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Comparative Efficacy of Intracuff 1% and 2% Alkalinized Lignocaine with Saline on Endotracheal Tube-Induced Hemodynamic Changes and Emergence Phenomena in Neurosurgical Patients

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Abstract

Introduction Extubation is associated with hemodynamic changes and emergence phenomena leading to cough, sore throat, dysphonia, and dysphagia in the postoperative period. The aim of our study was to compare intracuff 2% alkalinized lignocaine with 1% alkalinized lignocaine and saline in reducing endotracheal tube induced emergence phenomena and haemodynamic changes at extubation in neurosurgical patients.

Materials and Methods In this randomized controlled study, 90 adult patients of either sex, scheduled to undergo neurosurgical procedures were randomly divided into three groups of 30 each to receive either 1% alkalinized lignocaine (AL1), 2% alkalinized lignocaine (AL2), or saline as cuff inflation media. Intracuff pressures and haemodynamic variables were noted intraoperatively and during emergence. The presence of postextubation cough, sore throat, dysphonia, and dysphagia were monitored until 24 hours postoperatively. Data were analyzed using Chi-square test and ANOVA. A *p*-value of less than 0.05 was considered significant.

Results The intracuff pressures were significantly less with alkalinized lignocaine as compared to saline, after 3 hours of induction. Post extubation, hemodynamic parameters and incidence of coughing and bucking at extubation were significantly less in Groups AL1 ($p = 0.024$) and AL2 ($p = 0.02$) as compared to saline. On assessment of laryngotracheal morbidity, the incidence of coughing was found to be significantly less with 2% alkalinized lignocaine as compared to saline ($p = 0.021$) at 1 hour after extubation. Sore throat was significantly less in Groups AL1 and AL2 as compared with saline at 1 hour ($p = 0.008$, 0.002 respectively) and 8 hours ($p = 0.01$ in both groups), and in Group AL2 versus saline at 24 hours ($p = 0.044$) after extubation. The incidence

Keywords
- alkalinized lignocaine
- saline
- intracuff pressure
- hemodynamic response
- postextubation cough
- sore throat

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of dysphonia was significantly less in Groups AL1 and AL2 as compared with saline at 1 hour ($p = 0.016$, $p = 0.002$) and 24 hours ($p = 0.012$ in both groups) and in Group AL2 versus saline at 8 hours ($p = 0.03$) postoperatively. No significant differences were noted between 1% alkalinized lignocaine and 2% alkalinized lignocaine.

Conclusion Intracuff alkalinized lignocaine 1% and 2% were significantly better than saline in reducing coughing and bucking at extubation, post extubation haemodynamic changes and incidence of postoperative cough, sore throat, and dysphonia.

Introduction

Maintenance of airway with a cuffed endotracheal tube (ETT) is the gold standard for surgeries performed under general anesthesia (GA). The recommended intracuff pressure is between 20 and 30 cm H_2O.[1] Emergence from GA is associated with tachycardia, hypertension, and laryngotracheal (LT) morbidities such as cough, sore throat, dysphonia and dysphagia,[2] the incidence of which varies from 38 to 96%.[3] Coughing and bucking during extubation can result in tachycardia, hypertension, surgical bleeding, and raised intraocular, intracranial and central venous pressures.[4] These side effects may be especially deleterious in patients undergoing neurosurgical, ophthalmic, and vascular procedures.

The incidence of postoperative sore throat is higher with larger-sized ETTs, non-lubricated ETTs, multiple intubation attempts, and use of nitrous oxide (N_2O) during GA.[3] Various measures have been employed to reduce the incidence of postoperative laryngotracheal (LT) morbidity, including the use of smaller size ETTs, monitoring, and adjustment of intracuff pressure and replacement of intracuff air with liquid media such as saline and lignocaine to prevent the rise in cuff pressure caused by diffusion of N_2O.[5] Lignocaine diffuses across the cuff membrane to block the tracheal pain receptors and addition of sodium bicarbonate to lignocaine (alkalinization) further increases its diffusion.[6]

The primary aim of our study was to compare the efficacy of intracuff 2% alkalinized lignocaine with 1% alkalinized lignocaine and saline in reducing the incidence of post extubation cough (PEC) and postoperative sore throat (POST) and secondary aim was to study the incidence of hemodynamic changes at extubation in neurosurgical patients.

