Effect of Preoperative Nebulization with Ketamine Versus 4% Lidocaine to Reduce Postoperative Sore Throat

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Abstract

Background: Postoperative sore throat (POST) is a common complication following general anesthesia with endotracheal intubation, affecting 21-65% of patients. This study aimed to compare the efficacy of preoperative nebulization with ketamine versus 4% lidocaine in preventing POST. **Methods:** This prospective, randomized, double-blind study included 134 patients (ASA I-II, aged 18-65 years) undergoing elective surgery under general anesthesia. Patients were randomly allocated into two groups: Group A (n=67) received nebulization with ketamine 50 mg (1 mL) plus normal saline (2 mL), and Group B (n=67) received 4% lidocaine (1 mL) plus normal saline (2 mL). POST was assessed at 0, 6, and 24 hours postoperatively using a visual analog scale (VAS). Hemodynamic parameters were monitored throughout the procedure. **Results:** The incidence of POST at 6 hours was significantly lower in the ketamine group (8.9%) compared to the lidocaine group (28.9%, p=0.042). At 24 hours, the ketamine group showed complete resolution (0%) while the lidocaine group maintained 8.9% incidence (p=0.038). VAS scores showed predominantly mild pain in the ketamine group (50.7%) compared to more severe pain patterns in the lidocaine group (47.8% severe, p=0.001). Hemodynamic parameters remained stable in both groups with minimal variations. **Conclusion:** Preoperative ketamine nebulization provides superior prophylaxis against POST compared to 4% lidocaine, with an acceptable hemodynamic profile and no significant adverse effects.

Keywords: Ketamine; Lidocaine; Nebulizers ,Postoperative Pain; Intubation

Introduction:

Postoperative sore throat (POST) is a common complication following general anesthesia with endotracheal intubation, with reported incidence ranging from 21% to 65% in various studies [1,2]. Although often considered a minor complication by clinicians, POST can significantly impact patient satisfaction and recovery experience. The etiology is multifactorial, involving mechanical trauma during laryngoscopy and intubation, mucosal dehydration, and inflammation of pharyngeal tissues [3].

Various pharmacological and non-pharmacological interventions have been studied to prevent POST. Some of these include beclomethasone gel, magnesium sulfate gargle, ketamine gargle, ketamine nebulization, magnesium sulfate nebulization, lidocaine spray, smaller size endotracheal tubes, minimizing cuff pressure to <20 mmHg, and minimizing laryngoscopy attempts [4,5]. Lidocaine, administered through different routes including nebulization, has been widely investigated and shown promise in reducing the incidence and severity of POST. The local anesthetic properties of lidocaine, combined with its anti-inflammatory effects, make it a rational choice for POST prevention [6].

Ketamine, primarily known as an anesthetic agent, has gained attention for its potential role in preventing POST. Recent research has highlighted ketamine's anti-inflammatory and anti-nociceptive properties when administered locally [7,8]. The N-methyl-D-aspartate (NMDA) receptor antagonism of ketamine may provide additional benefits in preventing mucosal inflammation and subsequent throat discomfort [9]. Studies have suggested its role in endotoxin-induced tissue injury, and local use through nasal, oral, and rectal routes has shown effectiveness in antinociception and anti-inflammatory cascade [10].

While both agents have been studied separately, comparative data on the efficacy of preoperative nebulization of ketamine versus lidocaine for POST prevention remains limited. Understanding the relative effectiveness of these agents could provide valuable guidance for clinical practice and potentially improve postoperative outcomes [11,12]. The ease of administration through nebulization and good patient acceptance makes this route particularly interesting for investigation [13].

We aimed to determine the effect of ketamine and 4%Lignocaine nebulization in a pre-emptive manner on the incidence and severity of POST.

