COMPARISON OF THE EFFECT OF INTRA-CUFF KETAMINE VERSUS ALKALINIZED LIDOCAINE FOR PREVENTION OF POST-OPERATIVE SORE THROAT

Nadeem Naqvi, Arif Iftikhar Mallhi, Ali Asgher, Umer Rafique

Liaquat National Hospital & Medical College, Karachi Pakistan

ABSTRACT

Objective: To determine the Comparison of the effect of intra-cuff ketamine versus alkalinized lidocaine for prevention of post-operative sore throat at a tertiary care hospital at Karachi.

Study Design: Prospective comparative study.

Place and Duration of Study: Liaquat National Hospital & Medical College, Karachi, from Apr to Jul 2018.

Methodology: After taking informed written consent, severity of post operative sore throat pain, cough, hoarseness, laryngeal spasm & changes in heart rate & blood pressure was assessed and compared among patients undergoing General anesthesia with end tracheal intubation.

Results: A total of 70 participants who were going under general anesthesia with endotracheal intubation as per inclusion criteria were included. Patients were divided into two groups, group K (intra-cuff ketamine) and group LA (alkalinized lidocaine). Severity of sore throat pain, cough, hoarseness, laryngeal spasm, and changes in heart rate & blood pressure were noted less commonly in ketamine group as compare to group Lidocaine Alkalinized (p>0.05).

Conclusion: Intra-cuff alkalinized lidocaine significantly attenuated the severity of post, cough, hoarseness & laryngeal spasm especially in the early post-operative period, as compare to intra-cuff ketamine.

Keywords: Alkalinized lidocaine, Ketamine, Post-operative sore throat.

INTRODUCTION

Post-operative sore throat (POST) occurs in 21-65% of patients receiving general anesthesia (GA) with tracheal intubation[1,2]. Though considered as a minor complication, but it may cause significant post-operative morbidity and patient dissatisfaction[3]. Various non-pharmacological and pharmacological trials have been used for attenuating POST with no proven single modality. The pharmacological methods used to reduce POST include use of beclomethasone gel, gargling with azulenesulphonate, ketamine and licorice, intra-cuff ketamine & alkalinized lidocane[4-6]. Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist and has been used as a gargle for reducing the incidence and severity of POST due to its anti-nociceptive and anti-inflammatory effects[6,7].

Previous studies with in vitro and in vivo approaches that used large doses (200-500 mg) of lidocaine hydrochloride (L-HCl) instead of saline have shown that L-HCl could slowly diffuse through the cuff, and this could be dangerous if the cuff ruptured[8,9]. The purpose of our study was to evaluate the effectiveness of endotracheal intracuff lidocaine vs alkalinized lidocaine in reducing the POST. POST happens in 21-65% of patients accepting GA with tracheal intubation[1,2]. However considered as a minor complexity, yet it might cause huge post-ope-rative dismalness and persistent dissatisfaction[3]. Diffe-rent non-pharmacological and pharmacological preli-minaries have been utilized for weakening POST with no demonstrated single methodology.

The pharmacological strategies used to diminish POST incorporate utilization of beclomethasone gel, swishing with azulenesulphonate, ketamine and licorice, intra-cuff ketamine and alkalinized lidocaine[4-6]. Ketamine is a NMDA receptor foe and has been utilized as a wash for lessening the occurrence and seriousness of POST because it's enemy of nociceptive and calming effects[6,7].

Past investigations with in vitro and in vivo approaches that utilized substantial dosages (200-500 mg) of lidocaine hydrochloride (L-HCl) rather than saline have demonstrated that L-HCl could gradually diffuse through the sleeve, and this could be perilous if the cuff ruptured[8,9]. The motivation behind our examination was to assess the viability of endotracheal intracuff lidocaine versus alkalinized lidocaine in diminishing the POST.