Materials and Methods

This prospective interventional randomized controlled study was conducted from December 2017 to December 2018 in the Department of Anaesthesia and Intensive Care at Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi after obtaining approval from the Institutional Ethical Committee and written informed consent from the patients . The trial was registered with ctri.nic.in (Clinical Trial Number: CTRI/2018/04/013067) and adheres to the applicable CONSORT guidelines (►**Fig. 1**).

Ninety adult patients of either sex, aged between 18 and 65 years, with American Society of Anaesthesiologist's Grade I or II and Glasgow coma scale (GCS) of 15/15, scheduled to undergo neurosurgery were included in the study. Patients with history of sore throat, upper respiratory infection, uncontrolled hypertension, asthma, chronic obstructive airway disease, predicted difficult intubation, more than 2 attempts at intubation, those who received intravenous lignocaine or had allergy to local anesthetics, and were not immediately extubated after surgery, were excluded from the study.

The patients were randomly divided into three groups of 30 each, to receive either 2% alkalinized lignocaine, 1% alkalinized lignocaine, or saline as cuff inflation media, based on computer-generated random numbers and concealment allocation by sealed envelope system.

Group S ($n = 30$): 0.9% saline

Group AL1 ($n = 30$): 1% alkalinized lignocaine

Group AL2 ($n = 30$): 2% alkalinized lignocaine

Preparation of 2% alkalinized lignocaine: 9 ml of 2% lignocaine + 1 mL of 7.5% $NaHCO_3$

Preparation of 1% alkalinized lignocaine: 9 ml of 1% lignocaine (5 mL of 2% lignocaine +

5 ml of saline; discard 1 mL) + 1 mL of 7.5% $NaHCO_3$

Preoperatively, the patients were familiarized with the grading of cough, sore throat, dysphonia, dysphagia, and pain scoring system. All patients were made to fast as per guidelines. In the operating room, standard monitors were attached including electrocardiography (ECG), noninvasive blood pressure-systolic, diastolic and mean (SBP, DBP, MAP), pulse oximetry (SpO_2), and capnography. After preoxygenation with 100% oxygen (O_2) for 3 min, patients were induced with Inj. fentanyl 1.5 µg/kg IV and Inj. propofol 1 to 2 mg/kg, and muscle relaxation was provided with vecuronium bromide 0.1 mg/kg IV. Intermittent positive pressure ventilation (IPPV) with O_2, N_2O, and isoflurane was instituted. At the end of 3 min, N_2O, and isoflurane were switched off. An appropriate size ETT (polyvinyl chloride, low pressure and high-volume cuff) was inserted into the trachea. The test drug was loaded in a 10 mL syringe to make a total volume of 10 mL. It was prepared by a second anesthesiologist who did not take part in the study.

After insertion of the ETT, the cuff was inflated with test drug at the minimal occlusive volume, i.e., the volume sufficient to establish a cuff pressure between 25 and 30 cm H_2O (and eliminate audible inspiratory leak with IPPV). N_2O and isoflurane were switched on and mechanical ventilation was commenced. Inj. decadron 8 mg IV was given after induction. Anesthesia was maintained with O_2, N_2O,

