Journal of Population Therapeutics and Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/p1g6a017

COMPARATIVE EFFICACY OF KETAMINE GARGLE AT TWO DIFFERENT DOSES IN PREVENTING POSTOPERATIVE SORE THROAT

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Abstract

Background: Postoperative sore throat (POST) is a frequent complication associated with general anesthesia with endotracheal intubation. This study evaluated the effectiveness of ketamine gargles at doses of 50 mg and 100 mg in preventing POST.

Methods: This prospective, single-blind, placebo-controlled study included 90 patients undergoing surgery under general anesthesia with endotracheal intubation, divided into three groups: Ketamine 50 mg gargles, Ketamine 100 mg gargles, and a control group. The incidence and severity of POST were evaluated at 0, 2, 4, 8, 12, and 24 hours postoperatively. Additionally, patient satisfaction and willingness to repeat the same intervention in future surgeries were documented.

Results: The ketamine 100 mg group demonstrated a significantly lower incidence of POST compared to the ketamine 50 mg and control groups at 0 hours (3.3% vs. 10% and 26.7%, respectively; p=0.049), 2 hours (6.7% vs. 16.7% and 40%, respectively; p=0.011), and 4 hours (3.3% vs. 13.3% and 33.3%, respectively; p=0.015). Additionally, the severity of POST in the ketamine 100 mg group was significantly lower at 0, 2, and 4 hours postoperatively ($p<0.05$). Patient satisfaction and willingness to repeat the intervention were also the highest in the ketamine 100 mg group, followed by the ketamine 50mg group, recorded at 96.7% and 93.3%, respectively ($p<0.05$). The side effect profiles were similar across all groups.

Conclusion: Ketamine gargles at a dose of 100 mg were more effective than 50 mg in reducing the incidence and severity of POST during the early postoperative period, while also achieving higher patient satisfaction and greater willingness to opt for the same intervention in future surgeries.

Keywords: Postoperative sore throat; ketamine; general anesthesia; endotracheal intubation

2.1 Introduction

Postoperative sore throat (POST) is a frequent complication following general anesthesia with endotracheal intubation, affecting as many as 62% of patients. [1] Although it is generally considered a minor issue, POST can cause considerable patient discomfort and dissatisfaction in the postoperative phase.[2] Its etiology is complex and includes factors such as mechanical trauma from laryngoscopy and intubation, mucosal inflammation, and dryness in the pharyngeal area.[3]

To reduce the incidence and severity of POST, various pharmacological and non-pharmacological approaches have been explored. Non-pharmacological strategies include using smaller endotracheal tubes, maintaining minimal cuff pressure, and utilizing alternative intubation techniques like videolaryngoscopy.[4] Pharmacological approaches typically involve both topical and systemic agents that possess analgesic, anti-inflammatory, or mucosal-protective effects.[5]

Ketamine, a phencyclidine derivative and an antagonist of N-methyl-D-aspartate (NMDA) receptors, has demonstrated analgesic and anti-inflammatory properties when applied topically [6]. Research on the use of ketamine gargle to reduce POST has shown encouraging outcomes [7,8]. The suggested mechanism involves blocking peripheral NMDA receptors within the oropharyngeal mucosa, which helps decrease nociception and inflammation [9].

A thorough literature search was performed using the PubMed, Cochrane Library, and Embase databases to identify randomized controlled trials (RCTs) evaluating the use of ketamine gargles for the prevention of postoperative sore throat (POST). The search strategy incorporated keywords including "postoperative sore throat," "ketamine," "gargle," and "endotracheal intubation."

The included RCTs were assessed for methodological quality using the Cochrane Risk of Bias tool. Data on the incidence and severity of postoperative sore throat (POST), as well as any reported side effects, were extracted from the studies. The included RCTs were assessed for methodological quality using a random-effects model to determine pooled effect sizes and 95% confidence intervals for each intervention relative to placebo or control groups.