METHODOLOGY

This prospective comparative study was conducted by the department of anesthesiology, Liaquat

Correspondence: Dr Ali Asgher, Department of Anesthesiology, Liaquat National Hospital, Karachi Pakistan

Received: 31 Jan 2019; revised received: 01 Jul 2020; accepted: 07 Jul 2020

National Hospital and Medical College, Karachi, after the approval of the study from the Institutional Ethical Board, from April to July 2018. Non-probability (consecutive sampling technique was used using formula N=Z) 2 *p*(1-P) /d2 with confidence level = 95% and Power of d=80% with incidence of POST (with intra-cuff) ketamine versus alkalinized lidocaine = 34% vs 56%. The study was conducted. Once an eligible patient has been identified in the preoperative round meeting the inclusion and exclusion criteria, the study details were carefully discussed with the potential subject and informed consent attained. Randomization was done using a lottery method for the selected patient. If the patient was illiterate, then the informed consent form was read to the patient and if consent was given, it was signed and dated by an impartial witness who was independent of the Principal Investigator.

A performa was filled by the investigator as a data collecting tool for preoperative and postoperative assessment. A total of total 70 patients were selected using a non-probability consecutive sampling technique. Group were allocated randomly as group K & group LA using a lottery method. Once the patient was identified then General Anesthesia was given using induction dose of propofol 2-3 mg/kg , nalbuphine 0.1 mg/kg and atracurium 0.5 mg/kg and patients were intubated with 7.0 mm size ETT for females and 8.0 mm size ETT for male patients. All intubations were performed by an anesthesiologist with minimum of two year experience. ETT cuff was inflated by using Ketamine 2.5% in Normal Saline in group K and 2% lidocaine with 8.4% Sodium bicarbonate in LA group till the air leak was diminished. After surgery patient was assessed on extubation for any emergence phenomena and then were assessed for 1st 6th 12th and 24th hour post surgery for outcome. The assessment was done by the on call anesthesiology resident who was blinded of the study group. Any patient who developles post-operative sore throat was given dexamethasone 8 mg IV stat and advised warm normal saline gargles.

Principal investigator recorded all clinical history demography on a perfoma that was already designed, Informed on paper consent was taken before enrollment. Exclusion criteria was firmly followed to avoid confounding variables.

For analyzing the data SPSS-22 was used. Mean and standard deviation was computed for calculation of quantitative variables like age and for qualitative variables i.e. gender and paraprotienemia. Frequency and percentage was calculated. Chi-square test was applied for post satisfication; *p*-value ≤0.05 was taken as significant.

RESULTS

A total of 70 participants who were undergoing General anesthesia with endotracheal intubation as per inclusion criteria were included in our study. Patients were randomly divided into two groups, group K patients were given intra-cuff ketamine and group LA patients were given alkalinized lidocaine and assessed by severity of post operative sore throat, cough, Hoarseness, laryngeal spasm, heart rate & blood pressure.

Group 'K' included 35 subjects of which 20 (57%) were male while 15 (43%) were female, with mean age of 36.51 ± 14.13 years, group 'LA' also included 35 patients of which 21 (60%) were male while 14 (40%) were female, with mean age 36.29 ± 14.6 years as shown in table-I. The overall mean age came out to be 36.40 ± 14.26 years as shown in table-I.

Table-I: Age and gender distribution in two study groups.

Age 2 ± Groups	Kalimine Group	Alkalinized Lidocaine Group	*p*-value
Mean ± SD (years)	36.51 ± 14.13	36.29 ± 14.6	0.624
Gender			
Male	20 (57%)	21 (60%)	0.806
Female	15 (43%)	14 (40%)	

In our study the co-morbids in group K were diabetes mellitus (DM) in 2 (6%), hypertension in 4 (11%), Breast carcinoma in 1 (3%), hepatitis C in 1 (3%), Hypertension/Asthma in 1 (3%), Hypertension/Parkinson's disease in 1 (3%), No known co-morbids in 25 (71%), while in group LA Diabetes mellitus (DM) in 1 (3%), hypertension in 2 (6%), Breast carcinoma in 0 (0%), Hepatitis C in 0 (0%), Hypertension/Asthma in 1 (3%), DM/Hypertension 2 (6%), No known co-morbids in 27 (77%), as shown in table-II.