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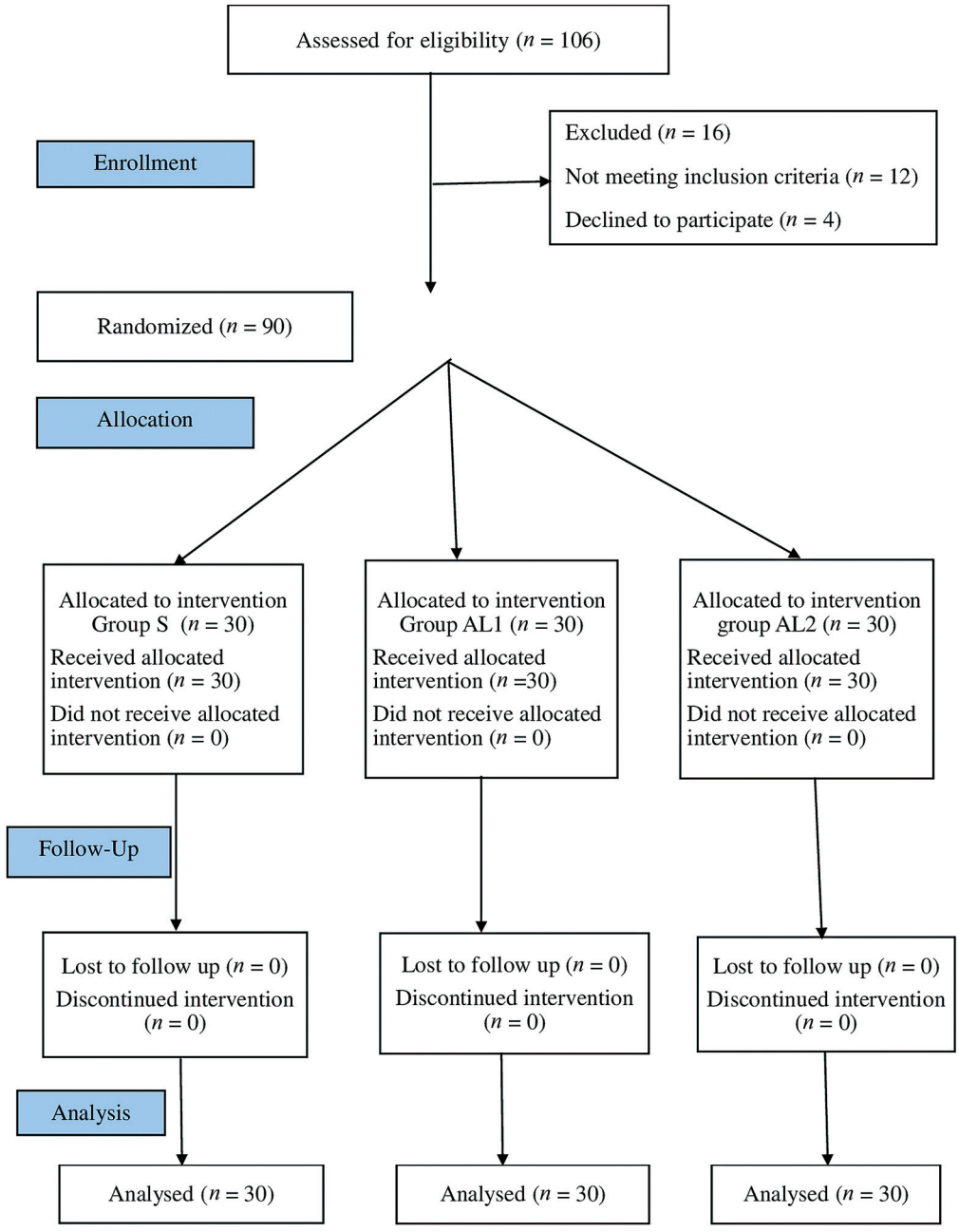

Fig. 1 Consort diagram showing random allocation to three different groups.

and isoflurane, vecuronium bromide and fentanyl. Hemodynamic parameters, exhaled tidal volume and peak airway pressures were monitored at 5 minutes, 15 minutes, and every 15 minutes thereafter until 5 minutes before extubation. Intracuff pressures were monitored every half hourly throughout the surgery using a cuff pressure manometer with an extension tubing of 100cm.

At the end of surgery, neuromuscular blockade was reversed and extubation was done when the patient was fully awake and responding to verbal commands. The presence of PEC was noted and graded as: grade 0 is no cough; grade 1 is cough lasting less than 15 seconds; grade 2 is cough lasting more than 15 seconds.[3] Smooth extubation was considered at a PEC grade of 0 or 1. The presence of bucking, laryngospasm, bronchospasm, fall in oxygen saturation (SpO_2), blood staining of ETT; tongue, lip or dental trauma and time of spontaneous ventilation (time between emergence of spontaneous breathing and extubation) were noted.

In the postoperative period, a note was made of laryngotracheal morbidity (cough, sore throat, dysphonia, and dysphagia), pain (assessed by Numeric Rating Scale) and postoperative nausea and vomiting at 1 hour, 8 hours, and 24 hours after surgery. Sore throat was graded as: Grade 0 is no sore throat; Grade 1 is mild (< cold); Grade 2 is moderate (= cold); Grade 3 is severe (> cold).[7] Dysphonia was graded as: Grade 0 is no hoarseness; Grade 1 is mild (noticed by the patient); Grade 2 is moderate (noticed at the time of interview); Grade 3 is severe (aphonia).[7] Dysphagia was graded

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Table 1 Baseline characteristics