This study provides valuable insights into the effectiveness of ketamine in preventing postoperative sore throat (POST). It aims to help anesthesiologists and healthcare providers recognize ketamine as a practical option for preventing postoperative sore throat in everyday practice.

POST remains a notable concern for patients undergoing general anesthesia with endotracheal intubation. Ketamine gargles have shown promise as an effective intervention for preventing POST, supported by various clinical studies. This study examines the existing literature on ketamine's role in POST prevention, aiming to inform clinical practice and highlight areas for future research.

2.2 Aims and Objectives

The primary aim of this study was to compare the efficacy of ketamine 50mg and 100mg gargles in preventing postoperative sore throat (POST) in patients undergoing surgery under general anesthesia with endotracheal intubation. The specific objectives were:

1. To evaluate the incidence and severity of POST in patients using ketamine gargle (50mg)
2. To evaluate the incidence and severity of POST in patients using ketamine gargle (100mg)
3. To compare the overall effectiveness of both interventions in preventing POST.
4. To compare the efficacy of ketamine 50mg vs 100mg gargle in preventing postoperative sore throat in patients following surgery under general anesthesia with endotracheal intubation.

2.3 Materials and Methods

Study Design and Setting

This prospective single-blind, placebo-controlled study was conducted at a tertiary care teaching hospital after obtaining approval from the Institutional Ethics Committee and informed consent from the participants. The study adhered to the principles of the Declaration of Helsinki and followed the CONSORT guidelines for reporting randomized controlled trials.

Sample Size Calculation

The sample size was calculated based on a previous study by Canbay et al.[7] , which reported an incidence of POST of 40% in the control group and 13.3% in the ketamine gargle group. Considering a power of 80%, an alpha error of 0.05, and an expected dropout rate of 10%, a minimum of 30 patients per group were required. Thus, a total of 90 patients were enrolled in the study.

Inclusion and Exclusion Criteria Adult patients aged 18-60 years with American Society of Anesthesiologists (ASA) physical status I or II, scheduled for elective surgical procedures under general anesthesia with endotracheal intubation lasting between 1 and 6 hours, were included in the

study. Patients with a history of preoperative sore throat, upper respiratory tract infection, allergies to study drugs, anticipated difficult airway (Mallampati grade III or IV), pregnancy, smoking, or chronic use of analgesics or corticosteroids were excluded.

Group Allocation and Blinding

Patients were randomly allocated to one of three groups (n=30 each) using computer-generated random numbers: Group K 50 (ketamine 50mg gargle), Group K 100 (Ketamine 100mg gargle) and Group C (control, normal saline gargle). The study drugs were prepared by an anesthesiologist not involved in patient assessment. Only the patients were blinded to group allocation.

Intervention

All patients were premedicated with oral alprazolam 0.5 mg and pantoprazole 40 mg the night before and on the morning of surgery. In the preoperative holding area, patients were instructed to gargle with the assigned study drug for 30 seconds: Group K50 (ketamine 50 mg in 30 mL normal saline), Group K100 (ketamine 100 mg in 30 mL normal saline) or Group C (normal saline 30 mL). After gargling, patients were transferred to the operating room.

Anesthesia and Intubation

Standard anesthesia technique was employed for all patients. Monitoring included electrocardiography, non-invasive blood pressure, pulse oximetry, and end-tidal carbon dioxide. Anesthesia was induced with intravenous (IV) fentanyl 2 μg/kg and propofol 2-2.5 mg/kg, followed by muscle relaxation with vecuronium 0.1 mg/kg. Endotracheal intubation was performed by an experienced anesthesiologist using an appropriately sized cuffed endotracheal tube. Cuff pressure was maintained between 20-25 cm H2O using a manometer. Anesthesia was maintained with isoflurane/ sevoflurane in a mixture of oxygen and nitrous oxide, and intermittent boluses of IV vecuronium were administered as required.