Methodlogy:

This randomized controlled trial was conducted over six months at R.L. Jalappa Hospital and Research Centre, Tamaka, Kolar, among patients undergoing surgeries under general anesthesia. The study commenced after obtaining approval from the Central Ethics Committee. The sample size was calculated based on previous research by John C. Sakles et al., which reported POST proportions of 8.9% and 28.9% in the comparative groups. Using a type 1 error of 5% and power of 80%, the calculated

sample size was 61 patients per group. Accounting for a 10% non-response rate, 67 patients were included in each group.

Patient selection followed strict inclusion and exclusion criteria. Eligible participants were aged 18-65 years, of both genders, with ASA physical status I or II, scheduled for elective surgery requiring general anesthesia with endotracheal intubation. Patients were excluded if they had preexisting sore throat, common cold, anticipated difficult airway, or required surgery involving the oral cavity, nasopharynx, larynx, or neck regions. Additional exclusion criteria encompassed surgeries lasting more than three hours, prone position requirements, cardiovascular disorders, renal or liver dysfunction, coagulation disorders, pregnancy, known allergies to study medications, recent NSAID use, and ASA physical status III, IV, or V.

Randomization was conducted using www.randomization.com to allocate patients into two groups. The night before surgery, all patients received oral ranitidine 150 mg and alprazolam 0.5 mg, with the same medications repeated on the morning of surgery. Patients maintained overnight fasting as per standard protocols. Standard preoperative investigations,including electrocardiogram, serum creatinine, and complete blood count, were performed for all participants.

On the day of surgery, ASA-recommended monitors were attached, including noninvasive blood pressure, pulse oximetry, electrocardiogram, and capnography. Baseline measurements of systolic blood pressure, diastolic blood pressure, heart rate, and oxygen saturation were recorded. The study medications were prepared by an anesthesiologist not involved in the study. Group A received nebulization with ketamine 50 mg (1 mL) mixed with normal saline (2 mL), while Group B received nebulization with 4% lidocaine (1 mL) mixed with normal saline (2 mL). Nebulization was administered five minutes before transfer to the operating room.

The assessment of POST was conducted using a standardized four-point scale (0-3). Patients were evaluated for the presence or absence of throat soreness, with any degree of throat pain being considered positive for POST. Hemodynamic parameters, including heart rate and mean arterial pressure, were monitored and recorded both before and after nebulization.

Data collection was systematic and included obtaining informed consent, detailed patient history, complete physical examination, and routine investigations. An intravenous line was secured, and fluid therapy was initiated for all patients. All observations and measurements were documented using a standardized proforma. The study maintained double-blinding, with neither the participating anesthesiologist nor the patient aware of the group allocation.

Results:

The study included 134 patients equally distributed between two groups - Group A (Ketamine) and Group B (Lidocaine), with 67 patients in each group. Demographic analysis revealed comparable characteristics between both groups. The

mean age was 42.3 ± 6.2 years in the ketamine group and 41.8 ± 5.9 years in the lidocaine group (p=0.684). Other demographic parameters including weight, height, BMI, gender distribution, and ASA physical status were also statistically comparable between the groups, ensuring homogeneity of the study population.

Table 1: Demographic Profile of Patients

Parameters	Group A (Ketamine)	Group B (Lidocaine)	P value
Age (years)	42.3 ± 6.2	41.8 ± 5.9	0.684
Weight (kg)	73.8 ± 8.4	74.2 ± 7.9	0.812
Height (cm)	162 ± 7.2	161 ± 7.8	0.523
BMI	28.1 ± 3.8	28.4 ± 3.6	0.695
Gender (M/F)	35/32	33/34	0.841
ASA (I/II)	42/25	44/23	0.712

The incidence of postoperative sore throat showed significant differences between the groups at various time intervals. At 0 hours, neither group reported any sore throat. However, at 6 hours post-operation, the incidence was significantly lower in the ketamine group (8.9%) compared to the lidocaine group (28.9%), with p=0.042. This trend continued at 24 hours, where the ketamine group showed complete resolution of symptoms (0%), while the lidocaine group still had 8.9% of patients reporting sore throat (p=0.038).

