthesia demonstrated a significant decrease in procedure-related complications in smoking patients.[13] Lidocaine has been used in various ways. (as an aerosol, lubricant jelly or ointment) to suppress cough and as a supplement to light planes of general anaesthesia in attempts to prevent the haemodynamic disturbances during the intubation and recovery phases of anaesthesia, and to prevent sore throat. However, following intravenous or intratracheal administration, lidocaine blood concentrations quickly decrease and the topical anaesthesia of the upper airway only lasts for 20-30 min.

When lidocaine is injected into the ETT cuff[14], it spreads through the semipermeable membrane wall and induces anesthetic action in the trachea. This increases tolerance to the placement of tracheal[15] and tracheotomy tubes. Hemodynamic alterations after tracheal extubation are thereby minimized, and the incidence of coughing is reduced. Only the non-ionized base form of the drug diffuses across the hydrophobic polyvinyl chloride walls of the ETT cuff.[10] Increasing the pH of the solution can predictably increase the percentage of the non-ionized fraction of the drug. Addition of bicarbonate resulted in a 63-fold increase in the diffusion of lidocaine across the ETT cuff[11], allowing to use lower lower doses of lidocaine (without exceeding the toxic limits). Inflation of the ETT cuff with alkalinized 2% lidocaine is superior to saline in decreasing the incidence of emergence coughing and preventing sore throat during the postoperative period in smokers[16]

It has recently been suggested that a lidocaine spray might be irritating and damaging to the tracheal mucosa. A different approach for the application of lidocaine to the trachea was suggested by Sconzoand colleagues.[17] They showed, by measuring increasing lidocaine concentrations in a water bath, that lidocaine diffuses across the cuff of the endotracheal tube. The amount of lidocaine diffusing across the cuff increased when the cuff was prefilled for 1-2.5 h before placing it in the water bath.[18] Based on this information, we also used the ETTcuff as a reservoir for lidocaine. We compared Saline, lidocaine and alkalinized lidocaine for determining rise in intracuff pressure and thereby incidence and signs of tracheal morbidity like emergence coughing, post-operative sore throat and hoarseness of voice.

Estebe et al 2005[19], reported that alkalinization of L-HCl allowed the diffusion of 65% of the neutral base form of L-HCl through the hydrophobic structure of the PVC cuff within a 6-hour period and showed that the use of a small dose (40 mg) of alkalinized L-HCl markedly improved ETT tolerance during the first postoperative day. They have also shown, *in vitro*, that variation in volumes of 8.4% of NaHCO3 (1to 7 mL) injected into the cuff had no effect on the diffusion of 40 mg L-HCl. The study helped us to determine efficacy and safety of intracuff lidocaine thus made us to study its effects in perspective of our study. 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 taken from Navarro et al.[12]

In our study, the average volume and pressure at the start of surgery to achieve adequate seal in saline group was 4.12 ± 0.46 ml and 20.47 ± 0.75 cm H_20, in lidocaine group was 4.50 ± 0.67 ml and 20.35 ± 0.61cm H_20 and 4.33 ± 0.69 ml and 20.32 ± 0.62 cm H_20 in alkalinized lidocaine group. Towards the end of surgery, the average volume and pressure was 4.28 ± 0.59 ml and 22.18 ± 1.03 cm H_2O in saline group, 4.35 ± 0.59 ml and 19.60 ± 0.78 cm H_2O in lidocaine group and 4.14 ± 0.63 ml and19.65 ± 0.90 cm H_2O in alkalinized lidocaine group. Our data confirmed the increased intracuff pressure at the end in saline group while stable intracuff pressure among lidocaine and alkalinized lidocaine group, while intracuff volume at the end was not changed significantly among the 3 study groups on comparing them together.

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. 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[20], the inflation of the cuff with a mixture of N_2O/O_2 in proportions identical to those used in the anesthesia[21], the use of a tracheal tube with a cuff impermeable to N_2O, and filling the cuff with 0.9% saline.[22] 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).[18,14,17] Lidocaine alkalinization[23] increases the rate of diffusion through the cuff wall, allowing a reduction of the lidocaine dose while achieving the same results.

In our 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 occur.

Limitation

There were limitations associated to our study. The sample size to study the individual group with the study parameters and the outcome was small enough to correlate them all together. We excluded <18 years old population, Mallampati Calssification > I, Patient with history of respiratory tract infection. We were missing at taking prior history of general anaesthesia which was whether had the same outcomes studied in our study. No visual inspection via fiber-optic scope of the cases was done to see the extent of tracheal mucosal damage and if any damage to airway due to intubation. We did not include those subjects who were maintained without nitrous oxide during general anaesthesia. Plasma lidocaine assessment was not done in the study. We need a better scoring and grading to study the outcomes.

CONCLUSION

In conclusion, our study demonstrated inflation of the ETT cuff with alkalinized 2% lidocaine decreases the incidence of emergence coughing and prevents sore throat and hoarseness during the postoperative period rather than ETT cuff filled with plain lignocaine and saline.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 10-02-2018; **Accepted:** 14-03-2018; **Published:** 30-03-2018