	Group S	Group AL1	Group AL2	
	Mean ± SD	Mean ± SD	Mean ± SD	*p*-Value
Age (y)	38.27 ± 12.62	42.97 ± 11.9	43.43 ± 14.33	0.269
Height (cm)	161.47 ± 6.82	161.27 ± 6.83	161.1 ± 6.3	0.977
Sex ratio (F/M)	15/15	16/14	16/14	0.96
Weight (kg)	61.73 ± 7.79	61.67 ± 6.96	61.43 ± 7.05	0.986
ETT size	7.75 ± 0.25	7.73 ± 0.25	7.73 ± 0.25	0.96
Duration of anesthesia	3.73 ± 0.66	4 ± 0.6	3.64 ± 0.71	0.057

as: Grade 1 is able to eat normally; Grade 2 is requires liquids with meals; Grade 3 is able to take only semisolid food; Grade 4 is able to take only liquids; Grade 5 is able to swallow saliva but not liquids; Grade 6 is complete dysphagia.[8]

Statistical Analysis

Navarro et al observed an incidence of cough of 80% in the intracuff saline group and 28% in the intracuff 2% alkalinized lignocaine group.[9] Taking the difference in cough as 30% to 50%, the minimum required sample size with 90% power of study and 5% level of significance is 25 patients in each study group. Data were analyzed using the SPSS latest version software. Quantitative variables were compared using ANOVA/Kruskal–Wallis test between three groups and unpaired *t*-test/Mann–Whitney test (when the data sets were not normally distributed) between two groups. Qualitative variables were compared with chi-square test or Fisher's exact test as indicated. A *p*-value less than 0.05 was considered as statistically significant.

Results

All patients were comparable with respect to age, height, weight, sex, size of ETT inserted and duration of anesthesia (►**Table 1**).

The incidence of coughing and bucking at extubation was significantly higher in Group S when compared to Group AL1 ($p = 0.024$) and Group AL2 ($p = 0.02$) (►**Fig. 2**).

On assessment of laryngotracheal morbidity in the postoperative period, the incidence of coughing at 1 hour after extubation was found to be significantly less in Group AL2 when compared to Group S ($p = 0.021$), and there was no significant difference between the groups at 8 hours and 24 hours, postoperatively (►**Fig. 3**). None of the patients in any of the groups had grade 2 cough.

Sore throat was found to be significantly less with alkalinized lignocaine 1% and alkalinized lignocaine 2% as compared to saline at 1 hour ($p = 0.008$, $p = 0.002$, respectively) and 8 hours ($p = 0.01$, $p = 0.01$, respectively) post extubation. At 24 hours post extubation, the incidence of sore throat was significantly less in Group AL2 as compared to saline ($p = 0.044$). Two patients in group S had grade2 sore throat at this point of time. No significant difference was found between groups AL1 and AL2 (►**Fig. 4**).

Dysphonia was higher in Group S when compared to Group AL1 ($p = 0.016$) and Group AL2 ($p = 0.002$) at 1 hour, in Group S when compared to Group AL2 ($p = 0.03$) at 8 hours and in Group S when compared to Group AL1 ($p = 0.012$) and Group AL2 ($p = 0.012$) at 24 hours. None of the patients had Grade 2 or 3 dysphonia. No significant difference was found between the groups AL1 and AL2 (►**Fig. 5**).

The groups were comparable with respect to dysphagia, pain, and nausea and vomiting at 1 hour, 8 hours, and 24 hours, postoperatively.

No significant difference was found in the intracuff pressures among the three groups from T0 (baseline) to T150

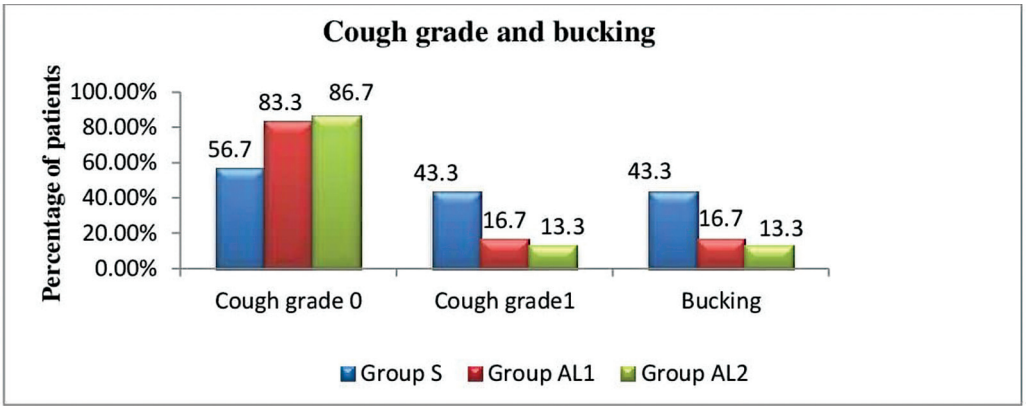

Fig. 2 Comparison of coughing and bucking at extubation among the groups.

