

Effect of Preoperative Ketamine on Sore Throat After Intubation: A Randomized Study

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Abstract:

Background: The term "sore throat" is a collection of multiple clinical features like coughing, hoarseness, coughing, tracheitis, laryngitis, and odynophagia that occurs due to endotracheal intubation under general anaesthesia. Ketamine, being an NMDA blocker, may be used in reducing the incidence of POST due to its anti-nociceptive, anti-inflammatory action. Advantages of nebulized forms include avoidance of bitter taste and requirement of lesser volume comparatively. This study with aim to know the efficacy of nebulized ketamine in decreasing POST in patients who underwent endotracheal intubation when compared to placebo (normal saline).

Materials and Methods: In this interventional single-blinding study, 100 patients scheduled for endotracheal intubation were included. They were randomized into 2 groups of 50 patients each. Group K received nebulized ketamine and group P received nebulized placebo (normal saline), which looks similar to ketamine. Age, gender, ASA status, Incidence and severity of post operative sore throat was noted and compared between each group.

Results: There is no significant difference in mean age, gender, ASA grade between two groups. Overall incidence of POST was 24%. It was significantly high in placebo group compared to ketamine group at 6 hours and 12 hours of postoperative period. The mean severity of POST was more in placebo group compared to ketamine group at 6 and 12 hours.

Conclusion: Nebulized ketamine is very effective in reducing the incidence and severity of post operative sore throat among patients scheduled for elective endotracheal intubation.

Nebulized ketamine is well accepted by patients and it didn't produce any side effects in our study population.

Key Words: Ketamine, post operative sore throat, nebulized form, randomized controlled study, placebo

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I. Introduction

The term "sore throat" is a collection of multiple clinical features like coughing, hoarseness, coughing, tracheitis, laryngitis, and odynophagia that occurs due to endotracheal intubation under general anaesthesia. Postoperative sore throat (POST) is a common complication seen after endotracheal intubation, causing significant annoyance, irritation and misery to the patient. Some authors reported the incidence of POST to vary from 21 to 65%.¹⁻² It is a minor complication, but it may interrupt the quality of recovery of patients from anaesthesia. It is caused by localized trauma to mucosa of upper airway during intubation, leading to aseptic inflammation of pharynx. Factors that contribute to POST include usage of non-lubricated large sized tube, multiple attempts of intubation, prolonged intubation, use of throat packs, high intra cuff pressure² and high anaesthetic gas flows. There are multiple interventions (nonpharmacological and pharmacological), which were studied previously in reducing the incidence of POST with varying results.⁴⁻⁶ They include using steroids, small endotracheal tube, lidocaine, ketamine gargle, benzydamine gargle etc. Zhu MM and Davidson et al reported that N-methyl-d-aspartate (NMDA) plays a vital role in inflammation and causing pain.⁷⁻⁸ Ketamine, being an NMDA blocker, may be used in reducing the incidence of POST due to its anti-nociceptive, anti-inflammatory action. It can be used as a gargle or in the nebulized form.⁹⁻¹⁰ But nebulized form is better found to be tolerated better by patients as per Ahuja et al. Advantages of nebulized forms include avoidance of bitter taste and requirement of lesser volume comparatively.¹¹

Objective: This study was done to know the efficacy of nebulized ketamine in decreasing POST in patients who underwent endotracheal intubation when compared to placebo (normal saline).

II. Material And Methods

This interventional, randomized, single-blinded study was carried out at the Department of anesthesia at NRI Institute of Medical Sciences, Chinakakani, Andhra Pradesh from July 2022 to December 2022.

Study Design: Interventional, randomized, single-blinded study

Study Location: This study was done at tertiary care teaching hospital in the Department of anesthesia at NRI Institute of Medical Sciences, Chinakakani

Study Duration: July 2022 to December 2022.

