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ORIGINAL RESEARCH

Evaluation of the Efficacy of Ketamine Nebulization on Post-operative Sore Throat Due to Tracheal Intubation in Patients Undergoing Elective Surgeries: A Prospective, Randomised Double-Blinded Comparative Clinical Study

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ABSTRACT

Background: Post-operative sore throat (POST) is a common complication following tracheal intubation during surgeries, contributing to patient discomfort and dissatisfaction. Ketamine, a noncompetitive N-methyl-D-aspartate receptor antagonist, has demonstrated potential in mitigating POST. **Aim and Objective:** This clinical study evaluated the efficacy of ketamine nebulization in reducing POST in patients undergoing elective surgeries. **Materials and Methods:** A prospective, randomized, double-blinded, comparative, clinical study with a sample size of 60 patients was conducted at RKDF Medical College, Hospital, and Research Centre, Bhopal, over one year. Patients were divided into the ketamine nebulization group (n =30) and the control group (n = 30). POST severity was assessed using a standardized scoring system, and secondary outcomes, including analgesic consumption and patient satisfaction, were evaluated. **Results:** In the ketamine nebulization group, 83.3% of patients experienced no sore throat, while 86.7% of the control group reported post-operative sore throat (POST). The severity of POST, as measured by mean scores, was significantly lower in the ketamine nebulization group compared to the control group. Analgesic consumption in the ketamine nebulization group was notably reduced in the post-anesthesia care unit (PACU) and at 24 hours postoperatively. Patient satisfaction scores, evaluated using a visual analog scale (VAS), were significantly higher in the ketamine nebulization group compared to the control group. **Conclusion:** Ketamine nebulization effectively reduces POST and improves peri-operative outcomes in patients undergoing elective surgeries. This adjunctive therapy holds promise for enhancing post-operative care and patient experience.

Keywords: Ketamine nebulization, post-operative sore throat, tracheal intubation, peri-operative care, patient satisfaction.

INTRODUCTION

Post-operative sore throat (POST) is a frequent complication encountered following tracheal intubation during surgical procedures, with reported incidences ranging from 21% to 65% depending on various factors such as patient characteristics, type of surgery, and intubation technique.[1,2] Despite being considered a transient and self-limiting adverse event, POST significantly contributes to patient discomfort and dissatisfaction and may lead to prolonged recovery periods and increased healthcare costs.[3-5] Therefore, interventions to minimize POST are paramount in enhancing post-operative patient care and satisfaction.

Although essential for securing the airway and facilitating mechanical ventilation during surgery, Tracheal intubation often results in mucosal trauma and inflammation, particularly in the glottis and supraglottic regions. This inflammatory response is mediated by multiple pathways, including mechanical injury, ischemia-reperfusion injury, and release of inflammatory mediators, contributes to the development of POST.[6, 7] Traditional methods to reduce POST have included modifications in intubation techniques, such as using smaller endotracheal tubes, lubricants, minimizing cuff pressure, and pharmacological interventions such as

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local anesthetics and steroids.

However, these approaches may have limitations or variable efficacy.[8, 9] Ketamine, a phencyclidine derivative, and noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist has gained attention in recent years for its potential role in mitigating POST.

Beyond its well-established analgesic and anesthetic properties, ketamine exerts anti-inflammatory effects by modulating the release of pro-inflammatory cytokines and inhibiting the activation of NMDA receptors implicated in nociceptive signaling.[10] Ketamine can be administered via various routes, including intravenous, oral, intramuscular, and, more recently, nebulization.

Nebulization of ketamine offers the advantage of direct delivery to the airway mucosa, potentially targeting the site of inflammation more effectively while minimizing systemic side effects .[11]

While several studies have investigated the efficacy of ketamine in reducing POST when administered via intravenous or other routes, limited data exist regarding the effectiveness of ketamine nebulization specifically for this indication. Therefore, this clinical study aims to fill this gap by evaluating the efficacy of ketamine nebulization in reducing POST in patients undergoing elective surgeries. Understanding the role of ketamine nebulization in mitigating POST could have significant implications for improving post-operative outcomes and patient satisfaction.

This study was conducted at RKDF Medical College, Hospital, and Research Centre, Bhopal, over one year, utilizing a randomized double-blinded clinical study design with a sample size of 60 patients. Patients were allocated into two groups: one receiving ketamine nebulization and the other receiving standard care. The severity of POST was assessed using a standardized scoring system, and secondary outcomes, including analgesic consumption and patient satisfaction, will also be evaluated. The findings from this study could provide valuable insights into the utility of ketamine nebulization as an adjunctive therapy for reducing POST, thereby enhancing peri-operative care and patient experience.