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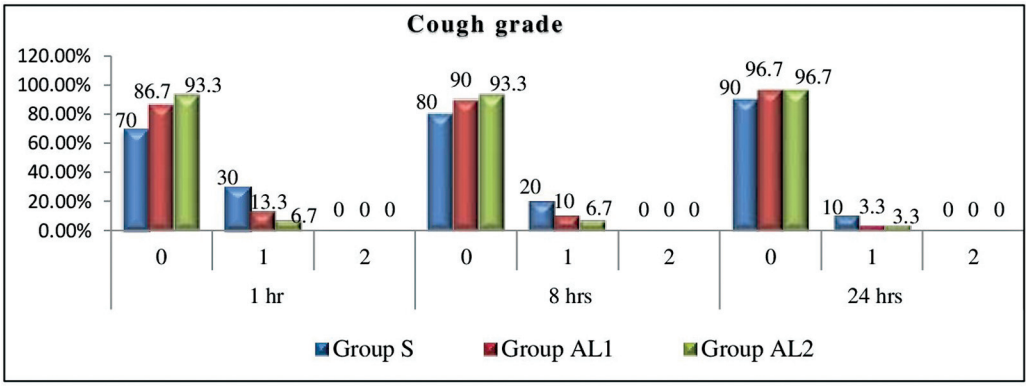
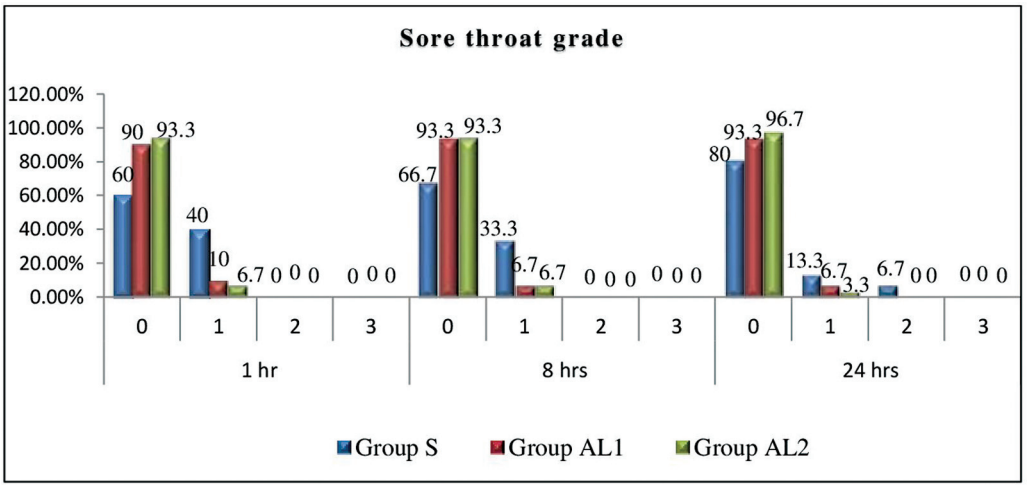


P value = 0.021* at 1 hour (Group S vs Group AL2)

Fig. 3 Comparison of cough among the groups postextubation.



At 1 hour, *p* value = 0.008* (Group S vs Group AL1), *p* value = 0.002* (Group S vs Group AL2)

At 8 hours, *p* value = 0.01* (Group S vs Group AL1 and AL2)

At 24 hours, *p* value = 0.044* (Group S vs Group AL2)

Fig. 4 Comparison of sore throat among the groups postextubation.

(150 min post intubation). The intracuff pressure was significantly higher in Group S at T180 (180 min post intubation) Group S greater than Group AL1 ($p = 0.045$) and Group S greater than AL2 ($p = 0.003$); T210 (210 min post intubation) Group S greater than Group AL1 ($p = 0.004$) and Group S greater than Group AL2 ($p = 0.002$); and T240 (240 min post intubation) Group S greater than Group AL1 ($p = 0.002$) and Group S greater than Group AL2 ($p = 0.011$), as compared with Groups AL1 and AL2 (►**Fig. 6**).

