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Original Article

Comparative Study between the Effects of 4% Lignocaine Solution through Endotracheal Tube Cuff and 1.5 mg/kg of Intravenous 2% Lignocaine on Coughing and Hemodynamics During Extubation in Neurosurgical Patients

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Abstract

Aim: A prospective, randomized, double-blind trial was performed to compare the effects of 4% endotracheal tube cuff lignocaine and 1.5 mg/kg intravenous lignocaine on coughing and hemodynamics during extubation in patients undergoing neurosurgical procedures.

Methods: Group A (*n* = 50) patients received 4% lignocaine into endotracheal tube cuff after intubation and Group B (*n* = 50) patients received intravenous lignocaine 2% at 1.5 mg/kg before extubation. Coughing was assessed by the scale of 3 at the time of extubation, 0–2 min, 2–4 min, and 4–8 min post-extubation. Hemodynamic parameters were recorded at 1 min, 2 min, 5 min, and 10 min and were compared with baseline values.

Results: Comparison of hemodynamic variables, incidence, and severity of cough at emergence was analyzed using unpaired *t*-test. The incidence and severity of cough were less in Group A when compared to Group B. There was no significant difference in hemodynamic variables in between the groups.

Conclusion: Intracuff 4% lignocaine was found to be superior to 2% intravenous lignocaine in suppressing cough during emergence.

Key words: Cough reflex, Endotracheal tube cuff, Hemodynamic response, Intravenous, Lignocaine

INTRODUCTION

Tracheal intubation with an endotracheal tube is necessary during general anesthesia. After intubation, inflating the cuff around the endotracheal tube maintains a seal. Smooth Emergence from general anesthesia is frequently complicated by coughing induced by stimuli from the endotracheal tube.[1] Irritant or stretch stimuli in the trachea caused by the tube and its cuff are presumed mechanisms in inducing cough. Rapidly acting receptors which are found throughout the trachea are thought to be the irritant receptors involved in the cough reflex. These nociceptive stimuli can be blocked by topically applied anesthetics.[2] Coughing during emergence can result in hypertension, tachycardia, raised intraocular and intracranial pressures, myocardial ischemia, bronchospasm, and surgical bleeding.[3] This can be of particular relevance in neurosurgical, ophthalmic, and vascular procedures.

2% preservative-free lignocaine solution can be given intravenously in a dose of 1.5 mg/kg to attenuate stress response during intubation as well as extubation.[4] Many

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studies proved its efficacy in attenuating stress response during emergence, but prior studies failed to prove that it effectively suppresses a cough during emergence.[5] Whereas 4% lignocaine hydrochloride containing 40 mg/mL given in a dose of 1–5 mL (40–200 mg) or 0.6–3 mg/kg anesthetizes mucus membranes. It can be used as spray/cotton applicator/packs/instilled into cavities.[6] 4% intracuff lignocaine diffuses across the endotracheal tube in a fashion that may enable the cuff to serve a potentially useful role as a reservoir for local anesthetic.[7]

Hence, it anesthetizes the tracheal mucosa surrounding the endotracheal tube cuff and may reduce the incidence of coughing during emergence. In this study, we evaluated its efficacy in reducing cough during emergence compared to intravenous lignocaine.

METHODS

After Institutional Ethics Committee approval and written informed consent, 100 patients of ASA Grades 1 and 2 were included in this randomized, prospective clinical study.

Inclusion Criteria

- Age: 16–56 years
- Sex: Both genders
- Neurosurgical procedures.

Exclusion Criteria

- Known H/o reactive airway disease
- H/o altered sensorium
- Signs of raised intracranial pressure
- Upper airway infection
- Known H/o smoking
- Airway pathology
- H/o anticipated difficult intubation
- Any contraindication to the study drug.

Group Allocation

A total of 100 patients were randomly allocated into two groups of 50 each by computer-generated random numbers into Groups A and B.

- Group A: Received 4% lignocaine solution into endotracheal tube cuff, volume according to minimal occlusion volume technique during cuff inflation.
- Group B: Received preservative-free 2% lignocaine (loxicard) at a dose of 1.5 mg/kg intravenously before extubation.