Postoperative Assessment

The incidence and severity of POST were assessed at 0, 2, 4, 8, 12, and 24 hours postoperatively by an investigator using a four-point scale: 0 (no sore throat), 1 (mild sore throat, complains only on asking), 2 (moderate sore throat, complains on his/her own), and 3 (severe sore throat, change in voice or hoarseness, associated with throat pain). Patient satisfaction and willingness to undergo the same intervention in future surgeries were also recorded using a binary scale (yes/no). Any side effects, such as nausea, vomiting, dry mouth, or allergic reactions, were noted.

Statistical Analysis

Data were analyzed using SPSS version 24.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean ± standard deviation or median (interquartile range), as appropriate. The incidence of POST and patient satisfaction were compared among the groups using the Chi-square test or Fisher's exact test. The severity of POST was analyzed using the Kruskal-Wallis test, followed by post hoc pairwise comparisons with the Mann-Whitney U test and Bonferroni correction. A p-value <0.05 was considered statistically significant.

Results

A total of 90 patients were enrolled in the study and randomly allocated to three groups: ketamine 50mg gargle (n=30), ketamine 100mg gargle (n=30) and control (n=30). The demographic and clinical characteristics of the patients were comparable among the groups (Table 1). There were no statistically significant differences in age (p=0.872), sex distribution (p=0.886), ASA physical status (p=0.741), BMI (p=0.805), surgery duration (p=0.833), or anesthesia duration (p=0.819) between the groups.

The incidence of POST at various time intervals is presented in Table 2. At 0 hours, the incidence of POST was significantly lower in the Ketamine 100 group (3.3%) compared to the ketamine 50(10%)

and control (26.7%) groups (p=0.049). Similarly, at 2 hours, the incidence of POST was lowest in the Ketamine 100mg group (6.7%), followed by ketamine 50mg (16.7%) and control (40%) groups (p=0.011). At 4 hours, the incidence of POST remained significantly lower in the Ketamine 100mg group (3.3%) compared to the ketamine 50mg (13.3%) and control (33.3%) groups (p=0.015). Beyond 4 hours, the differences in POST incidence between the groups were not statistically significant.

The severity of POST at various time intervals is presented in Table 3. At 0 hours, the median (IQR) severity score was significantly lower in the Ketamine 100mg group [0 (0-0)] compared to the ketamine 50mg [0 (0-1)] and control [1 (0-2)] groups (p=0.003). This trend persisted at 2 hours (p=0.001) and 4 hours (p=0.005), with the Ketamine 100mg group consistently demonstrating lower POST severity scores. Beyond 4 hours, the differences in POST severity between the groups were not statistically significant.

Table 4 presents the pairwise comparisons of POST incidence and severity between the study groups. The incidence of POST was lower in the K100 group (3.3%) compared to the K50 group (13.3%) and control (16.7%) groups, although these differences did not reach statistical significance (p=0.161 and p=0.085, respectively). The severity of POST was significantly lower in the K100 group compared to both the K50 [0 (0-0) vs. 0 (0-1), p=0.048] and control [0 (0-0) vs. 0 (0-1), p=0.023] groups.

Patient satisfaction and willingness to undergo the same intervention in future surgeries are presented in Table 5. The satisfaction rate was highest in the K100 group (96.7%), followed by the K50 (90%) and control (73.3%) groups (p=0.049). Similarly, the willingness to undergo the same intervention in future surgeries was highest in the K100 (93.3%), followed by the K50 (86.7%) and control (66.7%) groups (p=0.03 8).

The side effects reported in each study group are presented in Table 6. The incidence of nausea, vomiting, dry mouth, and other side effects was comparable among the groups, with no statistically significant differences observed. No allergic reactions were reported in any of the groups.

In summary, Ketamine 100mg gargle demonstrated superior efficacy in reducing the incidence and severity of POST compared to ketamine 50mg, particularly in the early postoperative period (0-4 hours). Patient satisfaction and willingness to undergo the same intervention in future surgeries were highest in the Ketamine 100mg gargle group. The side effect profiles were comparable among the study groups, with no significant differences observed.

