



# **Comparison of Ketamine Nebulisation with Ketamine Gargle in Attenuating Post Operative Sore Throat Following General Anaesthesia with Endotracheal Intubation**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Background & Objective:** In the post operative period, Sore throat is a common morbidity following tracheal intubation. The 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 18-64 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).

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**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.. None of the patients in either group experienced severe sore throat.

**Conclusion:** Ketamine nebulisation seemed to represent an effective alternative to ketamine gargle for relieving Post Operative sore throat.

*Keywords: Ketamine nebulisation; ketamine gargle; endotracheal intubation; postoperative throat.*

## 1. INTRODUCTION

Postoperative sore throat is one of the most common complications following endotracheal intubation for general anaesthesia.. Endotracheal intubation is often associated with varying degrees of trauma to the airway mucosa which may result in irritation and inflammation [1]. Lubrication of the endotracheal tube with lidocaine jelly, steroids such as betamethasone, and K-Y jelly are possible methods of reducing the occurrence of sore throat after endotracheal intubation [1].

It has been postulated that the post operative sore throat is due to mucosal injury in the trachea and other factors like oropharyngeal suctioning, intra cuff pressure, use of throat pack, size of the endotracheal tube, Duration of surgery and difficulty during intubation manoeuvres, also represent risk factors for post-operative sore throat.

The incidence of postoperative sore throat can be associated with different sizes of endotracheal tubes and cuff pressure. Cuff pressures of low pressure high volume cuffs less than or equal to 25 cmH<sub>2</sub>O have been demonstrated to successfully reduce the incidence of postoperative throat pain after endotracheal intubation [2]. This makes a cuff pressure less than 25 cmH<sub>2</sub>O or less ideal for most patients [2,3]. Inappropriate tube size and cuff pressure increases the pressure effect on the tracheal mucosa with consequent ischemia and inflammatory changes that increase the risk of developing postoperative sore throat.

Ketamine a phencyclidine derivative is a non-competitive antagonist of N –Methyl D Aspartic acid (NMDA) receptor. NMDA receptors 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-operative sore throat.

Many studies have been conducted, showing the effectiveness of ketamine gargle 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 [4]. Nebulization 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 operative sore throat between ketamine gargle and ketamine nebulization.

### 1.1 Aims and Objectives

#### 1.1.1 Aim

General aim was to compare the effect of ketamine nebulization with ketamine gargle in attenuating post operative sore throat following general anaesthesia with endotracheal intubation. In particular, our primary objective was to study the incidence and severity of postoperative sore throat following the use of ketamine nebulization and gargling, Secondary objective were to study the time of onset of postoperative sore throat following ketamine gargle and ketamine nebulisation and to evaluate the correlation of duration of intubation with the occurrence of postoperative sore throat.

## 2. MATERIALS AND METHODS

The study was conducted after approval of the ethical committee clearance of Jawaharlal Nehru Medical College, DMIMS (DU), Acharya Vinoba Bhave Rural Hospital (AVBRH), affiliated to Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha.

### 2.1 Study Design

Study period: One year  
Study area: Department of Anaesthesiology JNMC & AVBRH.  
Research design: Randomized, prospective study

### 2.2 Inclusion Criteria

- 1) Patients aged between 18- 64years
- 2) ASA Class I & II patients.

- 3) Patients willing for the study.
- 4) Female and male patients
- 5) Patient posted for elective procedures under GA with endotracheal intubation.

### 2.3 Exclusion Criteria

1. Patients not willing for the study.
2. Age :<18 &> 64 years ( male or female )
3. Known allergy to any drug in the study.
4. Patient who suffered from pre-operative sore throat.
5. Kidney, Endocrine & Metabolic disease.
6. Mallampati grades more than 2
7. Use of NSAID's recently
8. Patients with throat pack and Ryles tube passage.
9. Patients with comorbidities; asthma, heart block, left ventricular failure, diabetes mellitus, ischemic heart disease, hypertension, aortic stenosis

### 2.4 Methods

Written and informed consent were obtained from the patients who were posted for elective surgeries and those who fit into the inclusion criteria . Pre anaesthetic check up was done prior to the procedure.

**Group GK** (gargled ketamine) received 30ml of gargle solution containing 1ml ketamine (50mg) in 29 ml of normal saline.

**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 .The patients were randomly allocated to each study group (Grp GK and NK) by lucky dip via letters which was kept in opaque envelopes.

### 2.5 Study Procedure

A complete preoperative history, physical examination, and investigations were performed for each eligible patient the day before anaesthesia. Full blood count, serum electrolyte, urea and creatinine levels, as well as urine analysis, were all performed as part of routine tests. Other laboratory tests were carried out as needed for each instance. The study protocol with risks and benefits were explained to the understanding of these patients. Informed written consent were obtained thereafter during the pre-operative review. The patients were randomly assigned to each study group (i.e., Group GK

and NK) by lucky dip via letters which were kept in envelopes.

Pre-operative checks of all equipment and anaesthetics were performed upon arrival in the operating room. Each patient had a multi-parameter monitor linked to them, and their baseline vital signs were recorded. A 18G cannula was used to establish intravenous access.