Sample size: 100 patients

Sample size calculation: The sample size was estimated on the basis of population proportion design. Around 44% of patients suffered from POST after endotracheal intubation as per Mehta et al.¹²

At confidence level of 90%, taking error as 8%, and the proportion as 44%, the minimum sample size obtained was 105. So, we included 105 patients in our study, but the data was incomplete for 5 patients.

So, finally we included 100 patients for data analysis.

Subjects & selection method: The study population was drawn from patients scheduled for elective endotracheal intubation at NRI Institute of Medical Sciences.

Patients were divided into two groups (each group had 50 patients) as per the drug given.

Group P (N=50 patients) –Nebulized placebo – 4ml of normal saline was used.

Group K (N=50 patients) –Nebulized Ketamine- 50mg of ketamine in 4ml of normal saline was used.

Inclusion criteria:

1. Patients belonging to ASA grade I and II
2. Either sex
3. Aged 20 to 60 years,
4. Patients undergoing elective endotracheal intubation in supine position
5. Patients who provided informed consent

Exclusion criteria:

1. Pregnant and lactating women
2. Patients with contraindication to ketamine
3. Patients with severe hepatic and renal disorders
4. Patients using corticosteroids
5. Patients who need nasal intubation
6. Patients who need more than 2 attempts
7. Usage of throat packs
8. Patients scheduled for surgeries of head and neck, oral cavity, airway

III. Methodology:

Patients were randomized into two groups using a computer-generated software.

All the patients were given capsule omeprazole 20mg, Tab. Metoclopramide 10 mg, Tab Alprazolam 0.25 mg before intubation. Patient was asked to fast for minimum 8 hours. General anaesthesia was induced in ten minutes after nebulization. Fentanyl, Midazolam, Glycopyrrolate were given. After 3 minutes of pre oxygenation, general anaesthesia was given using 2 mg/kg propofol and intubation was done after giving vecuronium using properly sized endotracheal tube. Cuff was inflated with air. Anaesthesia was maintained using nitrous oxide and oxygen at appropriate ratio. Continuous pulse oximetry, ECG, blood pressure, heart rate monitoring was done. In case of more cough, lignocaine was given by intravenous route. Once the patient becomes completely conscious; trachea was extubated after deflating the cuff. At the end, neuromuscular blockage was reversed with inj. Neostigmine and glycopyrrolate.

POST was assessed at 6 and 12 hours after extubation.

Informed consent is taken from every patient. All 100 patients accepted to participate in this study and gave written ICF. All the patients underwent proper physical examination and required blood testing. Medical history was taken from all patients as per the case record form (CRF). The patients who were involved in randomization and drug preparation doesn't know the information about the type of drug that was given to them (single-blinded).

We have used numerical rating scale (NRS) score to identify the severity of pain among patients.

NRS 0 = no sore throat

NRS score of 1 to 3 = mild sore throat

NRS score of 4 to 6- moderate sore throat

NRS score of 7 to 10: severe sore throat

Parameters assessed:

Age

Gender

ASA grade
Incidence of POST
Severity of POST as per NRS

Ethical considerations:

Permission was obtained from the Institutional ethical committee attached to NRI Institute of Medical Sciences before conducting the study. Every patient was explained the whole process and advantages of the study. After he/she accepts, an informed consent form is given in local language or patient understandable language and the person was asked to sign it or put a thumb impression.

Statistical analysis

Data was analyzed using Epi info software version 7.2.5. Student's *t*-test was used to compare numerical parameters between two groups. Chi square test was used to compare categorical values between two groups. P value <0.05 was considered significant.

IV. Results

The current study included 100 patients divided into groups P and K.

Age:

There is no significant difference in the mean age of patients of both groups, as per the T-test. Hence the comparison is justifiable without age-related bias. Mean age of patients in group P was 43.2±5.6 years and mean age of patients in group K was 42.8±6.2 years.

Table no 1: Shows the mean age of patients in both groups.