Severity of sore throat pain in group K at 15 minutes was mild in 10 (28.5%) & no pain in 25 (71.5%), at 1 hour was mild in 8 (22.8%) & no pain in 27 (77.1%), at 3 hours was mild in 2 (5.7%) & no pain in 33 (94.3%) & 24 hours was mild in 0 (%) & no pain in 35 (100%), while in group LA severity of sore throat pain at 15 minutes was mild in 10 (28.5%) & no pain in 25 (71.5%), at 1 hour was mild in 2 (5.7%) & no pain in 33 (94.3%), at 3 hours was mild in 2 (5.7%) & no pain in 33 (94.3%) & 24 hours was mild in 0 (0%) & no pain in 35 (100%) as shown in table-III.

Cough in group Kat 15 minutes post operatively was noted in 4 (11.5%), at 1 hour in 3 (8.5%), at 3 hours in 0 (0%) & at 24 hours in 1 (2.8%), while in group LA at 15 minutes post operatively was noted in 9 (25.7%), at 1 hour in 5 (14.2%), at 3 hours in 0 (0%) & at 24 hours was noted in none patient 0 (0%), as shown in table-III.

Hoarseness was only noted in group K at 15 minutes in 1 (2.8%), at 1 hour in 1 (2.8%), not noted at 3 hours & at 24 hours, while in group LA also noted at

Table-II: Co-morbids distribution in two study groups.

Co-Morbids	Kalimine Group	Alkalinized Lidocaine Group	*p*-value
Diabetes mellitus (DM)	2 (5.7%)	1 (2.8%)	0.806
Hypertension	4 (11.4%)	2 (5.7%)	
Breast carcinoma	1 (2.8%)	1 (2.8%)	
Hepatitis C	1 (2.8%)	1 (2.8%)	
Hypertension/Asthma	1 (2.8%)	1 (2.8%)	
Hypertension/Parkinson's disease	1 (2.8%)	-	
Diabetes Mellitus/ Hypertension	-	2 (5.7%)	
No known co-morbids	25 (71.4%)	27 (77.1%)	

Table-III: Severity of pain at 15 minutes, 1 hour, 3 hours & 24 hours, Cough at 15 minutes, 1 hour, 3 hours & 24 hours distribution with is study groups.

Severity of Sore Throat Pain	Kalimine Group		Alkalinized Lidocaine Group		*p*-value
	Mild pain	No Pain	Mild pain	No Pain	
15 minutes	10 (28.5%)	25 (71.5%)	10 (28.5%)	25 (71.5%)	1.000
1 hour	8 (22.8%)	27 (77.2%)	2 (5.7%)	33 (94.3%)	0.04
3 hours	2 (5.7%)	33 (94.3%)	2 (5.7%)	33 (94.3%)	1.000
24 hours	-	35 (50%)	-	35 (50%)	1.000
Cough	**Kalimine Group**		**Alkalinized Lidocaine Group**		
	Yes	**No**	**Yes**	**No**	
15 minutes	4 (11.5%)	31 (88.5%)	9 (25.7%)	26 (74.3%)	0.12
1 hour	3 (8.57%)	32 (91.43%)	5 (14.3%)	30 (85.7%)	0.70
3 hours	-	35 (50%)	-	35 (50%)	1.000
24 hours	1 (2.8%)	34 (97.2%)	-	35 (50%)	0.999
Hoarseness	**Kalimine Group**		**Alkalinized Lidocaine Group**		
	Yes	**No**	**Yes**	**No**	
15 minutes	1 (2.8%)	34 (97.3%)	1 (2.8%)	34 (97.2%)	1.000
1 hour	1 (2.8%)	34 (97.2%)	1 (2.8%)	34 (97.2%)	1.000
3 hours	-	35 (50%)	-	35 (50%)	1.000
24 hours	-	35 (50%)	-	35 (50%)	1.000
Laryngeal Spasm	**Kalimine Group**		**Alkalinized Lidocaine Group**		
	Yes	**No**	**Yes**	**No**	
15 minutes	1 (2.8%)	34 (97.2%)	3 (8.5%)	32 (91.5%)	0.62
1 hour	-	35 (50%)	-	35 (50%)	1.000
3 hours	-	35 (50%)	-	35 (50%)	1.000
24 hours	-	35 (50%)	-	35 (50%)	1.000

Table-IV: Pre-operative heart rate, heart rate at 15 minutes, 1 hour, 3 hours & 24 hours.

