

Effect of Preoperative Nebulized Ketamine on Incidence and Severity of Postoperative Sore Throat in Patient Undergoing General Anaesthesia with Endotracheal Intubation

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ABSTRACT

Introduction

Postoperative sore throat (POST) has a reported incidence of up to 62% following general anaesthesia. POST was rated by patients as the eighth most undesirable outcome in the postoperative period. The objective of this study was to compare the incidence and severity of postoperative sore throat after saline and ketamine nebulization in patients undergoing general anaesthesia with endotracheal intubation.

Methods

The study was prospective double blinded randomized controlled trial . One hundred patients belonging to American Society of Anesthesiologists physical status I–II undergoing surgery under general anaesthesia with endotracheal intubation were randomized into two groups; group Saline (S) received nebulization with 5 ml of normal saline and group Ketamine (K) received nebulization with 1 ml of ketamine of concentration 50 mg/ml mixed with 4 ml saline. POST was assessed at zero hour, two hour, four hour, six hour, eight hour and 24 hour.

Results

The overall incidence of POST was 28%. Twenty two (44%) patients in group S and six (12%) patients in group K had postoperative sore throat at some point of the study. The POST was significantly reduced in group K at zero hour 3(6%), two hour 3(6%), four hour 4(8%), six hour 5(10%) and eight hour 3(6%) with p value <0.05 . The severity of POST was also significantly decreased in group K at zero hour, two hour, four hour, six hour, eight hour with p value <0.05.

Conclusion

Preoperative nebulization with ketamine reduces the incidence and severity of POST after general anaesthesia with endotracheal intubation.

Keywords: Endotracheal intubation, ketamine nebulization, post-operative sore throat

INTRODUCTION

Sore throat includes specific symptoms such as: dysphagia, dysphonia, hoarseness, continuous throat pain and pharyngeal dryness.¹ Postoperative sore throat (POST) was rated by patients as the eighth most undesirable outcome in the postoperative period.² POST has a reported incidence of up to 62% following general anaesthesia (GA).³ The incidence of POST is more common in GA with tracheal intubation than GA with supraglottic airway.⁴ The other factors associated with increased risk for POST are young age, prolong duration of surgery, high tracheal tube cuff pressure, large size tube, non use of muscle relaxant for intubation, trauma during intubation.³ Postoperative sore throat is at its peak in the early postoperative period, 2 to 6 hours after extubation, but the incidence decreases rapidly with time.⁵ There are various pharmacological methods available to prevent POST and locally used ketamine is one of them.³ The primary objective of the study was to compare the incidence and severity of POST after ketamine nebulization and saline nebulization. Secondary objective was to look for side effect in the study group.

METHODS

The study was conducted in Tribhuvan University Teaching Hospital (TUTH) after ethical approval from Institutional Review Committee of Institute of Medicine. The sample size was calculated

presuming the incidence of POST to be 60%. The sample size was estimated from the assumption that a 50% reduction in the incidence of POST would be clinically relevant. The power analysis (taking $\alpha = 0.05$ and power = 0.90) suggested that 45 patients are required in each group. On adding 10% patients for possible loss to follow-up, the sample size required was 50 patients per group. A total of 100 patients of American Society of Anesthesiologist Physical Status (ASA PS) I-II, either sex, age 18-60 years undergoing general anaesthesia with endotracheal intubation with surgery duration less than two hour were included in the study. Patient with history of sore throat or upper respiratory tract infection, intraoral surgery, patient with history of chronic obstructive airway disease or Asthma, patient with Mallampati grade more than II, known allergic to study drug, more than one attempt required to intubation, psychiatry patients and perioperative use of anti-inflammatory drugs (Non steroidal anti-inflammatory drug or steroid) were among the exclusion criteria.

Using computer generated randomization technique; opaque sealed sequentially numbered envelopes were prepared by an anaesthesiologist who was not involved in the study. The envelopes were opened by the staff nurse, and nebulization solution was prepared according to group allocation. The staff nurse who prepared the study drugs did not participate in subsequent assessment of these patients. Patients were blinded as both the preparations were colorless.

