

## Comparison of ketamine nebulisation with ketamine gargle in attenuating post-operative sore throat

Bhagyashree Amingad<sup>1,\*</sup>, Shruthi Jayaram<sup>2</sup>

<sup>1,2</sup>Assistant Professor, Dept. of Anaesthesiology, Hassan Institute of Medical Sciences, Hassan

\*Corresponding Author:

Email: cooldubhagya@gmail.com

### Abstract

**Background & Objective:** Sore throat is a common morbidity following tracheal intubation in the post operative period. Our aim was to compare ketamine nebulisation with ketamine gargle to see the effectiveness of nebulisation over gargle in reducing the incidence and severity of post operative sore throat (POST).

**Methods:** In this prospective, randomized study 80 patients between 20-60 year, of either sex belonging to ASA I/II, scheduled for elective surgery under general anaesthesia, were assigned into two groups of 40 patients each. Group GK received preservative free ketamine 50mg in 29 ml of saline, gargled for 30 seconds and Group NK received ketamine 50 mg in 4ml of normal saline via nebulisation for 15 min. General anaesthesia was induced 5 min later in both the groups. Postoperatively sore throat was assessed at 0, 2, 4, 24 hrs using four point scale(0-3).

**Results:** The incidence of POST at 0, 2, 4, 24 hrs was 27%, 25%, 20% and 17% respectively in GK group and 20%, 17.5%, 12.5% and 7.5% in NK group respectively with no statistical difference between the two. Both the groups showed more than 50% reduction from the reported incidence of 21-65% of POST. None of the patients in either group experienced severe sore throat.

**Conclusion:** Ketamine nebulisation is an effective alternative to ketamine gargle in attenuating POST.

**Key words:** Ketamine gargle, Ketamine nebulisation, Post-operative sore throat, Endotracheal intubation, General anaesthesia.

Access this article online	
Quick Response Code:	Website:
	www.innovativepublication.com
	DOI: 10.5958/2394-4994.2016.00060.3

### Introduction

Post-operative sore throat (POST) is ranked by American anaesthesiologist as the 8<sup>th</sup> most undesirable subjective complaint following general anaesthesia.<sup>1</sup> It has a incidence of 21-65%.<sup>2,3</sup> In this era of quality care, factors responsible for post-operative morbidity and patient dissatisfaction have to be taken care of. It has been postulated that the POST is due to mucosal injury in the trachea<sup>4</sup> and other factors like oropharyngeal suctioning, intra cuff pressure, use of throat pack, size of the endotracheal tube, duration of surgery, difficult in intubation, also contribute as risk factors for post-operative sore throat.<sup>5,6,7</sup> To overcome this problem many studies have been conducted using various non-pharmacological and pharmacological methods to attenuating POST but with variable success.

Ketamine a phencyclidine derivative is a non-competitive antagonist of N –Methyl D Aspartic acid (NMDA) receptor.<sup>8</sup> NMDA receptor are found not only in the central nervous system(CNS) but also in the peripheral nerves. Experimental studies show that peripherally administered NMDA receptor antagonists

are involved with anti-nociception and anti-inflammatory cascade, thus preventing POST.<sup>9</sup>

Many studies have been conducted, showing the effectiveness of ketamine gargle<sup>10-13</sup> in reducing sore throat, however the larger volume used may carry the risk of aspiration if accidentally swallowed and the bitter taste of ketamine is unpleasant, for the patients. Nebulisation<sup>14</sup> is another mode of delivering ketamine which can overcome the bitter taste and large volume used for gargling. Hence we intended to compare incidence and severity of POST between ketamine gargle and ketamine nebulisation.

### Materials and Methods

This prospective randomized study was conducted after obtaining approval from the Institutional Ethical Committee. Written informed consent was taken from 80 patients belonging to ASA physical status I and II, in the age group of 20 to 60 year of either sex. Patients undergoing elective surgeries under general anaesthesia in supine position, lasting up to 2 hours were included. Patients with history of pre-operative sore throat, asthma, COPD, smoking, recent non-steroidal anti-inflammatory drug intake, patients with Mallampatti grade more than 2, those who required more than 1 attempt of intubation and in whom intubation time taken was greater than 20 seconds were excluded from the study. Detailed pre-operative anaesthetic check-up was done a day before the surgery and patients were pre-medicated with tab diazepam 10 mg orally at night. Patients were randomized into two groups(Group GK and Group NK) with 40 patients in each group using help of computer generated random number tables in

opaque envelope prepared by the anesthesiologist not involved in the study.