The three groups were comparable with each other with regard to heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, oxygen saturation, exhaled tidal volumes and peak airway pressures intraoperatively. Heart rate was found to be higher with intracuff saline when compared to alkalinized lignocaine 1% and 2% at 3 min, 5 min, and 10 min post extubation (►**Table 2**). On comparing trends in mean arterial blood pressure, it was found to be significantly higher in the saline group at 3 minutes, 5 minutes, 10 minutes, 30 minutes, and 60 minutes post extubation as compared to Groups AL1 and AL2 (►**Table 3**).

The mean time to spontaneous ventilation in Group S was 6.67 ± 1.12 min, in GroupAL1 was 7.07 ± 0.94 min, and in Group AL2 was 6.87 ± 0.9 min. The three groups were comparable with each other ($p = 0.302$).

Also, 100% of the patients had smooth extubation and the groups were comparable with each other ($p = 1.00$). None of the patients had complications such as laryngospasm, bronchospasm, fall in saturation, blood staining of ETT and tongue and lip or dental trauma during extubation.

Discussion

Tracheal intubation with a cuffed endotracheal tube is considered to be standard practice for airway management during general anesthesia. Prolonged surgery may result in an increase in cuff pressure, which hampers tracheal mucosal blood flow and can lead to tracheal ischemia.[10]

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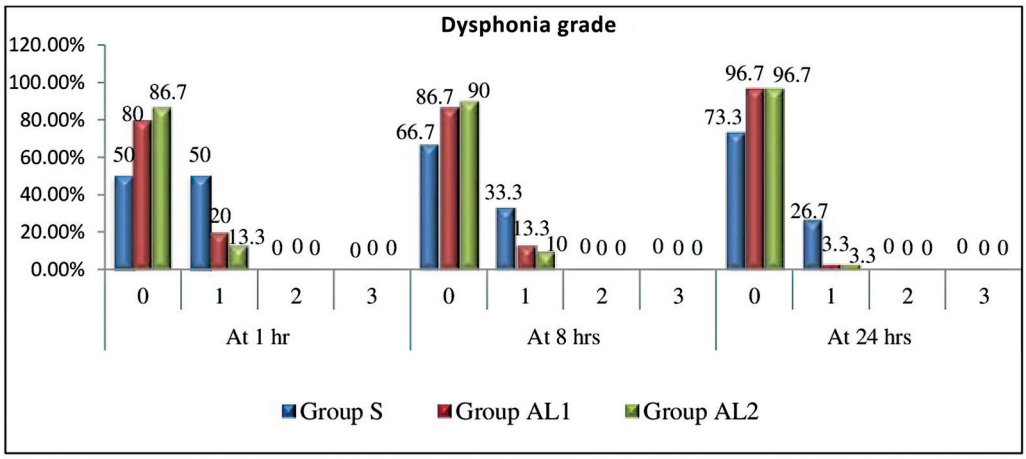

At 1 hour, p value = 0.016* (Group S vs Group AL1), p value = 0.002* (Group S vs Group AL2)

At 8 hours, p value = 0.03* (Group S vs Group AL2)

At 24 hours, p value = 0.012* (Group S vs Group AL1 and AL2)

Fig. 5 Comparison of dysphonia among the groups postextubation.

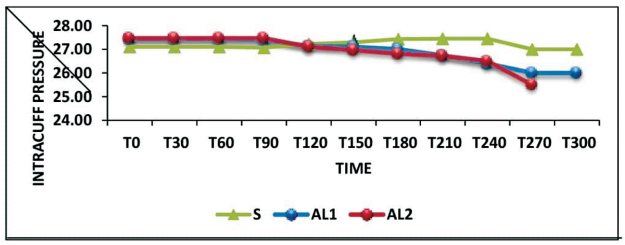

Fig. 6 Trends in intracuff pressure.