A high volume low pressure cuff tube with a cuffed endotracheal tube with an internal diameter of 7.0-7.5 mm for females and internal diameter of 8.0 mm and 8.5 mm for males were prepared.

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

**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).

To boost the oxygen reserve and denitrogenate the lungs, each patient was pre-oxygenated with hundred percent oxygen for five minutes.

Patients were premedicated with injection glycopyrrolate 4 microgram per kg, injection midazolam 0.03 mg/kg. Anaesthesia was induced with propofol at 2mg/kg and injection fentanyl 2microgram per kg. A senior consultant anaesthetist performed laryngoscopy to limit trauma to oropharyngeal structures and lower the incidence of postoperative sore throat. Serial auscultation was used to check proper insertion of the endotracheal tube immediately after intubation, and the endotracheal tube cuff was then inflated.

The close circuit breathing system was used to connect the endotracheal tube to the anaesthetic machine, and the patient was mechanically ventilated using intermittent positive pressure ventilation mode. A balanced method was used to maintain anaesthesia, with sevoflurane titrated to effect. With 0.1 mg/kg vecuronium, muscle relaxation was obtained.

All patients received intravenous fentanyl 1mcg/kg and 15mg/kg paracetamol for intra-operative analgesia. The amount of blood loss was calculated and restored with normal saline

or Ringer's lactate. The patient's pulse rate and oxygen saturation were monitored every five minutes until the surgery was completed. A capnograph was also utilised to track end-tidal carbon dioxide levels. Patient's oropharynx were softly suctioned at the end of operation with as little instrumentation as feasible.

The patient was reversed with myopyrolate. The durations of surgery and endotracheal intubation were noted respectively. Following extubation, each patient was transferred to the Post Operative ward for additional observation and vital sign monitoring.

Post-operative ward patients were interviewed for sore throat by a blinded investigator at 0 hr (on arrival to post operative room), 2nd hr, 4th hr, 8<sup>th</sup> hr, 12<sup>th</sup> hr, 24hr.

On a three-point scale, post-operative sore throat was assessed (0-2)

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)

### 2.6 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. Leven1s 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.

### 2.7 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.

### 3. RESULTS

There were 80 patients in the study, 40 in the gargled ketamine (GK) group and 40 in the nebulization group (NK group). In terms of age, gender, body weight, and anaesthetic duration, there were no significant variations between the groups.

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.

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.

**Table 1. Demographic data**

Groups	GK(n=40)	NK(n=40)	P-Value
Age(yr)	40.17±10.92	40.71±12.86	0.844
Sex(F:M)	18:22	21:19	0.340
Weight(Kg)	55.31±6.64	56.30±5.81	0.476
Duration of anaesthesia(min)	120.62±8.59	123.00±9.08	0.233

**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%)
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	

#### 4. 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 compared with people who did not complain of POST [5]. The overall incidence of POST is 21- 65% [2,3,6]. 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 nebulized ketamine had shown decreased in the incidence of POST. The present study is aimed to compare the effectiveness of preoperative ketamine gargle (group GK) with preoperative ketamine nebulization (group NK) in reducing the incidence and severity of POST [7].

Post-operative Sore throat is mostly seen between 2 and 4 hours. By this time, the patients are fully awake and more willing to participate in the research.. 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% [8]. Our study is in accordance with many other studies which had showed the decrease in incidence of POST [9-13]. 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. (Table2)

The mechanism of attenuating the sore throat was possibly due to the topical effect of ketamine either given by gargle or by nebulization 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 [14]. Studies have supported anti-inflammatory action of ketamine in an experimental model with rats [15].

Furthermore, animal studies have shown that peripherally given ketamine can activate the L-arginine/Nitric oxide (NO)/cyclic guanosine monophosphate (CGMP) pathway, resulting in peripheral anti-nociception.

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 [16] while few studies show POST to be more in elderly [17] Studies have found sore throat, to be more common in females [18,17,19]. 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 operative sore throat.

As the mucosal injury in the trachea [20] or vocal cord [21] contributes for POST, all patients were intubated by experienced anaesthesiologist in our study. Jaensson et al. [22] considered the experience of person performing intubation as significant for POST, whereas Monroe et al [19] and Edomwonyi et al. [23] found no correlation between POST and the skill of anaesthesiologist.

The most common cause of POST was tracheal mucosal injury caused by cuff trachea contact, and it was discovered that narrowing cuffs, which reduce the amount of cuff trachea contact, reduces Post operative sore throat.

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 [24] 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. Because humidified gas has been linked to the growth of POST, we employed a heat moisture exchanger in the gas distribution circuit.

Higgins et al. [25] 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 nebulization group as the patient's active

involvement was not required. Hence we found that ketamine nebulization is a good alternative method for reducing the post-operative sorethroat.

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. [23] showed lower serum levels of ketamine and nor ketamine, which were not sufficient to produce systemic effects.

## 5. CONCLUSION

We studied a single drug which was Ketamine, and studied the different route of administration, which was nebulization and gargle. We found that Ketamine nebulization before surgery is as effective as ketamine gargle in lowering the occurrence and severity of post-operative sore throat.

## CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

The study was conducted after obtaining approval from the ethics and screening committee of Jawaharlal Nehru Medical College, DMIMS (DU), Acharya Vinobha Bhave Rural Hospital (AVBRH), Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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