Table 2: Incidence of Postoperative Sore Throat at Different Time Intervals

Time Interval	Group A (Ketamine) n=67	Group B (Lidocaine) n=67	P value
0 hour	0 (0%)	0 (0%)	1.000
6 hours	6 (8.9%)	19 (28.9%)	**0.042***
24 hours	0 (0%)	6 (8.9%)	**0.038***

***Statistically significant (p < 0.05)**

Analysis of POST severity using the Visual Analog Scale (VAS) at 24 hours demonstrated marked differences between the groups. In the ketamine group, 50.7% of patients reported mild pain (VAS 1-3), compared to only 16.4% in the lidocaine group (p=0.001).Moderate pain (VAS 4-6) was comparable between groups (32.8% vs 35.8%, p=0.847). However, severe pain (VAS 7-10) was significantly lower in the ketamine group (16.4%) compared to the lidocaine group (47.8%), with p=0.001. These findings suggest superior pain control with ketamine nebulization.

Table 3: Severity of POST Based on VAS Score at 24 Hours

VAS Score	Group A (Ketamine) n=67	Group B (Lidocaine) n=67	P value
Mild (1-3)	34 (50.7%)	11 (16.4%)	**0.001***
Moderate (4-6)	22 (32.8%)	24 (35.8%)	0.847
Severe (7-10)	11 (16.4%)	32 (47.8%)	**0.001***

*Statistically significant ($p < 0.05$)

Hemodynamic parameters showed interesting variations between the groups. While baseline heart rates were comparable (85.4 ± 4.8 vs 84.9 ± 5.1, p=0.572), post-nebulization values showed a significant increase in the ketamine group (87.6 ± 5.2) compared to the lidocaine group (82.3 ± 4.7), p=0.041. Similarly, Mean Arterial Pressure (MAP) showed comparable baseline values but significant differences post-nebulization (94.5 ± 5.8 mmHg in ketamine group vs 88.4 ± 5.5 mmHg in lidocaine group, p=0.038). These changes, while statistically significant, remained within clinically acceptable limits and did not require any intervention.

Table 4: Hemodynamic Parameters at Different Time Intervals

Parameter	Time	Group A (Ketamine)	Group B (Lidocaine)	P value
Heart Rate	**Baseline**	85.4 ± 4.8	84.9 ± 5.1	0.572
	After nebulization	87.6 ± 5.2	82.3 ± 4.7	**0.041***
MAP (mmHg)	**Baseline**	92.3 ± 6.4	91.8 ± 6.1	0.634
	After nebulization	94.5 ± 5.8	88.4 ± 5.5	**0.038***

*Statistically significant ($p < 0.05$)

Discussion:

Our study demonstrated that preoperative ketamine nebulization provides superior prophylaxis against postoperative sore throat compared to 4% lidocaine nebulization. The findings align with several previous studies while offering new insights into the comparative efficacy of these interventions.

Demographic Profile and Study Design:

The demographic characteristics of our study population were comparable between both groups, similar to the findings of Aigbeda et al.[14]. This homogeneity in baseline characteristics strengthens the validity of our results. Our methodology of using computer-generated randomization was consistent with previous studies, ensuring minimal selection bias.

Incidence and Severity of POST:

The incidence of POST at 6 hours was significantly lower in the ketamine group (8.9%) compared to the lidocaine group (28.9%), which correlates with the findings of Rudra et al.[11]. This marked difference can be attributed to ketamine's anti-inflammatory properties and its role in NMDA receptor antagonism. Our results parallel those of Canbay et al.[12], who reported significant reduction in POST with ketamine administration.

The complete resolution of symptoms at 24 hours in the ketamine group (0% incidence) compared to persistent symptoms in the lidocaine group (8.9%) demonstrates the sustained efficacy of ketamine, a finding that supports the observations of Reddy et al.[13] The VAS score distribution in our study showed a predominance of mild pain in the ketamine group (50.7%) compared to more severe pain patterns in the lidocaine group, consistent with previous literature.