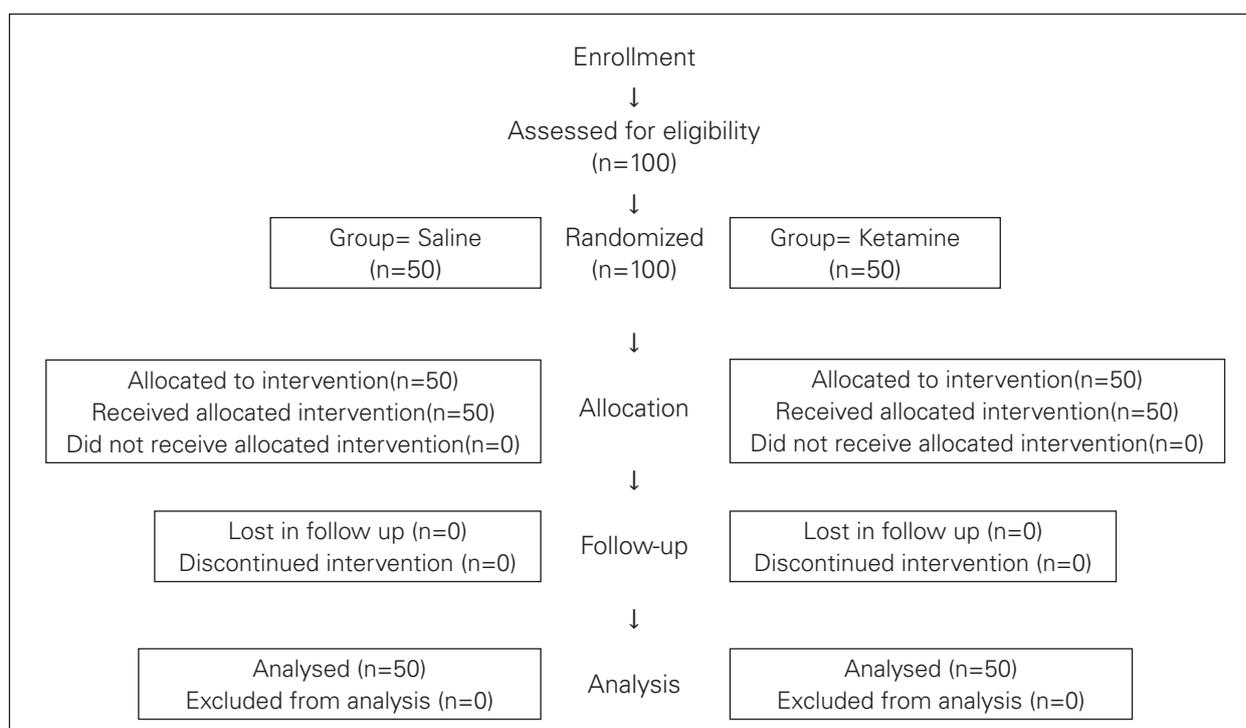


Fig 1. CONSORT flow diagram

After obtaining the full informed consent patients were kept nil per oral for 8 hours before surgery. Diazepam 5 mg (patient weighing less than 60 kg) or Diazepam 10 mg (patient weighing more than 60 kg) was administered orally as pre-medication at night and morning 6am on the day of surgery. Preoperative counseling was done regarding POST assessment. Intravenous access was established with 18 Gauge cannula and base line heart rate, blood pressure and SPO₂ were recorded before nebulization.

The 100 enlisted patients were randomly allocated to two groups of 50 each: Group S received saline nebulization (5ml) an Group K received ketamine 50mg (1.0 ml with 4.0 ml of the saline) nebulization .

The patients received solution via nebulization. The technique used was oxygen driven nebulization method.⁶ After the completion of nebulization heart rate, blood pressure and SPO₂ was recorded. Patient was then transferred to operation theatre 10mins after completion of nebulization. Monitor was attached. (NIBP, ECG electrodes, pulse oximeter, ETCO₂). Inj Ringer's lactate I.V at 8-10ml/kg was administered. Inj fentanyl 2mcg/kg was given for analgesia. All patients were induced with propofol titrating dose. Muscle relaxant inj vecuronium 0.1mg/kg was given. Direct laryngoscopy with a standard Macintosh Laryngoscope blade (size 3) was performed which was followed by oral endotracheal intubation. Oral endotracheal intubation with a soft seal cuffed sterile polyvinyl chloride tracheal tube (low pressure cuff) was used. Size of endotracheal tube (ETT) used in men-7.5mm ID and in female-7mm ID. Oral Intubation was done by the investigator in a single attempt. Correct tube placement was confirmed by ETCO₂. ETT cuff pressure was maintained at 20-25cmH₂O by using manometer (Portex pressure gauge/cuff inflator). Anaesthesia was maintained on oxygen with isoflurane , intermittent positive pressure ventilation and vecuronium. After the completion of surgery the oropharynx was gently suctioned with blunt end suction catheter. The neuromuscular block was reversed with IV neostigmine 50 µg/kg and glycopyrrolate 10 µg/kg while awaiting the return of spontaneous ventilation. After the patient fulfilled the extubation criteria, cuff was fully deflated then extubation was done.