Group GK (gargled ketamine) received 30ml of gargle solution containing 1ml ketamine 50mg in 29 ml of normal saline by the operation theater nurse. Patients were asked to gargle for 30 sec in 2 divided parts as to prevent chances of swallowing the large volume.

In Group NK (nebulised ketamine) patients received 1ml ketamine 50mg in 4 ml of normal saline for nebulisation for 15 min through the wall mounted oxygen source (8L, 50PSI).

Patients could not be blinded because of the different route of administration of the two preparations. Anaesthesia was induced after 5 min in both the groups.

Patients were connected to standard anaesthesia monitors ECG, Pulse Oxymeter, non-invasive blood pressure, end tidal carbon di oxide. Patients were pre-oxygenated with 100% oxygen for 3 mins and pre-medicated with inj glycopyrolate 4µg/kg, inj midazolam 0.03mg/kg. Anaesthesia was induced with inj fentanyl 2µg/kg and inj propofol 2mg/kg. Tracheal intubation was facilitated by vecuronium bromide 0.1mg/kg, done by anaesthesiologist with more than 5 years of experience. Trachea was intubated with sterile soft seal cuffed poly vinyl chloride tube, with internal diameter of 7-7.5 mm for females and 8-8.5 mm for males lubricated with lignocaine jelly 2%. Throat packing and oral airway were avoided. General anaesthesia was maintained with oxygen 33% in air and supplemented with halothane. The cuff was inflated with air and the pressure in the cuff was maintained between 20 to 22 cm of water using pressure manometer. The peak airway pressure was maintained below 25cm of water. To prevent the mucosal dryness we used heat and moisture exchanger (HME). Intra operatively analgesia was supplemented with inj fentanyl. Inj ondansetron 4mg and inj dexamethasone 8mg was given 30 min before completion of surgery. At the end of the surgery oropharynx was suctioned gently under visualization, halothane was turned off, O<sub>2</sub> concentration was increased to 100%. Neuromuscular blocked was reversed with inj neostigmine 50µg/kg and inj glycopyrolate 10µg/kg. After the extubation criteria were met, patients were extubated. Patients who coughed and bucked during extubation were excluded from the study. All patients received inj paracetamol 1gm iv in the post-operative ward and repeated 6<sup>th</sup> hourly to control pain.

Post-operative ward patients were interviewed for sore throat by a blinded investigator at 0 hr (on arrival to post operative room), 2nd hr, 4<sup>th</sup> hr, 24hr. POST was graded on four point scale (0-3).<sup>15</sup>

0=no sore throat,

1= mild sore throat (upon asking patients complains of sore throat),

2= moderate sore throat (patient himself complains of sore throat).

3=severe sore throat (hoarseness of voice)

### Statistical Methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumptions on data is made, **Assumptions:** 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. LevenIs test for homogeneity of variance has been performed to assess the homogeneity of variance.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant Fig.

+ Suggestive significance (P value: 0.05<P<0.10)

\* Moderately significant (P value: 0.01<P ≤ 0.05)

\*\* Strongly significant (P value: P≤0.01)

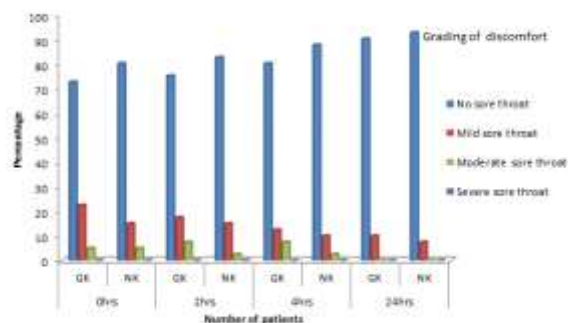


Fig. 1: Severity of Post

### Statistical software

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate Graphs, Tables.