Heart Rate	Kalimine Group		Alkalinized Lidocaine Group		*p*-value
	57-85	86-135	57-85	86-135	
Pre-operative heart rate	16 (45.7%)	19 (54.3%)	13 (37.2%)	22 (62.8%)	0.47
Mean heart rate	88.20 ± 18.52		86.97 ± 11.12		
Post operative at 15 minutes	11 (31.4%)	24 (68.6%)	5 (14.3%)	30 (85.7%)	0.090
Mean & standard deviation	89.86 ± 12.79		96.83 ± 11.28		
At 1 hours	16 (45.7 %)	19 (54.3%)	7 (20%)	28 (80%)	0.020
Mean & standard deviation	86.63 ± 13.25		91.34 ± 8.26		
At 3 hours	20 (57.1%)	15 (42.9%)	15 (42.9%)	20 (57.1%)	0.230
Mean & standard deviation	84.60 ± 13.27		88.74 ± 8.90		
At 24 hours	25 (71.4%)	10 (28.6%)	14 (40%)	21 (60%)	0.010
Mean & standard deviation	81.74 ± 12.14		87.44 ± 8.21		

15 minutes in 1 (2.8%), at 1 hour in 1 (2.8%), not noted at 3 hours & at 24 hours, as shown in table-III.

Laryngeal spasm was only noted at 15 minutes in group K in 1 (2.8%), while in group LA in 3 (8.57%), it was not noted at 1 hour, at 3 hours & at 24 hours, as shown in table-III.

The mean heart rate in group K, per operatively was 88.20 ± 18.52 b/min, post operatively at 15 mins was 89.86 ± 12.79, at 1 hours 86.63 ± 13.25, at 3 hours 84.60 ± 13.27 & at 24 hours was 81.74 ± 12.14, while in group LA heart pre operatively was 86.97 ± 11.11, at 15 mins was 96.83 ± 11.28, at 1 hour 91.34 ± 8.26, at 3 hours 88.74 ± 8.90 & at 24 hours was 87.44 ± 8.21, as shown in table-IV. Blood pressure in both groups pre operatively, at 15 minutes, 1 hour, 3 hours & at 24 hours is given in table-V.

Table-V: Pre-operative blood pressure, blood pressure at 15 minutes, 1 hour, 3 hours & 24 hours distribution with in the study groups.

Blood Pressure	Kalimine Group		Alkalinized Lidocaine Group		*p*-value
	100/50-140/90	141/91-170/118	100/50-140/90	141/91-170/118	
Pre-operative blood pressure	27 (77.1%)	8 (28.9%)	29 (82.9%)	6 (17.1%)	0.540
Post operative blood pressure at 15 minutes	30 (85.7%)	5 (14.3%)	23 (65.7%)	12 (34.3%)	0.050
At 1 hours	29 (82.9%)	6 (17.1%)	29 (82.9%)	6 (17.1%)	1.000
At 3 hours	33 (94.3%)	2 (5.7%)	32 (91.4%)	3 (8.6%)	0.999
At 24 hours	32 (91.4%)	3 (8.6%)	32 (91.4%)	3 (8.6%)	1.000

DISCUSSION

Many of the general anesthetic procedures in the modern anesthetic practice are carried out with endotracheal intubation. Post-operative sore throat is a well recognized minor complication after general anesthesia[10], rated by patients as the 8th most undesirable outcome in the post-operative period[11]. Prophylactic management for decreasing its frequency and severity is still recommended to improve the quality of post anesthesia care though the symptoms resolve spontaneously without any treatment[12]. POST is a parsimonious description representing a broad constellation of signs and symptoms of laryngitis, tracheaitis, hoarseness, cough or dysphagia[11], with incidence varying from 14.4-100% after endotracheal intubation[10]. Research indicates that POST can be attenuated using a multi model approach consisting of pharmacological and non-pharmacological interventions. Identification of the factors associated with an increased risk of POST will allow anesthesia providers to avoid combination of controllable factors, decrease the incidence of POST and improve patients' anesthetic outcome. Many pharmacological interventions like steroids and non-steroidal anti-inflammatory drugs, lignocaine, have been used to attenuate POST by various authors. But all such maneuvers had their own limitations. Ketamine is in the middle of the affinity range of the uncompetitive NMDA antagonists which has been found by various authors to attenuate POST[12]. An increasing amount of experimental data shows that NMDA receptors are found not only in central nervous system but also in the peripheral nerves. Peripherally administered NMDA receptor antagonists are involved with anti-nociception and anti-inflammatory cascade[13], by reducing NFK beta activity and TNF alpha production[14], expression of inducible nitric oxide synthase[15], serum C-reactive protein IL-6 and IL-10[16].