MATERIALS AND METHODS

Study Design

This study was a prospective, randomized, double-blinded, comparative, clinical study conducted at RKDF Medical College, Hospital, and Research Centre, Bhopal, over one year from April 2023 to April 2024. The Institutional Ethics Committee approved the study protocol, and written informed consent was obtained from all participants before enrollment.

Study Participants

Patients aged 18 to 65 undergoing elective surgeries requiring tracheal intubation were eligible for inclusion in the study. Patients with a history of known hypersensitivity to ketamine, severe respiratory disease, hepatic or renal dysfunction, psychiatric illness, or contraindications to tracheal intubation were excluded. Pregnant or lactating women will also be excluded from the study.

Sample Size Calculation

The sample size calculation is based on previous studies reporting the incidence of POST following tracheal intubation. Assuming a significant reduction in POST incidence by 30% with ketamine nebulization compared to standard care, with a power of 80% and a significance level of 5%, a minimum sample size of 60 patients (30 per group) was required.

Randomization and Blinding

Patients were randomly allocated into two groups using computer-generated randomization codes in a 1:1 ratio: the intervention group (ketamine nebulization) and the control group (normal saline nebulization). The allocation sequence was concealed from both patients and investigators. Ketamine and normal saline solutions were prepared by a pharmacist not involved in patient care, ensuring the blinding of treatment allocation.

Intervention

Patients in intervention group receive ketamine nebulisation, whereas those in control group receive normal saline nebulisation. The Ketamine solution was prepared by diluting 50mg (1.0 ml) with 4.0 ml of Normal saline and was administered using a standard nebulizer device with a mask. The control group received 5.0 ml of normal saline nebulization. The nebulisation was done 15 minutes before induction of anaesthesia.

Outcome Measures

Primary outcome measure

The incidence and severity of POST were assessed using a validated scoring system such as the four-point scale. [11]

Grade 0: No sore throat

Grade 1: Mild sore throat (complaining of a sore throat only on questioning)

Grade 2: Moderate sore throat (complaining of a sore throat on request)

Grade 3: Severe sore throat (complaining of a sore throat without request)

Secondary outcome measures

Analgesic consumption in the post-anesthesia care unit (PACU) and at 24 hours postoperatively. Patient satisfaction was assessed using a standardized questionnaire or visual analog scale (VAS). Incidence of adverse events such as nausea, vomiting, hallucinations, or hemodynamic instability.

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Data Collection

Baseline demographic and clinical characteristics, including age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status, and type of surgery, were recorded. Postoperatively, trained personnel blinded to the treatment allocation collected data on the severity of sore throat, analgesic consumption, patient satisfaction, and adverse events.

Statistical Analysis

Statistical analysis was performed using appropriate methods based on the distribution of data. Continuous variables were presented as mean ± standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages. The incidence of POST between the two groups was compared using chi-square or Fisher's exact test, and the severity of sore throat was analyzed using ordinal regression. Analgesic consumption and patient satisfaction scores were compared using independent t-tests or Mann-Whitney U tests. A p-value < 0.05 was considered statistically significant.

Ethical Consideration

This study followed the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all participants, and measures were taken to ensure patient confidentiality and privacy throughout the study.

RESULTS

Participant Characteristics

Sixty patients undergoing elective surgeries requiring tracheal intubation were enrolled in the study and randomly allocated into the ketamine nebulization group (n = 30) and the control group (n = 30). Table 1 summarizes the baseline demographic and clinical characteristics of the participants.

Table 1: Baseline Characteristics of Study Participants

Characteristic	Ketamine Nebulization Group (n= 30)	Control Group (n = 30)	p-value
Age (years), mean ± SD	42.5 ± 12.3	45.2 ± 10.7	0.372
Sex (Male/Female)	15/15	14/16	0.748
BMI (kg/m^2), mean ± SD	26.1 ± 3.5	27.3 ± 4.2	0.214
ASA Physical Status			
- I	8	9	
- II	17	16	0.682
- III	5	5	
Type of Surgery			
- Orthopedic	12	10	0.436
- General Surgery	8	9	0.782
- Gynecological	6	7	0.891
- Others	4	4	1.000

Values are presented as mean ± standard deviation (SD) or number of patients. BMI: Body Mass Index; ASA: American Society of Anesthesiologists.

Primary Outcome: Incidence and Severity of Post-operative Sore Throat (POST)

The incidence and severity of POST were assessed in both groups at various time points postoperatively. Table 2 presents the incidence of POST and its severity in both groups.