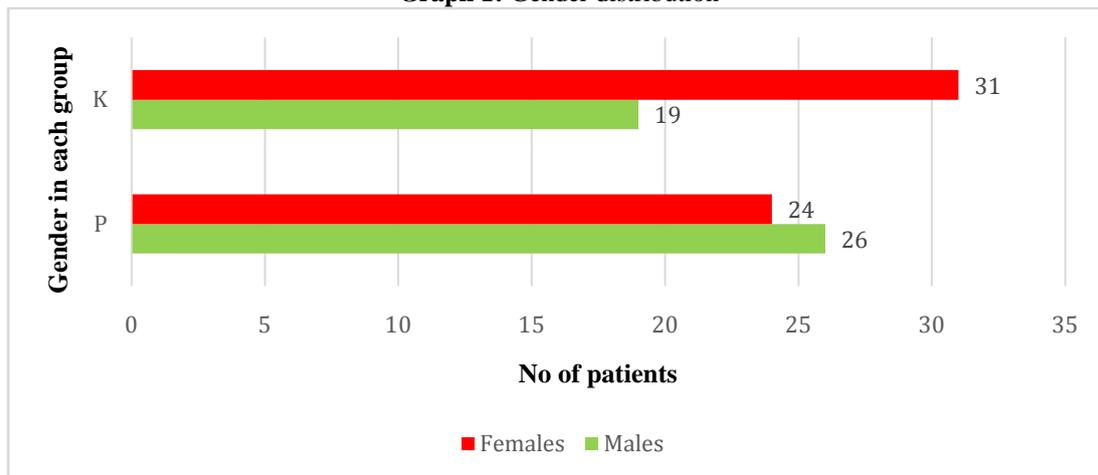
Groups	Mean age	P Value
P	43.2±5.6 years	0.735
K	42.8±6.2 years	

Gender:

Females were more compared to males. Among 55 female patients, 31 belonged to group K. But there is no significant difference in gender distribution between the two groups, as per the chi-square analysis(p=0.159).

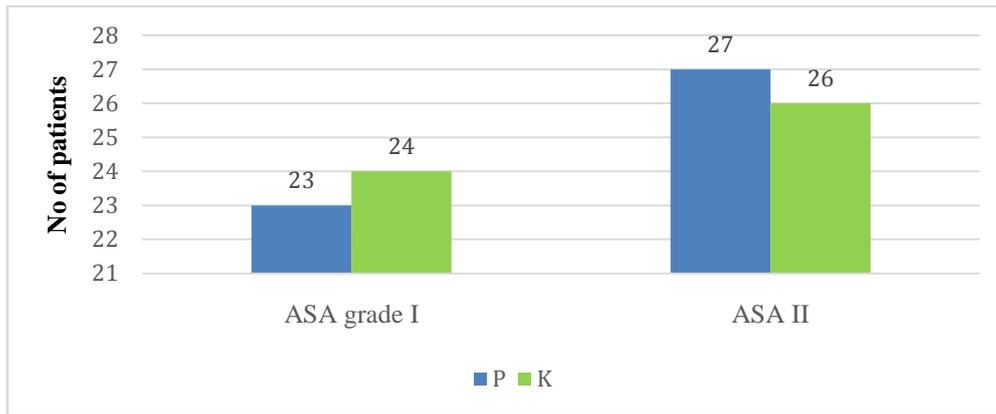
Hence the comparison is justifiable without any gender-related bias.

Graph 1: Gender distribution



ASA grade: There is no significant difference in ASA grade in both groups(p=0.841).