Sore throat assessment was done: immediately after recovery(when the patient is oriented with time, place and person) 0hr and then at 2hr, 4hr, 6hr, 8hr and 24hr. Nurses in wards were informed and taught about the assessment of postoperative sore throat. When the patients were transferred to the respective wards POST assessment was done by nurses using the four point scale at different time as follows:

Grading of POST was done in four point scale (0-

3) as follows. The similar grading was used in the study by Canbay O and colleagues.⁷

- 0 = No sore throat
- 1 = Mild sore throat (complains of sore throat only on asking)
- 2 = moderate sore throat (complains of sore throat on his/ her own)
- 3 = severe sore throat (change of voice or hoarseness, associated with throat pain).

Other side effects like nausea, vomiting, cough and dry mouth if occurred were noted. Injection paracetamol 1 gm 6 hourly IV and Injection tramadol 50mg IV 6 hourly were used for post operative analgesia in both groups. The patient with severe sore throat was planned to treat with benzydamine gargle .

The collected data was analyzed using IBM SPSS statistics version 20. The hemodynamic variables before and after nebulization within the groups were compared with paired t-test. The differences in the incidence of POST among the groups were compared with Chi square test. The groups were compared with Mann–Whitney U test for severity of POST and p<0.05 was considered statistically significant.

RESULTS

The patients in both the groups were comparable for age, sex, weight, height and duration of surgery as shown in Table 1.

Out of 100 patients, the total number of POST in this study was 28 (28%). The POST was experienced by 22 (44%) in control group but only 6 patients(12%) in ketamine group had POST which was statistically significant p<0.001.

The sore throat was assessed in post operative care unit,(0 hour) and then in ward every 2 hour for 8 hour and then at 24 hour . At 0 hour , 12 patients in group S complained of sore throat but only 3 patients in group K complained of sore throat. The prevalence increased with time with peak at 4 hour in group S and 6 hour in group K. At 24th hour , 13

Table 1. Demographic profile

| Variables | Group S N= 50 | Group S N= 50 | p- value |
|---------------------------|------------------|------------------|-------------|
| Age (yrs) | 38.4±10.06 | 38.9±10.67 | 0.80 |
| Weight (kg) | 63.5±5.88 | 63.6±6.53 | 0.94 |
| Height (cm) | 160.4±3.92 | 160.7±4.86 | 0.74 |
| M:F ratio* | 1:1.08 | 1:1.08 | - |
| Duration of surgery (min) | 86.80±14.59 | 88.20±15.60 | 0.64 |

*M:F ratio = male:female ratio

Table 2. Comparison of POST between the groups at different interval of time

| Time (hour) | Group S N=50 | Group K N= 50 | p-value |
|-------------|-----------------|------------------|---------|
| 0 | 12 (24%) | 3 (6%) | 0.03** |
| 2 | 15 (30%) | 3 (6%) | 0.004** |
| 4 | 16 (32%) | 4 (8%) | 0.006** |
| 6 | 15 (30%) | 5 (10%) | 0.03** |
| 8 | 13 (26%) | 3 (6%) | 0.01** |
| 24 | 8 (16%) | 2 (4%) | 0.10 |

patients in group S still had sore throat but in group K only 2 patients had sore throat. Table 2

The patients in group S not only had high prevalence but also the severity of POST was higher when compared to group K and it was statistically significant $p < 0.05$ except at 24 hour of observation. Table 3

There was also no significant changes in Heart rate (HR), Systolic blood pressure SBP, diastolic blood pressure DBP and SPO_2 in group K and group S after nebulization as shown in Table 4.

There were no adverse effects such as nausea, vomiting, cough and dry mouth in the ketamine group during study period.