In the pre-operative period, after selection of the patients who met the inclusion criteria, all the routine laboratory investigations were done. On the day of surgery, patient's baseline parameters of HR, NIBP, SPo2, and RR were noted. In the operating room, two 18 gauze IV cannulas were secured. Monitoring devices such as SpO_2, electrocardiogram (ECG), NIBP, and temperature were connected to all the patients. General anesthesia was induced using a standard regimen in all the patients of both groups. Premedication was done with injection glycopyrrolate 5 μg/kg IV and injection fentanyl 2 μg/kg IV, just before induction.

After preoxygenation for 5 min, all the patients were induced with injection thiopentone sodium 5 mg/kg IV and intubation was done using suxamethonium 2 mg/kg IV with appropriate sized polyvinyl chloride (PVC) cuffed endotracheal tube, and then, the tube was secured after checking for bilateral air entry at the angle of the mouth to the desired length.

Group A endotracheal tube cuff was inflated with 4% lignocaine solution, the volume decided by the minimum occlusion volume technique. Group B endotracheal tube cuff was inflated with 0.9% saline solution, the volume according to minimal occlusion volume technique in the same manner as in Group A. Precautions taken while inflating the cuff are slow inflation than usual to prevent damage to tracheal mucosa and to see that no air bubble enters the cuff while inflating with 4% lignocaine.

Anesthesia gas mixture was administered through closed circuit of an anesthesia workstation with N_2O, O_2, and sevoflurane in a concentration of 66.6%, 33.3%, and 0.5% (1–1.5%), respectively. Neuromuscular blockade was maintained with vecuronium in a dose of 0.08 mg/kg. Neuromuscular blockade was antagonized with neostigmine in a dose of 70 μg/kg and glycopyrrolate 5 μg/kg IV at the end of the surgical procedure.

In Group B, just before extubation, 2% lignocaine (preservative-free) was given intravenously. At the same time in Group A, the same amount of normal saline was administered intravenously to ensure blinding. Three anesthesiologists were involved in this study, namely, principal investigator, Observer A and B. The solutions to be injected into the inflatable cuffs of endotracheal tube were loaded by the Principal investigator who was aware of the group allocation. They were supplied to the operating room in sealed envelopes. The intravenous solutions are given just before extubating the patients were also loaded by the principal investigator, and they were also supplied in sealed envelopes. The sealed envelopes were labeled according to their route of administration and were opened just before administration of drugs. The observer anesthesiologist A administered all the study drugs according to their route. The principal investigator went out of the operating room after administering the drugs. Just before extubation, the observer anesthesiologist A administered IV drugs according to the group allocation. The observer anesthesiologist B

monitored all the patients throughout the surgery and made the following observations.

Continuous monitoring was done in all the patients with pulse oximetry, ECG, systolic blood pressure (SBP), and diastolic blood pressure (DBP) every 1 min for the first 15 min, followed by every 5 min till the end of surgery.

During extubation, hemodynamic monitoring was done at 1 min, 2 min, 5 min, and 10 min immediately following extubation.

All the patients were assessed for incidence of coughing and its severity at the time of emergence.

Three category scale for scoring severity of cough[8] during emergence was used in this study.

- Mild - single episode
- Moderate - 1 episode of unsustained cough for <5 s
- Severe - sustained bouts of coughing for >5 s.

All the data were statistically analyzed. Demographic data were analyzed using Fischer exact test. Comparison of hemodynamic variables, incidence, and severity of coughing at emergence was analyzed using unpaired *t*-test. $P < 0.05$ was considered statistically significant. Data were expressed as mean, standard deviation, and percentage.

RESULTS

A total of 100 ASA I/II patients were included in this randomized prospective study. All the patients completed the study.

The patients of both the groups were comparable with respect to demographic characteristics such as age, gender, weight, ASA grading, and duration of surgery. $P > 0.05$ was statistically not significant [Table 1].