### Results

The study population consisted of 80 patients, 40 patients in gargled ketamine (GK group) and 40 patients in nebulisation group (NK group). There were no significant differences in the groups in terms of age, gender body weight, duration of anaesthesia (Table 1)

**Table 1: Demographic data**

Groups	GK(n=40)	NK(n=40)	P-Value
Age(yr)	40.18±10.93	40.70±12.85	0.844
Sex(F:M)	29:11	25:15	0.340
Weight(Kg)	55.30±6.65	56.30±5.82	0.476
Duration of anaesthesia(min)	120.63±8.58	123.00±9.07	0.233

In group GK the incidence of postoperative sore throat at 0, 2, 4, and 24 hrs was 27.5%, 25%, 20% and 10% respectively. At corresponding time point in group NK it was 20%, 17.5%, 12.5% and 7.5%. (Table 2). The difference between the groups were not significant statistically.

**Table 2: Inter group comparison of incidence and severity of post-operative sore throat (POST)**

Grading of discomfort	Number of patients							
	0hrs		2hrs		4hrs		24hrs	
	GK (n=40)	NK (n=40)	GK (n=40)	NK (n=40)	GK (n=40)	NK (n=40)	GK (n=40)	NK (n=40)
No sore throat	29(72.5%)	32(80%)	30(75%)	33(82.5%)	32(80%)	35(87.5%)	36(90%)	37(92.5%)
Mild sore throat	9(22.5%)	6(15%)	7(17.5%)	6(15%)	5(12.5%)	4(10%)	4(10%)	3(7.5%)
Moderate sore throat	2(5%)	2(5%)	3(7.5%)	1(2.5%)	3(7.5%)	1(2.5%)	0(0%)	0(0%)
Severe sore throat	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Total no of patients having post	11(27.5%)	8(20%)	10(25%)	7(17.5%)	8(20%)	5(12.5%)	4(10%)	3(7.5%)
P value	0.804		0.685		0.677		1.000	

Regarding severity among the groups, in group GK at 0, 2, 4, 24 hrs mild sore throat was observed in 9, 7, 5, 4 patients respectively and moderate sore throat was observed in 2, 3, 3, 0 patients respectively. In NK group at 0, 2, 4 24 hrs mild sore throat was observed in 6, 6, 4 and 3 patients respectively and moderate sore throat in 2, 1, 10 patients respectively. No significant differences in mild and moderate sore throat were noted among the groups. None of the patients in both group had severe sore throat. No systemic side effects were noted in both groups.

## Discussion

Post operative sore throat, a common complication of general anaesthesia contributes to postoperative morbidity in the patients. Along with causing discomfort to the patient, it prolongs the post-operative stay by 14 minutes compared with people who did not complain of POST.<sup>16</sup> The overall incidence of POST is 21- 65%.<sup>2,3,17</sup> Many studies have shown that gargling with ketamine prior to induction is one of the effective means of reducing the incidence and severity of POST by 50% and only one study on pre induction nebulised ketamine had shown decreased in the incidence of POST. The present study is done to compare the effectiveness of preoperative ketamine gargle (group GK) with preoperative ketamine nebulisation (group NK) in reducing the incidence and severity of POST.

POST is found to be peak at 2 to 4 hrs.<sup>18</sup> By this time the patients are completely conscious and more cooperative to participate in the study. In our study the incidence of POST at 2hr was 25% and 17.5% in GK

and NK group respectively and at 4hr it was 20% and 12.5% in GK and NK groups respectively (Table 2). These observations showed more than 50% reduction in the incidence of sore throat from the reported incidence of 21-65%. Our study is in accordance with many other studies which had showed the decrease in incidence of POST.<sup>10-14</sup> Though the incidence of sore throat is less in NK group than in GK group, there was no statistical significance difference between the groups. Comparing the severity of POST in both groups, we observed that among the patients who had sore throat, were more of mild degree than moderate. We did not find any patients having severe sore throat at any time point in both groups. (Table 2)