Emergence from GA is often associated with hemodynamic sequelae such as tachycardia, hypertension, and laryngotracheal (LT) morbidities such as cough, sore throat, dysphonia and dysphagia. Extubation responses particularly coughing and hypertension can result in an increase in intracranial pressure, which is deleterious in neurosurgical patients.[11] Hence, we should aim for a smooth extubation in such patients. The use of nitrous oxide is one of the factors that results in LT morbidity due to its diffusion into the cuff filled with air leading to an increase in the intracuff pressure.[12] Replacement of intracuff air with liquid media such as saline and lignocaine is one of the measures to decrease the responses post extubation. Alkalinization of lignocaine with sodium bicarbonate increases its diffusion across the ETT cuff and blocks the tracheal pain receptors.[13]

In our study, 1% and 2% alkalinized lignocaine were found to be significantly better than saline for reducing coughing and bucking at extubation, post extubation hemodynamic sequelae and sore throat at 1 and 8 hours and dysphonia at 1 and 24 hours after extubation. Alkalinized lignocaine 2% was significantly better than saline in decreasing the incidence of cough at 1 hour, sore throat at 24 hours and dysphonia at 8 hours after extubation. No significant difference was noted between alkalinized lignocaine 1% and alkalinized lignocaine 2%.

On studying the incidence of coughing and bucking at extubation, it was found that 83.3% of patients in AL1 group, 86.7% in AL2 group, and 56.7% in saline group had no coughing and bucking. Though all patients in our study had a smooth extubation (PEC Grade 0 or 1), difference between the saline and the alkalinized lignocaine groups was statistically significant. Navarro et al did a study on 50 smokers, who were divided into two groups of intracuff saline versus 2% alkalinized lignocaine. The incidence of coughing at extubation was 80% in the saline group and 28% in the alkalinized lignocaine group, with the difference between groups being significant statistically, as was found in our study. The high incidence of coughing in both their study groups can be explained by the exaggerated airway reflexes found in smokers.[9]

In our study, the incidence of coughing was significantly less in the AL2 group, compared with saline, 1 hour postoperatively. No significant differences were noted at any other time intervals. Rizvanovic et al found that the incidence of coughing at 2 hours, 6 hours, and 24 hours postoperatively was 16.7%, 10%, and 6.7%, respectively, with intracuff saline and 13%, 10%, 3.3%, respectively, with 2% alkalinized lignocaine.[14] We observed a similar decreasing trend over time in our study, the incidence of cough at 1, 8, and 24 hours being 30%, 20%, and 10%, respectively, with saline, and 6.8%, 6.7%, and 3.3%, respectively, with 2% alkalinized lignocaine. We did not find any significant differences between Groups AL1 and AL2.

Sore throat was significantly less with 1% and 2% alkalinized lignocaine as compared to saline at 1 hour and 8 hours post extubation. At 24 hours postoperatively, the difference was statistically significant between AL2 and saline. No significant difference was found in sore throat between groups AL1 and AL2. A decreasing trend in the incidence of sore throat at 1 hour, 8 hours, and 24 hours postoperatively was observed with saline, 40%, 33.3%, and 20%, respectively, 1% alkalinized lignocaine, 10%, 6.7%, and 6.7%, respectively, and 2% alkalinized lignocaine, 6.7%, 6.7%, and 3.3%, respectively. A systematic review and meta-analysis by Lam et al demonstrated that intracuff lignocaine was associated with

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Table 2 Trends in heart rate and their intergroup comparison

Heart rate (beats/min)	Group S	Group AL1	Group AL2	*p*-Value	S vs. AL1	S vs. AL2	AL1 vs. AL2
	Mean ± SD	Mean ± SD	Mean ± SD				
Baseline	88.97 ± 10.45	89.27 ± 9.6	85.63 ± 8.7	0.274	1.00	0.551	0.443
Post extubation 1 min	93.53 ± 5.61	90.80 ± 5.2	91.03 ± 4.4	0.077	0.123	0.184	1.00
3 min	89.60 ± 5.21	86.43 ± 4.39	86.07 ± 5.2	0.012*	0.014*	0.011*	1.00
5 min	83.67 ± 4.86	80.40 ± 5.76	80.80 ± 5.07	0.036*	0.021*	0.029*	1.00
10 min	78.43 ± 3.98	75.43 ± 5.4	75.73 ± 4.22	0.024*	0.017*	0.014*	0.8
30 min	73.77 ± 3.32	72.33 ± 4.15	72.0 ± 3.51	0.149	0.406	0.200	1.00
60 min	72.43 ± 3.49	71.87 ± 3.39	72.13 ± 3.6	0.821	1.00	1.00	1.00

Note: *Statistically significant

significantly reduced incidence of postoperative sore throat at 1 and 24 hours.[15] In a study by Rakhi et al, the incidence of sore throat and cough was significantly reduced with intracuff lignocaine when compared to saline.[16]