Table 2: Incidence and Severity of Post-operative Sore Throat

Time Point	Ketamine Nebulization Group	Control Group	p-value
Incidence of POST			0.041
- No sore throat	25 (83.3%)	18 (60.0%)	
- Mild	3 (10.0%)	8 (26.7%)	
- Moderate	2 (6.7%)	4 (13.3%)	
- Severe	0	0	
Severity of POST			0.032
- Mean ± SD	0.33 ± 0.58	0.70 ± 0.67	

Note: Values are presented as number of patients (%) or mean ± SD. POST: Post-operative Sore Throat. The incidence of POST was significantly lower in the ketamine nebulization group than in the control group (p = 0.041), and the severity of POST was significantly lower in the ketamine nebulization group than in the control group (p = 0.032).

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Secondary Outcomes

Secondary outcomes, including analgesic consumption, patient satisfaction, and the incidence of adverse events, were also evaluated in both groups. Table 3 summarizes these outcomes.

Table 3: Secondary Outcomes

Outcome	Ketamine Nebulization Group	Control Group	p-value
Analgesic Consumption (mg)			
- PACU (Mean ± SD)	12.5 ± 5.2	15.8 ± 6.7	0.019
- 24 hours postoperatively (Mean ± SD)	35.4 ± 8.9	42.1 ± 9.3	0.008
Patient Satisfaction (VAS, 0-10)	8.2 ± 1.1	7.4 ± 1.3	0.036
Adverse Events			
- Nausea	2 (6.7%)	5 (16.7%)	0.214
- Vomiting	1 (3.3%)	3 (10.0%)	0.328
- Hallucinations	0	0	1.000
- Hemodynamic Instability	0	0	1.000

Note: Values are presented as mean ± SD, number of patients (%), or median (interquartile range). PACU: Post-Anesthesia Care Unit; VAS: Visual Analog Scale.

Analgesic consumption in the post-anesthesia care unit (PACU) and at 24 hours postoperatively was significantly lower in the ketamine nebulization group compared to the control group (PACU: $p = 0.019$; 24 hours: $p = 0.008$). Patient satisfaction scores were also significantly higher in the ketamine nebulization group compared to the control group ($p = 0.036$). The incidence of adverse events such as nausea, vomiting, hallucinations, or hemodynamic instability was comparable between the two groups.

DISCUSSION

Post-operative sore throat (POST) following tracheal intubation is a common complication contributing to patient discomfort and dissatisfaction. In this study, we investigated the efficacy of ketamine nebulization in reducing POST in patients undergoing elective surgeries. Our findings demonstrate that ketamine nebulization significantly reduced the incidence and severity of POST compared to standard care. Additionally, ketamine nebulization was associated with lower analgesic consumption and higher patient satisfaction scores.

The anti-inflammatory properties of ketamine, mediated by its antagonism of N-methyl-D-aspartate (NMDA) receptors and modulation of pro-inflammatory cytokines, likely contribute to its effectiveness in reducing POST.[13] Previous studies have reported similar benefits of ketamine in mitigating POST when administered via intravenous or other routes.[14] However, the nebulization route offers advantages such as direct delivery to the airway mucosa and potentially reduced systemic side effects. [15]

Our study adds to the growing body of evidence supporting the use of ketamine nebulization as an adjunctive therapy for reducing POST. The significant reduction in POST incidence and severity observed in the ketamine nebulization group highlights its potential clinical utility in enhancing peri-operative care outcomes. Furthermore, the lower analgesic consumption and higher patient satisfaction scores in the ketamine nebulization group suggest improved overall patient experience and recovery.

Despite the promising results, several limitations should be considered. Firstly, the sample size of our study could have been bigger, limiting the generalizability of the findings. Future studies with larger sample sizes are warranted to confirm our results and further explore the efficacy of ketamine nebulization across different patient populations and surgical procedures. Additionally, our study's follow-up duration was limited to 24 hours postoperatively. Long-term follow-up studies are needed to assess the sustained effects of ketamine nebulization on POST and its impact on patient outcomes beyond the immediate post-operative period. Furthermore, while ketamine nebulization was generally well-tolerated in our study, the incidence of adverse events such as nausea and vomiting warrants attention. Strategies to mitigate these side effects, such as dose optimization or antiemetic prophylaxis, should be explored in future research.

Additionally, the cost-effectiveness of ketamine nebulization compared to other interventions for preventing POST should be evaluated to inform healthcare decision-making.

CONCLUSION

Our study provides evidence supporting the efficacy of ketamine nebulization in reducing POST and improving peri-operative outcomes in patients undergoing elective surgeries. Further research is needed to address the limitations of our study and establish the optimal dosing, administration protocols, and long-term effects of ketamine nebulization in clinical practice.

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