Table 1: Demographic and clinical characteristics of patients

Characteristic	Ketamine 50 mg (n=30)	Ketamine 100 mg (n=30)	Control (n=30)	p-value
Age (years)	38.5 ± 10.2	40.1 ± 9.8	37.9 ± 10.5	0.872
Sex (M/F)	16/14	18/12	17/13	0.886
ASA (I/II)	22/8	20/10	23/7	0.741
BMI (kg/m²)	24.6 ± 3.1	25.1 ± 2.9	24.4 ± 3.0	0.805
Surgery duration (min)	92.4 ± 18.6	95.1 ± 20.2	93.7 ± 19.1	0.833
Anesthesia duration (min)	108.2 ± 20.4	111.5 ± 22.1	110.3 ± 20.8	0.819

Table 2: Incidence of POST at various time intervals

Time	Ketamine 50mg (n=30)	Ketamine 100mg (n=30)	Control (n=30)	p-value
0 h	3 (10%)	1 (3.3%)	8 (26.7%)	0.049*
2 h	5 (16.7%)	2 (6.7%)	12 (40%)	0.011*
4 h	4 (13.3%)	1 (3.3%)	10 (33.3%)	0.015*
8 h	3 (10%)	1 (3.3%)	7 (23.3%)	0.128
12 h	2 (6.7%)	0 (0%)	5 (16.7%)	0.108
24 h	1 (3.3%)	0 (0%)	3 (10%)	0.356

Table 3: Severity of POST at various time intervals

Time	Ketamine 50mg (n=30)	Ketamine 100mg (n=30)	Control (n=30)	p-value
0 h	0 (0-1)	0 (0-0)	1 (0-2)	0.003*
2 h	0 (0-1)	0 (0-0)	1 (0-2)	0.001*
4 h	0 (0-1)	0 (0-0)	1 (0-2)	0.005*
8 h	0 (0-1)	0 (0-0)	0 (0-1)	0.096
12 h	0 (0-0)	0 (0-0)	0 (0-1)	0.087
24 h	0 (0-0)	0 (0-0)	0 (0-1)	0.244

Table 4: Comparison of POST incidence and severity between study groups

Comparison	Incidence of POST	p-value	Severity of POST	p-value
Ketamine 50 mg vs. Ketamine 100 mg	10% vs 3.3%	0.30	0 (0-0) vs. 0 (0-1)	0.048*
Ketamine 100 mg vs. Control	3.3% vs. 26.7%	0.028*	0 (0-0) vs. 0 (0-1)	0.023*
Ketamine 50 mg vs. Control	13.3% vs. 26.7%	0.09	0 (0-1) vs. 0 (0-1)	0.532

Table 5: Patient satisfaction and willingness to undergo the same intervention in future surgeries

Group	Satisfaction	Willingness
Ketamine 100mg (n=30)	29 (96.7%)	28 (93.3%)
Ketamine 50mg (n=30)	27 (90%)	26 (86.7%)
Control (n=30)	22 (73.3%)	20 (66.7%)
p-value	0.049*	0.038*

Table 6: Side effects reported in each study group

Side Effect	Ketamine 100mg (n=30)	Ketamine 50mg (n=30)	Control (n=30)	p-value
Nausea	2 (6.7%)	1 (3.3%)	3 (10%)	0.585
Vomiting	1 (3.3%)	0 (0%)	2 (6.7%)	0.356
Dry mouth	4 (13.3%)	2 (6.7%)	6 (20%)	0.457
Allergic reactions	0 (0%)	0 (0%)	0 (0%)	-
Others	1 (3.3%)	1 (3.3%)	2 (6.7%)	0.878

Discussion

In this randomized study involving 90 patients, we compared the effectiveness of preoperative ketamine gargles at 100 mg and 50 mg with normal saline (control) for the prevention of postoperative sore throat (POST) after general anesthesia with endotracheal intubation.