The hemodynamic parameters such as heart rate, SBP, and DBP in our study were monitored at extubation, 1 min, 2 min, 5 min, and 10 min post-extubation and compared between 2 groups and found that they were not significant statistically, ($P > 0.05$).

The mean heart rate was higher at the time of extubation and subsequently lower at 1 min, 2 min, 5 min, and 10 min after extubation in both the groups. The attenuation of heart rate was comparable between the groups, ($P > 0.05$), not significant [Table 2].

The mean SBP was higher at the time of extubation and gradually decreased at 1 min, 2 min, 5 min, and 10 min post-extubation, in both the groups. The attenuation of mean SBP was comparable between the groups, $P > 0.05$, not significant [Table 3].

The mean DBP was higher at the time of extubation and gradually decreased at 1 min, 2 min, 5 min, and 10 min post-extubation in both the groups. The attenuation of mean DBP was comparable between the groups. The hemodynamic data and SpO_2 were similar for both the groups [Table 4].

The incidence of coughing was compared between the two groups at extubation within first few minutes [Table 5 and Graph 1].

For initial 2 min after extubation, the incidence of coughing was significantly higher in the 2% IV lignocaine group than 4% cuff lignocaine group (A vs. B: 16% vs. 38%) ($P = 0.05$), statistically significant.

Table 1: Demographic characteristics of the studied patients

Data	Mean±SD (*n*=50)		*P* value
	Group A	Group B	
Age (years)	32.64±9.26	33.26±9.21	0.73
Weight (kg)	64.86±7.76	65.12±8.14	0.87
Sex (%)			
Male	27 (54)	31 (62)	
Female	23 (46)	19 (38)	
ASA (I/II)	31+19	28+22	
Duration of surgery (in min)	78.40±50.12	82.10±47.28	0.70

Values are expressed as mean±SD or ratio or absolute numbers. Student *t*-test, *Fischer's exact test, †Chi-square test. *P*<0.05 statistically significant. SD: Standard deviation

Table 2: Heart rate of the patients in the two groups at different intervals.

Time interval	Mean±SD *n*=50		*P* value
	Group A	Group B	
HR 1st min after extubation	80.60±6.38	80.34±5.83	0.83
HR 2nd min after extubation	81.32±7.35	81.48±6.78	0.91
HR 5st min after extubation	82.32±7.13	81.24±5.64	0.40
HR 10st min after extubation	81.64±7.13	81.44±7.12	0.88

Values are expressed as mean±SD or ratio or absolute numbers. Student *t*-test, *P*<0.05 statistically significant. SD: Standard deviation

Table 3: Systolic blood pressure of the patients in the two groups at different intervals

Time interval	Mean±SD *n*=50		*P* value
	Group A	Group B	
SBP 1st min after extubation	117.20±8.93	120.04±8.86	0.11
SBP 2nd min after extubation	119.28±10.66	120.16±8.91	0.65
SBP 5st min after extubation	119.96±8.75	120.32±9.30	0.84
SBP 10st min after extubation	120.16±8.91	120.92±8.57	0.66

Values are expressed as mean±SD or ratio or absolute numbers. Student *t*-test, *P*<0.05 statistically significant. SD: Standard deviation

The incidence of coughing at 2–4 min after extubation was also significantly higher in 2% IV lignocaine group than 4% cuff lignocaine group (A vs. B: 11% vs. 36%) $P < 0.05$, statistically highly significant.

At 4–8 min after extubation, 2% IV lignocaine group had 34% incidence of coughing while none of the patients in 4% cuff lignocaine group had coughing after 4 min ($P < 0.05$), statistically highly significant.

The severity of cough was compared between two groups. The incidence of mild cough was significantly higher in 2% IV lignocaine group when compared to 4% cuff lignocaine group (A vs. B: 15% vs. 40%) $P < 0.05$, statistically significant [Table 6 and Graph 2].

The incidence of moderate cough was also significantly higher in the 2% IV lignocaine group when compared to 4% cuff lignocaine group ($P < 0.05$), statistically significant.