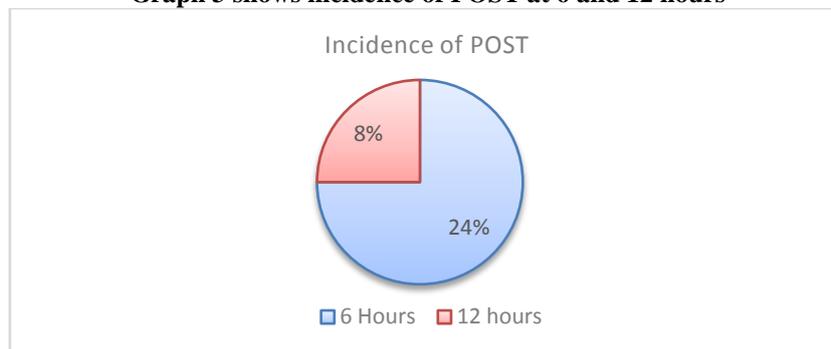
Graph 2: ASA distribution among study patients



Incidence of POST:

Overall incidence of POST was 24% in our study within 1st 12 hours of postoperative period.

Graph 3 shows incidence of POST at 6 and 12 hours



The incidence of POST was significantly more in placebo group compared to ketamine group at 6 and 12 hours. 16 patients in group P had POST at 6 hours and 8 patients in group P had POST at 12 hours. Overall, 24 patients had POST at 6 hours. Among them, 9 had persistent POST at 12 hours.

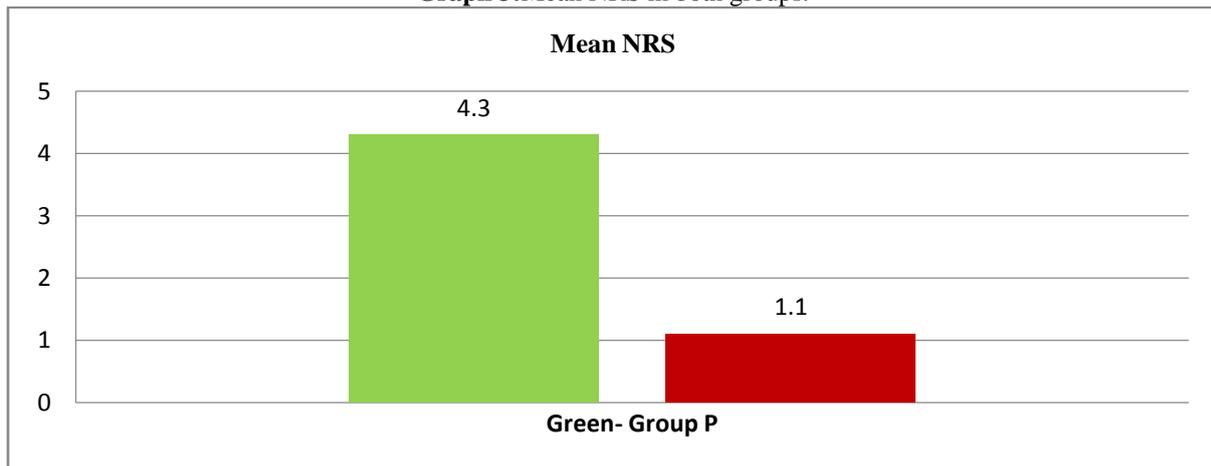
Only 1 patient in ketamine group had POST at 6 hours and it persisted even at 12 hours of postoperative period. Table 2 shows the incidence of POST in both groups.

Group	Incidence of POST at 6 hours(n)	Incidence of POST at 12 hours(n)	P Value
P	23 patients out of 50	8	<0.0001
K	1	1	0.01

Severity of POST:

POST severity was assessed using NRS. The mean NRS was significantly more in placebo group compared to ketamine group(p=0.0001).

Graph 3: Mean NRS in both groups.



Hemodynamic parameters: There are no significant differences in heart rate, systolic, diastolic blood pressure (SBP and DBP), and oxygen saturation in both groups at baseline, 6 and 12 hours of post-operative period.