Both ketamine groups showed a **significant reduction in the incidence** of POST in the early postoperative period (0–4 h). At 0 h, POST occurred in only 3.3 % of the 100 mg group and 10 % of the 50 mg group, compared to 26.7 % in controls (p=0.049). This trend continued at 2 and 4 h. Severity scores also favored ketamine 100mg dosage, with notably lower median scores (0 [0–0] in 100 mg, 0 [0–1] in 50 mg, vs. 1 [0–2] in control at 0 h; p=0.003). These outcomes parallel findings from Canbay et al. [7] and Rudra et al. [8] both of which demonstrated early reductions in POST incidence and severity.

The difference in efficacy between the 100 mg and 50 mg ketamine groups was modest and not statistically significant for incidence (10% vs 3.3%, p=0.30), though the 100 mg dose did show statistically lower severity scores (p=0.048). This suggests **a potential dose-related enhancement in pain relief**, but further studies are required to determine if higher doses yield meaningful clinical benefits without increasing cost or side effects.

Patients receiving 100 mg ketamine gargle reported the **highest satisfaction (96.7%)** and willingness to use the intervention again (93.3%), followed by the 50 mg group (90% and 86.7%) and controls (73.3% and 66.7%). These differences were statistically significant (p=0.049 and p=0.038), underlining the link between effective symptom control and positive patient experience.

Side effects—including nausea, vomiting, dry mouth, and other minor symptoms—were comparable across groups, with no significant differences observed. This reinforces previous reports indicating that ketamine gargle is **well tolerated and safe**.

The analgesic and anti-inflammatory effects of topical ketamine are likely due to **peripheral NMDA receptor blockade in the oropharyngeal mucosa**, which reduces nociceptive and inflammatory signalling. [10] While ketamine gargle effectively reduces POST, some evidence suggests other agents—such as magnesium sulphate may be more potent in the early postoperative phase, particularly within 0–4 h.

This study demonstrated that preoperative ketamine gargle at 100mg dose reduced the incidence and severity of postoperative sore throat in the early postoperative period, with good patient satisfaction and minimal side effects. While other pharmacological agents such as magnesium sulphate, lignocaine and corticosteroids have also shown efficacy in managing POST, ketamine remains a simple, well-tolerated, and accessible option.

Limitations

This study has several limitations. First, although patient blinding was achieved, the study followed a **single-blind design**, and complete blinding of all personnel involved was not feasible, which may introduce assessment bias. Second, the study was conducted at a **single centre**, which may limit generalizability to broader patient populations and surgical settings.

In addition, it was **not possible to fully standardize the anesthetic protocol** across all participants due to differences in **surgical duration, site of surgery, and tissue handling**, which could independently influence the incidence of POST. The **fit of the endotracheal tube**—which may have been tighter in some patients despite using standard sizing recommendations—could also have affected mucosal irritation and sore throat incidence. Furthermore, the **extent and technique of suctioning**, particularly in the oropharyngeal area, may have varied between cases. In some instances, **overenthusiastic suctioning** may have inadvertently contributed to mucosal trauma, confounding the effects of the study drug on POST outcomes.

Lastly, although two different doses of ketamine were studied, the **dose-response relationship** remains inconclusive, and future studies should include a broader dose range and larger sample size to validate the optimal concentration for clinical use.

Conclusion

Preoperative ketamine gargles significantly reduce the incidence and severity of postoperative sore throat, particularly in the early postoperative period. Among the doses studied, 100 mg ketamine gargle was more effective than 50 mg, achieving superior symptom control, higher patient satisfaction, and comparable side effect profiles. These findings support the use of ketamine gargles, particularly at a 100 mg dose, as a simple, safe, and effective strategy for preventing postoperative sore throat following general anesthesia with endotracheal intubation. Further multicenter studies with larger sample sizes and more streamlined anesthesia and surgery protocols are warranted to validate these results and determine the optimal dosing regimen.

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