28% of patients in 2% IV lignocaine group had severe cough while none of the patients in 4% cuff lignocaine group had severe cough. $P < 0.05$, statistically significant.

Table 4: Diastolic blood pressure of the patients in the two groups at different intervals

Time interval	Mean±SD *n*=50		*P* value
	Group A	Group B	
DBP 1st min after extubation	79.90±5.21	80.20±5.38	0.77
DBP 2nd min after extubation	76.88±5.30	79.82±6.24	0.01
DBP 5st min after extubation	78.28±6.29	78.26±8.12	0.98
DBP 10st min after extubation	79.96±5.67	79.88±6.22	0.94

Values are expressed as mean±SD or ratio or absolute numbers. Student *t*-test, *P*<0.05 statistically significant. SD: Standard deviation

Table 5: Incidence of cough after extubation in the two groups

Time interval (min)	Number of patients (%)	
	Group A (*n*=50)	Group B (*n*=50)
0–2	9 (18)	15 (30)
2–4	6 (12)	14 (28)
4–8	3 (6)	12 (24)

Data expressed as % and absolute numbers

Table 6: Severity of cough after extubation in two groups

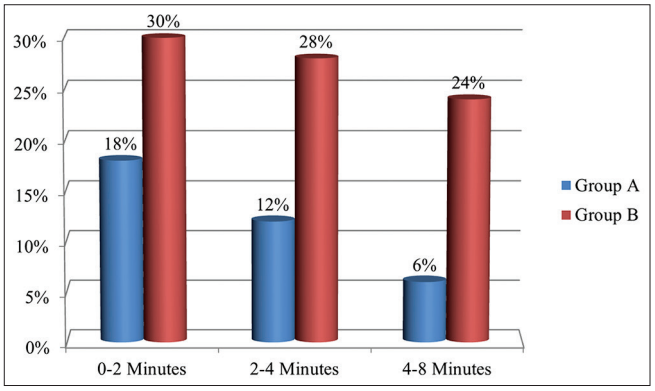
Grade	Number of patients (%)	
	Group A (*n*=50)	Group B (*n*=50)
Mild	10 (20)	17 (34)
Moderate	8 (16)	14 (28)
Severe	1 (2)	10 (20)

Data expressed as % and absolute numbers

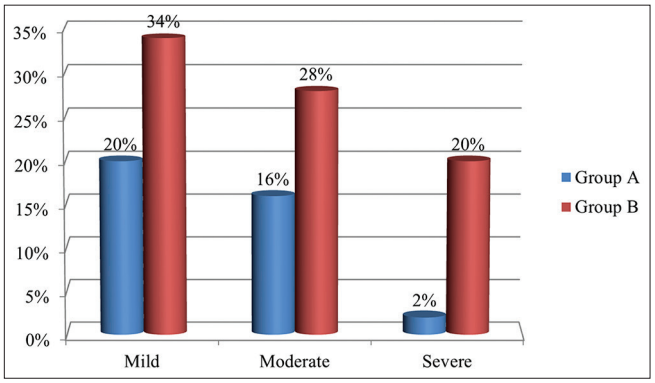
DISCUSSION

A technique that would allow patients from anesthesia to tolerate an endotracheal tube while also affording airway protection with intact supraglottic reflexes would be desirable in a selected group of surgical patients. Various methods have been employed to attenuate hemodynamic responses and also to decrease the incidence of coughing which include extubation in deep plane of anesthesia and administering intravenous agents like lignocaine, opioids like fentanyl, α-agonists such as dexmedetomidine and topical or intracuff application of lignocaine 4%, and IV lignocaine 2% have been a traditional method which is employed in various clinical trials as a control.[9] Although IV lignocaine has shown to suppress both mechanically and chemically induced airway reflexes, it is not very much effective against cough during emergence which was proved in many clinical studies.[10] The effects of 4% intracuff lignocaine were studied and compared with 2% IV lignocaine as control in this study. In this study, intracuff lignocaine has demonstrated success in attenuating hemodynamic responses and decreasing the incidence and severity of cough during emergence when compared to IV lignocaine.