In the present examination, the rate of POST at 3 and 24 hours was diminished significantly, and the constriction of seriousness of POST happened in the both groups however more generally in ketamine group at 15 minutes and 1 hour. The instrument of impact was potentially the topical impact of intra-cuff ketamine that lessened the nearby inflammation[17]. Writing bolsters the topical impact of ketamine by means of its NMDA-hostile activity and mitigating impact dependent on creature demonstrate data[18]. Ketamine is a NMDA receptor foe with the essential site of activity in the focal sensory system, and parts of the limbic framework while its utilization by means of nasal course, rinse, and rectal course proposes its fringe effect[19]. Trial creature thinks about have demonstrated a defensive impact on airway inflammatory damage with ketamine[20].

The utilization of a little measurement of alkalized L-HCl uniquely enhanced ETT resistance amid a more delayed time frame. The utilization of alkalinized neighborhood soporifics in the ETT cuff offers the upsides of negligible pressure reaction to smooth extubation and hack free development. No cuff break was recorded in our examination which is like Estebe *et al*[21], think about and different previous studies[22-25]. This

outcome affirmed that presentation of lidocaine isn't injurious for the cuff. Previous researches[22-25], have demonstrated that L-HCl set inside the cuff of an ETT can gradually diffuse through its hydrophobic structure.

Severity of sore throat pain in group K at 15 minutes was mild in 10 (28.5%) & no pain in 25 (71.5%), at 1 hour was mild in 8 (22.8%) & no pain in 27 (77.1%), at 3 hours was mild in 2 (5.7%) & no pain in 33 (94.3%) & 24 hours was mild in 0 (%) & no pain in 35 (100%), while in group LA severity of sore throat pain at 15 minutes was mild in 10 (28.5%) & no pain in 25 (71.5%), at 1 hour was mild in 2 (5.7%) & no pain in 33 (94.3%), at 3 hours was mild in 2 (5.7%) & no pain in 33 (94.3%) & 24 hours was mild in 0 (0%) & no pain in 35 (100%), as compare to one previous study in which overall postoperative sore throat was less in Ketamine group with 17 (34%) patients when compared to Alkalinized lidocaine group with 28 (56%) patients complaining of it with p=0.043.

STUDY LIMITATION

The main limitation was the small sample size. There were also different Anesthesiologists involved. Only 200 patients were enrolled in this study due to incomplete data, missing case notes or exclusion criteria.