DISCUSSION

The postoperative sore throat is the unwanted complication of General anaesthesia. There are various established factors that contribute to POST like use of large size tube, high cuff pressure, tracheal intubation without complete relaxation and trauma during intubation.³ In our study these factors were eliminated by use of 7.0mm ID size tube for female and 7.5mm ID size tube for male, cuff pressure monitoring and maintaining between 15- 25mm Hg, tracheal intubation after complete relaxation. In addition we exclude the case requiring more than one attempt and duration of surgeries more than 2 hours. The overall incidence of POST in our study was 28% but the incidence in control group(S) was 44%. In the study done by Haider HS et al, the incidence of POST in the control group was 57.5% which was higher than the incidence in our study as they had not used manometer for cuff pressure monitoring.⁸ Liu et al. found that the use of manometer to measure endotracheal tube cuff pressure and maintaining it between 15-25 mmHg can reduced the incidence of POST up to 24hrs.⁹

In our study, there were 12 patients who complained of sore throat at 0 hr post extubation in control group and it reached peak at 4 hour and the prevalence declined over time after 8 hour. These findings in control group was consistent with study

Table 3. Inter group comparison of severity of POST

| Time (hour) | Severity of POST (Grade) | Group S N= 50 | Group K N= 50 | p-value |
|-------------|--------------------------|------------------|------------------|---------|
| 0 | 1 | 3 | 9 | 0.01** |
| | 2 | 0 | 3 | |
| 2 | 1 | 3 | 10 | 0.002** |
| | 2 | 0 | 5 | |
| 4 | 1 | 3 | 11 | 0.003** |
| | 2 | 1 | 5 | |
| 6 | 1 | 4 | 11 | 0.01** |
| | 2 | 1 | 4 | |
| 8 | 1 | 3 | 10 | 0.006** |
| | 2 | 0 | 3 | |
| 24 | 1 | 2 | 6 | 0.04 |
| | 2 | 0 | 2 | |

by Jaensson et al⁵ and Shrestha et al.¹⁰

There are various pharmacological methods for prevention of POST and include steroid both in intravenous and topical preparation, topical benzydamine hydrochloride, topical magnesium and topical liquorice.³ The experimental studies in animals had found the antinocicetive and anti inflammatory action of ketamine when given peripherally.^{11,12} There was no benefit seen with Intravenous ketamine in reducing POST.¹³ There are literatures which use ketamine gargle for post operative sorethroat.^{7,10,14-16} Although these studies had shown to decrease the incidence and severity of POST with ketamine gargle, bitter taste and need for large volume may be uncomfortable for the patients. This was also one of the drawbacks of ketamine gargle in study by Amingad B et al.¹⁷ We decided to administer ketamine by nebulization due to above reason.

In our study, the total number of patients with POST in group K was 6 (12%) and it was statistically

Table 4. Comparison of hemodynamic variable Pre and Post nebulization

| Group | Vitals | Pre-nebulization | Post-nebulization | p-value |
|-------|---------|------------------|-------------------|---------|
| K | HR | 75.0±6.8 | 75.4±0.98 | 0.39 |
| | SBP | 118.0±9.2 | 119.0±8.4 | 0.19 |
| | DBP | 73.6±6.5 | 73.5±6.5 | 0.57 |
| | SPO_2 | 98.1±0.97 | 97.9±1.1 | 0.18 |
| S | HR | 76.1±6.4 | 76.1±5.5 | 0.93 |
| | SBP | 120.4±5.2 | 120.6±4.7 | 0.53 |
| | DBP | 76.5±4.3 | 76.4±4.2 | 0.53 |
| | SPO_2 | 97.6±1.02 | 97.6±1.02 | 1.00 |

significant compared to group S (p value = <0.001). The comparison of POST at 0 hr, 2 hr, 4 hr, 6hr and 8 hr between ketamine and saline also showed decrease number of POST in group K and statistically significant (p<0.05). Although, there were POST in group K, most of them were of grade 1. The comparison of severity of POST between two groups showed decrease severity in group K at 0hr, 2 hr, 4 hr and 8 hr which was also statistically significant. The effect of locally used ketamine in decreasing incidence and severity of POST is consistent with other studies.^{7,10,14-17} There were no grade 3 POST in both the groups. In our study, the decrease in number and severity of POST was not significant at 24 hour of observation. This was also observed in study done by Kang HJ et al.¹⁵ From this observation we can assume that action of locally used ketamine does not last for 24 hours.

We didn't observe significant hemodynamic changes and any side effects in group K after nebulization and in postoperative period. In fact, the level of ketamine in blood was much lower after ketamine gargle to produce the systemic effect in study done by Chan L et al.¹⁴

Limitation: The blood plasma level of ketamine was not measured in our study. Another limitation was we did not measure the incidence of POST beyond 24 hrs.

CONCLUSION

Preoperative nebulized ketamine reduces both the incidence and severity of postoperative sore throat after general anaesthesia with endotracheal intubation.

CONFLICT OF INTEREST

None declared.

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