Lignocaine instilled in the endotracheal tube cuff diffuses slowly across the cuff membrane. The cuff acts as a reservoir for lignocaine, allowing diffusion and subsequent



Graph 1: Incidence of cough minutes after extubation



Graph 2: Incidence of severity of cough after extubation

anesthesia of tracheal mucosa in contact with the cuff. This method reduces emergence phenomena including post-operative coughing and sore throat.

Various *in vitro* studies demonstrated that lignocaine diffused across the membrane of the cuff of the endotracheal tube, the diffusion of which depended on various factors such as the non-ionized fraction of local anesthetic, alkalinization, temperature, duration of procedure, and concentration of local anesthetic.[11,12]

The mean volume which was inflated into ET tube cuff was 7 ± 2 mL, but no sign of lignocaine toxicity was observed during the intra-operative and post-operative period in our study. The deflated volumes were always less than the inflated volumes, in the study group; the deflated volumes amounted to 6.2 ± 1.5 mL.

The protective cough reflexes above the tube cuff and of the vocal cords should remain intact. However, if cuff damage may occur, there is always the risk of leakage and systemic absorption of local anesthetic with its consequences.[13]

It was observed that none of the patients in this study had signs of lignocaine toxicity and all the cuffs of ET tubes were found intact after extubation. The cuffs of ET-tubes being intact, the concern for lignocaine toxicity was negligible because the amount of drug diffused among the ET tube cuff would be very less.

One limitation of this study was, plasma levels of lignocaine were not measured unlike in the other studies, due to lack of feasibility to this investigation in our institution.

The plasma levels required to suppress coughing during emergence were found to be around 3 μg/mL of lignocaine in previous studies.

Venkatesan and Korula conducted a similar randomized clinical trial comparing the effects of 4% ET cuff lignocaine versus IV lignocaine on coughing and hemodynamics on extubation in patients undergoing elective craniotomies and reported that there were no significant differences in terms of hemodynamic responses and also coughing during extubation.[14] Our study differs from this study with respect to incidence and severity of coughing as there was significant attenuation of coughing in cuff lignocaine group in our study.

Fagan *et al.* suggested that local anesthetic lignocaine instilled into the ET cuff might cause anesthesia of the trachea by diffusing across the PVC membrane, anesthesia confining to the mucosa in contact with the cuff and protective cough reflexes above the tube cuff and below the cords would remain intact.[15] The preservation of cough reflexes in post-extubation period can be explained by the above.

Wetzel *et al.* suggested similar results in intracuff lignocaine group compared with the saline group, but they did the study in smokers.[16]

Navarro *et al.* compared alkalinized intracuff 2% lignocaine with intracuff saline and concluded that intracuff lignocaine was superior to saline in decreasing incidence of emergence coughing and sore throat during the post-operative period in smokers.[17]

George *et al.* compared IV 2% lignocaine versus 2% lignocaine spray down the ET tube versus placebo for extubation response in neurosurgical patients. They concluded that the effectiveness of IV lignocaine versus lignocaine spray to attenuate extubation response was comparable. Lignocaine spray instilled into the ET tube was not superior to IV lignocaine in their study because the installation of 2% lignocaine spray was done 20–30 min before extubation which was in contrast to our study where we have administered intracuff lignocaine at the time of intubation so that there is adequate time for cuff lignocaine to be absorbed into tracheal mucosa and cause anesthetic effect.[18]

Snigdha *et al.* compared the installation of 4% lignocaine into ET cuff versus air and concluded that cuff lignocaine has significantly reduced post-extubation coughing, nausea, vomiting, dysphonia, hoarseness, and sore throat compared to air.[19]

The above studies were correlating to the observations of our study with few differences in the methodology, study drugs and time of administration.

Our study concluded that both intracuff 4% lignocaine and IV were similar in attenuating hemodynamic responses during extubation and intracuff 4% lignocaine has been superior to 2% IV lignocaine in suppressing cough during emergence.

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