CONCLUSION

Intra-cuff alkalinized lidocaine significantly attenuated the severity of POST, cough, hoarseness & laryngeal spasm especially in the early post-operative period, as compare to intra-cuff ketamine.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Higgins PP, Chung F, Mezei G. Postoperative sore throat after ambulatory surgery. Br J Anaesth 2002; 88(4): 582–84.
2. Loeser EA, Bennett GM, Orr DL, Stanley TH. Reduction of postoperative sore throat with new endotracheal tube cuffs. Anesthesiol 1980; 52(1): 257–59.
3. Macario A, Weinger M, Carney S, Kim A. Which clinical anesthesia outcomes are important to avoid. The perspective of patients. Anesth Analg 1999; 89(1): 652–58.
4. Sumathi PA, Shenoy T, Ambareesha M, Krishna HM. Controlled comparison between betamethasone gel and lidocaine jelly applied over tracheal tube to reduce postoperative sore throat, cough, and hoarseness of voice. Br J Anaesth 2008; 100(2): 215–18.
5. Ogata J, Minami K, Horishita T. Gargling with sodium azulene sulfonate reduces the postoperative sore throat after intubation of the trachea. Anesth Analg 2005; 101(1): 290–93.
6. Canbay O, Celebi N, Sahin A, Celiker V, Ozgen S, Aypar U. Ketamine gargle for attenuating postoperative sore throat. Br J Anaesth 2008; 100(1): 490–93.
7. Zhu MM, Zhou QH, Zhu MH, Rong HB, Xu YM, Qian YN, et al. Effects of nebulized ketamine on allergen-induced airway hyperresponsiveness and inflammation in actively sensitized Brown-Norway rats. J Inflamm (Lond) 2007; 4(1): 10-12.
8. Fagan C, Frizelle HP, Laffey J. The effects of intracuff lidocaine on endotracheal-tube-induced emergence phenomena after general anesthesia. Anesth Analg 2000; 91(1): 201–5.
9. 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(1): 436–42.
10. Hung NK, Wu CT, Chan SM, Lu CH, Huang YS, Yeh CC, et al. Effect on postoperative sore throat of spraying the endotracheal tube cuff with benzydamine hydrochloride, 10% lidocaine, and 2% lidocaine. Anesth Analg 2010; 111(1): 882–86.
11. Agarwal A, Nath SS, Goswami D, Gupta D, Dhiraaj S, Singhet PK. An evaluation of the efficacy of aspirin and benzydamine hydrochloride gargle for attenuating postoperative sore throat: a prospective, randomized, single blind study. Anesth Anal 2006; 103(4): 1001-3.
12. Canbay O, Celebi N, Sahin A, Celiker V, Ozgen S, Aypar U. Ketamine gargle for attenuating postoperative sore throat. British J Anaesth 2008; 100(4): 490–93.
13. Scuderi PE. Post-operative sore throat: more questions than answers. Anesth-Analgesia 2010; 111(4): 831-33.
14. Christensen AM, Willemoes-Larsen H, Lundby L, Jakobsen KB. Postop throat complaints after tracheal intubation.Br J Anaesth 1994; 73(6): 786-87.
15. Keller C, Sparr HJ, Brimacombe JR. Laryngeal mask lubrication–a comparative study of saline versus 2% lignocaine gel with cuff pressure control. Anaesth 1997; 52(1): 586-2.
16. Loerser EA, Bennett GM, Orr DL, Stanley TH. Reduction of postoperative sorethroat with new endotracheal tube cuffs. Anesthesiol 1980 ; 52(3): 257-59.
17. Khatavkar SS, Bakhshi RG. Comparison of nasal midazolam with ketamine versus nasal midazolam as a premedication in children. Saudi J Anaesth 2014; 8(1): 17–21.
18. Damle SG, Gandhi M, Laheri V. Comparison of oral ketamine and oral midazolam as sedative agents in pediatric dentistry. J Ind Soc Pedod Prev Dent 2008; 26(1): 97–00.
19. Hirota K, Lambert DG. Ketamine: New uses for an old drug. Br J Anaesth 2011; 107(2): 123-26.
20. Zhu MM, Qian YN, Zhu W, Xu YM, Rong HB, Ding ZN, et al. Protective effects of ketamine on allergen-induced airway inflammatory injure and high airway reactivity in asthma: Experiment with rats. Zhonghua Yi Xue Za Zhi 2007; 87(19): 1308–13.
21. Estebe JP, Dollo G, Le Corre P, Le Naoures A, Chevanne F, Le Verge R, et al. Alkalinization of intracuff lidocaine improves endotracheal tube-induced emergence phenomena. Anesth Analgesia 2002; 94(1): 227-30.
22. Sconso JM, Moscicki JC, Difazio CA. In vitro diffusion of lidocaine across endotracheal tube cuffs. Reg Anesth 1990; 15(1): 37-40.
23. Navarro RM. Lidocaine in the endotracheal tube cuff reduces postoperative sore throat. J Clin Anesth 1997; 9(5): 394–97.
24. Fagan C, Frizelle HP, Laffey J. The effects of intracuff lidocaine on endotracheal-tube-induced emergence phenomena after general anesthesia. Anesth Analg 2000; 91(1): 201–5.
25. 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(7): 436–42..