The mechanism of attenuating the sore throat was possibly due to the tropic effect of ketamine either given by gargle or by nebulisation which attenuated the local inflammation of the airway. Literature supports the peripheral effect of ketamine, and its use via nasal route, gargle and rectal route.<sup>19</sup> Studies have supported anti-inflammatory action of ketamine in an experimental model with rats.<sup>20</sup> Besides, experimental studies with animal have pointed out that peripherally administered ketamine was capable of activating the L-arginine/Nitric oxide (NO)/cyclic guanosine monophosphate (CGMP) pathway, thus eliciting peripheral anti-nociception.<sup>21</sup>

Of the various factors which attributes for POST, age and gender of the patient are two of them. Few studies reports POST to be more in younger age group<sup>16</sup> while few studies show POST to be more in elderly.<sup>7</sup> Studies have found sore throat, to be more common in

females.<sup>5,7,16</sup> In our study out of 54 female patients 16 patients had sore throat and out of 26 males, 3 patients complained of sore throat. As in our study we had more female patients in both groups, we could not come to the conclusion if gender had any role in the occurrence of sore throat. We did not find any association between age of the patient and occurrence of POST.

As the mucosal injury in the trachea<sup>4</sup> or vocal cord<sup>22</sup> contributes for POST, all patients were intubated by experienced anaesthesiologist in our study. Jaensson et al<sup>23</sup> considered the experience of person performing intubation as significant for POST, whereas Monroe et al<sup>18</sup> and Edomwonyi et al<sup>24</sup> found no correlation between POST and the skill of anaesthesiologist.

Major cause of POST was due to tracheal mucosal damage secondary to cuff trachea contact and it was found out that narrow cuffs by reducing the area of cuff trachea contact, attenuates POST.<sup>17</sup> Intra cuff pressure of endotracheal tube is also one of the factor for POST. Maintaining cuff pressure of 20 mm of hg decreases the incidence of POST.<sup>25</sup> In our study we had maintained tracheal cuff pressure 20 to 22 cm of water using a pressure manometer, and maintained a peak airway pressure of below 25 cm of water. We had used heat moisture exchanger in the gas delivery circuit as the humidified gas have been implicated in the development of POST.

Higgins et al<sup>16</sup> showed in their study that use of succinylcholine increases the incidence of POST due to sarcolemmal tears during fasciculation's. Because of this we avoided succinylcholine in our study.

In our study in the gargle group we divided the volume used for gargle of 30 ml into two parts, to avoid the chances of aspiration if accidentally swallowed. We found many patients were not comfortable with the bitter taste of ketamine and hence they were unable to do gargling in a proper way. This problem was not encountered in nebulisation group as the patient's active involvement was not required. Hence we found that ketamine nebulisation is a good alternative method for reducing the post-operative sore throat.

The limitation of our study was not measuring the serum ketamine and nor ketamine levels to rule out the systemic effect of ketamine in anti-nociception/ anti-inflammatory action. However the study done by Chan et al<sup>26</sup> showed lower serum levels of ketamine and nor ketamine, which were not sufficient to produce systemic effects.

## Conclusion

Pre-operative ketamine nebulisation is comparable with ketamine gargle in reducing the incidence and severity of post-operative sore throat.