The incidence of dysphonia was significantly less with alkalinized lignocaine 1% and 2% as compared with saline at 1 hour and 24 hours, and at 8 hours, the difference was significant between AL2 and saline. None of the patients had Grade 2 or Grade 3 dysphonia. No significant difference was found between the groups AL1 and AL2. Our findings are similar to Rizvanovic et al's study who compared intracuff air, saline, and 2% alkalinized lignocaine and found that alkalinized lignocaine had a lower incidence of dysphonia at 2 hours ($p = 0.015$) and 6 hours ($p = 0.001$) post extubation.[14]

The three groups were comparable with respect to dysphagia, pain at the operative site and postoperative nausea and vomiting. This can be explained by the fact that plasma concentrations of lignocaine are negligible with the intracuff route of administration, thus explaining the each of difference between the groups. Plasma levels of lignocaine vary with different routes of administration. With intracuff alkalinized lignocaine, the plasma levels were found to be less than 0.08 µg/mL[17] with IV administration, the levels were about 2 to 3 µg/mL[18] and with topical application, the levels were found to be 0.43 to 1.5 µg/mL.[19] This small plasma concentration with intracuff lignocaine produces a local effect without any systemic effect.

Navarro et al, on comparing intracuff saline with 2% of alkalinized lignocaine observed that the intracuff pressure was significantly less with alkalinized lignocaine by the end of surgery.[9] We had similar findings, as cuff pressures rose significantly higher in the saline group compared to both the alkalinized lignocaine groups, after 150 minutes of induction.

Though there was no difference in haemodynamic variables in the intraoperative period, heart rate was significantly less until 10 minutes and mean arterial pressure till 60 minutes postoperatively, in the alkalinized lignocaine 1% and 2% groups, as compared with saline. Our results are comparable with other studies. Acharya et al found that hemodynamic responses were lower with 4% alkalinized lignocaine when compared with air.[20] They too found a significant difference in heart rate and mean arterial pressures at 30, 60, 90, and 120 minutes following extubation. Soares et al in their study found that postextubation hemodynamic response was less with intracuff alkalinized lignocaine when compared to intracuff air and saline.[21]

Limitations

We did not measure the plasma lignocaine levels to find out the amount of the drug, which diffuses across the cuff.

Table 3 Trends in MAP and their intergroup comparison

MAP (mmHg)	Group S	Group AL1	Group AL2	*p*-Value	S vs. AL1	S vs. AL2	AL1 vs. AL2
	Mean ± SD	Mean ± SD	Mean ± SD				
Baseline	95.80 ± 7.36	91.37 ± 9.94	94.43 ± 9.96	0.472	0.278	0.991	0.277
Post extubation							
1 min	106.97 ± 3.91	104.97 ± 3.94	104.53 ± 4.08	0.069	0.052	0.156	0.384
3 min	103.53 ± 3.20	101.2 ± 4.05	101.17 ± 3.8	0.013*	0.008*	0.014*	0.853
5 min	99.73 ± 3.23	96.17 ± 4.11	95.93 ± 3.67	0.026*	0.012*	0.036*	0.602
10 min	93.77 ± 2.31	91.87 ± 2.92	91.63 ± 2.82	0.013*	0.009*	0.01*	0.922
30 min	91.10 ± 2.09	89.63 ± 3.36	88.17 ± 3.21	0.001*	0.057	0.00*	0.084
60 min	89.80 ± 2.75	87.67 ± 4.18	86.87 ± 4.41	0.021*	0.036	0.006*	0.449

Note: *Statistically significant

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Nitrous oxide was used in the study that can increase theintracuff pressure. This was however obviated by the fact that N_2O was used in all the groups. We measured the intracuff pressure with a manometer manually, which may not give accurate readings.

Conclusion

Intracuff alkalinized lignocaine 1% and 2% were significantly better than saline in decreasing the incidence of haemodynamic changes and coughing and bucking at extubation in patients undergoing neurosurgical procedures. All patients had a smooth extubation and there was no incidence of laryngospasm, bronchospasm, desaturation, bloodstaining of ETT, or trauma. Alkalinized lignocaine 1% and 2% were significantly better than saline in decreasing the incidence of post extubation cough until 1 hour and sore throat and dysphonia until 24 hours postoperatively. There was no significant difference between 1% alkalinized lignocaine and 2% alkalinized lignocaine.

Conflict of Interest
None declared.

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