Table 3 Shows hemodynamic parameters in both groups

Parameters	Ketamine	Placebo	P Value
Heart rate at Baseline	82.17±6.37	80.62±6.98	0.24
HR 6 hours	77.2±6.32	75.8±6.62	0.28
HR 12 hours	76.15±7.97	75.22±7.88	0.46
SBP at baseline	125.12±7.87	128.6±8.7	0.35
SBP at 6 hours	123.13±8.17	124.97±9.3	0.6
SBP at 12 hours	125.733±7.7	127.97±8.2	0.4
DBP at baseline	77.167±7.8	78.73±8.16	0.5
DBP at 6 hours	73.21±6.32	77.3±7.2	0.3
DBP at 12 hours	77.3±7.63	77.73±6.9	0.61
Spo2 at baseline	98.3±1.3%	97.8±1.2%	0.30
SPO2 at 6 hours	97.63±1.3%	96.96±1.3%	0.31
SPO2 at 12 hours	97.2±1.3%	97.2±1.1%	0.84

Side effects: No patient suffered from any side effect other than POST in our study.

V. Discussion

In the current study, 50 patients received nebulized ketamine (Group K) and 50 patients received placebo or normal saline (group P) for post operative sore throat prevention after endotracheal intubation under general anesthesia.

There is no significant difference in the mean age of patients of both groups. Mean age of patients in group P was 43.2 ±5.6 years and mean age of patients in group K was 42.8±6.2 years in our study.

Females were more compared to males. Among 55 female patients, 31 belonged to group K. But there is no significant difference in gender distribution between the two groups. There is also no significant difference in the ASA grade between two groups in our study.

Overall incidence of POST was 24% in our study within 1st 12 hours of postoperative period. The incidence of POST was significantly more in placebo group compared to ketamine group at 6 and 12 hours. The mean NRS was significantly more in placebo group compared to the ketamine group. Both groups showed hemodynamic stability.

Significant decline in POST incidence in our study can be due to topical effect of ketamine, by its NMDA-blocking and anti-inflammatory action, that relieves local inflammation and produced analgesic effect peripherally.¹³⁻¹⁵

In the study of **Thomas D** et al. 96 patients of ASA status 1 and 2 aged 18 to 60 years were included. Patients were randomized to receive ketamine and saline. Results showed that the overall incidence of POST was 25%, almost similar to our study findings. POST was experienced seen by 14.6% of patients of ketamine group and 35.4% of saline group. There was a significant decrease in the incidence of POST in the ketamine group, similar to our study results. Also, the severity of sore throat was found to be more in the saline group compared to ketamine post-extubation, similar to our study.¹⁶

Chan et al., used ketamine gargle in his research for decreasing for POST, and also assessed serum ketamine levels. They found low levels of ketamine and reported that topical ketamine caused attenuation of POST.¹⁷

Ahuja *et al.*,¹¹ also reported decline in the incidence of POST in patients of ketamine group. It was significant statistically at 2 hours and 4 hours of postoperative period. In contrast, we measured at 6 hours and 12 hours of postoperative period in our study. One animal study also proved that nebulized ketamine to provide a shielding effect on airway inflammation. They also reported that antipro-inflammatory processes, that was triggered after injury, can be prevented by ketamine.¹⁸ Gupta SK *et al* used 225 mg of magnesium sulfate, which is an NMDS blocker and found attenuation in POST at various time intervals during postoperative period.¹⁹

VI. Conclusion

Nebulized ketamine is very effective in reducing the incidence and severity of post operative sore throat among patients scheduled for elective endotracheal intubation.

It doesn't cause disturbances in heart rate, pulse rate, oxygen saturation and blood pressure, implying that it is hemodynamically stable. Nebulized ketamine is well accepted by patients and it didn't produce any side effects in our study population. But larger population studies and measurement of serum ketamine levels is required to identify better dose of ketamine for nebulization to reduce the incidence and severity of postoperative sore throat.

The study is self-sponsored and there are no conflicts of interest.

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