## References

1. Macario A, Weinger M, Truong P, Lee M. Which clinical anesthesia outcomes are both common and important to

- avoid? The perspective of a panel of expert anaesthesiologists. *Anesth Analg*. 1999;88:1085-91.
2. Mc Hardy F E, Chung F. Postoperative sore throat: cause, prevention and treatment. *Anaesthesia* 1999;54:444-53.
3. Christensen A M, Willemoes L H, Lundby L, Jacobsen K B. Postoperative throat complaints after tracheal intubation. *Br J Anaesth* 1994;73:786-7.
4. Beebe D S. Complications of tracheal intubation. *Semin Anesth Perioperative Med Pain*. 2001;20(3):166-172.
5. Biro P, Seifert B, Pasch T. Complaints of sore throat after tracheal intubation: A prospective evaluation. *Eur J Anaesthesiol* 2005;22:307-11.
6. Chen K T, Tzeng J I, Lu C L, et al. Risk factors associated with postoperative sore throat after tracheal intubation: an evaluation in the post anesthetic recovery room. *Acta Anaesthesiol Taiwan*. 2004;42(1):3-8.
7. Ahmed A, Abbasi S, Ghafoor A H, et al. Postoperative sore throat after elective surgical procedures. *J Ayub Med Coll Abbottabad*. 2007;19(2):12-14.
8. Kurdi M S, A Kaushic, Threeth, S Radhika, Deva .*Anesth Essays Res*.2014;8(3):283-89
9. Carlton S M, Coggeshall R E. Inflammation induced changes in peripheral glutamate receptor populations. *Brain Res*1999;820:63-70.
10. Canbay O, Celebi N, Sahin A, et al. Ketamine gargle for attenuating postoperative sore throat. *Br J Anaesth* 2008;100:490-3.
11. Rudra A, Ray S, Chatterjee S, et al. Gargling with ketamine attenuates the postoperative sore throat. *Indian J Anaesth* 2009;53:40-3.
12. Rajkumar G, Eshwori L, Konyak P Y, et al. Prophylactic ketamine gargle to reduce post-operative sore throat following endotracheal intubation. *J Med Soc*. 2012 ;26(3):175-9.
13. Kamble N P, Gajbhare M N. Efficacy of ketamine gargles in the prevalence of postoperative sore throat after endotracheal intubation. *I J C A* 2015;2(4):251-55.
14. Ahuja V, Mitra S, Sarna R. Prophylactic ketamine gargle to reduce post-operative sore throat following endotracheal intubation. *Indian J Anaesth* 2015;59:37-42.
15. Ayoub C M, Ghobashy A, Koch M E et al. Widespread application of topical steroids to decrease sore throat, hoarseness, and cough after tracheal intubation. *Anesthesia Analgesia* 1998;87:714-16.
16. Higgins P P, Chung F, Mezei G. Postoperative sore throat after ambulatory surgery. *Br J Anaesth* 2002;88:582-4.
17. Loeser E A, Bennett G M, Orr D L, Stanley T H. Reduction of postoperative sore throat with new endotracheal tube cuffs. *Anesthesiology* 1980;52: 257-9.
18. Monroe M C, Gravenstein N, Saga - Rumley S. Post airway in orotracheally intubated patients. *Anesth Analg* 1990;70:512 -6.
19. Khatavkar S S, Bakhshi R G. Comparison of nasal midazolam with ketamine versus nasal midazolam as a premedication in children. *Saudi J Anaesth* 2014;8:17-21.
20. Zhu M M, Zhou Q H, Zhu M H et al. Effects of nebulized ketamine on allergen-induced airway hyper responsiveness and inflammation in actively sensitized Brown-Norway rats. *J Inflamm (Lond)* 2007;4:10.
21. Romero T R, Galdino G S, Silva G C et al. Ketamine activates the L-arginine/Nitric oxide/cyclic guanosine monophosphate pathway to induce peripheral antinociception in rats. *Anesth Analg* 2011;113:1254-9.
22. Mencke T, Echtermach M, Kleinschmidt S, et al. Laryngeal morbidity and quality of tracheal intubation: a randomized controlled trial. *Anaesthesiology*. 2003;98(5)1049-1056.

23. Jaensson M, Olowsson L L, Nilsson U. Endotracheal tube size and sore throat following surgery: a randomized controlled study. *Acta Anaesthesiol Scand.* 2010;54(2):147-15.
24. Edomwonyi N P, Ekwewe I T, Omo E, Rupasinghe A. Postoperative throat complication after tracheal intubation. *Annals of African Medicine.* 2006;5:28-32.
25. Ratnaraj J, Todorov A, McHugh T, et al. Effects of decreasing endotracheal tube cuff pressures during neck retraction for anterior cervical spine surgery. *J Neurosurg.* 2002 Sep;97(2 Suppl):176-9.
26. Chan L, Lee M L, Loo Y L. Postoperative sore throat and ketamine gargle. *Br J Anaesth.* 2010;105(1):97.