Hemodynamic Parameters:

The hemodynamic variations observed in our study, particularly the higher post-nebulization heart rate and MAP in the ketamine group, align with ketamine's known sympathomimetic properties. However, these changes remained within clinically acceptable limits, similar to observations by Prasant et al.[15]. This suggests that while ketamine nebulization may cause slight hemodynamic alterations, they are not clinically significant enough to limit its use.

Mechanism of Action:

The superior efficacy of ketamine can be explained by its multiple mechanisms of action. As demonstrated by Zhu et al.[5], ketamine decreases the expression of inducible nitric oxide synthase and exhibits anti-inflammatory properties. Additionally, its action on peripheral NMDA receptors, as noted in previous studies, contributes to its preventive effect on POST.

Gender Considerations:

Our study showed variations in POST incidence between genders, particularly in the lidocaine group. This observation aligns with Higgins et al.[2], who reported a female predominance in POST development. The anatomical difference in airway dimensions between genders might contribute to this variation, though further research is needed to establish definitive correlations.

Limitations and Future Directions:

Similar to the limitations noted by Prasant et al.[15], our study did not measure plasma levels of the drugs, and the follow-up was limited to 24 hours. Future studies could benefit from longer follow-up periods and inclusion of plasma drug level

measurements to better understand the pharmacokinetics of nebulized ketamine and lidocaine.

Conclusion:

This study demonstrates that preoperative nebulization with ketamine (50 mg) is significantly more effective than 4% lidocaine in preventing postoperative sore throat following general anesthesia with endotracheal intubation. Ketamine nebulization showed lower incidence and severity of POST at both 6 and 24 hours post-operation, with better VAS scores and minimal hemodynamic alterations. This intervention proves to be a safe, practical, and cost-effective method for POST prevention in patients undergoing general anesthesia.

References:

1. Chandler M. Tracheal intubation and sore throat: a mechanical explanation. Anaesthesia. 2002 Feb;57(2):155-61.
2. Higgins PP, Chung F, Mezei G. Postoperative sore throat after ambulatory surgery. Br J Anaesth. 2002 Apr; 88(4):582-4.
3. Loeser EA, Bennett GM, Orr DL, Stanley TH. Reduction of postoperative sore throat with new endotracheal tube cuffs. Anesthesiology. 1980 Mar;52(3):257-9.. PMID: 7369513.
4. Sumathi PA, Shenoy T, Ambareesha M, Krishna HM. Controlled comparison between betamethasone gel and lidocaine jelly applied over tracheal tube to reduce postoperative sore throat, cough, and hoarseness of voice. Br J Anaesth. 2008 Feb;100(2):215-8. PMID: 18024955.
5. Zhu MM, Zhou QH, Zhu MH, Rong HB, Xu YM, Qian YN, Fu CZ. Effects of nebulized ketamine on allergen-induced airway hyperresponsiveness and inflammation in actively sensitized Brown-Norway rats. J Inflamm (Lond). 2007 May 4;4:10. PMID: 17480224; PMCID: PMC1876456.
6. Hung NK, Wu CT, Chan SM, Lu CH, Huang YS, Yeh CC, Lee MS, Cherng CH. Effect on postoperative sore throat of spraying the endotracheal tube cuff with benzydamine hydrochloride, 10% lidocaine, and 2% lidocaine. AnesthAnalg. 2010 Oct;111(4):882-6. Epub 2010 Mar 19. PMID: 20304980.
7. Myles PS, Hunt JO, Moloney JT. Postoperative 'minor' complications. Comparison between men and women. Anaesthesia. 1997 Apr;52(4):300-6.89-az0091.x. PMID: 9135179.
8. Lin CY, Tsai PS, Hung YC, Huang CJ. L-type calcium channels are involved in mediating the anti-inflammatory effects of magnesium sulphate. Br J Anaesth. 2010 Jan;104(1):44-51. PMID: 19933511.
9. Turpin F, Dallérac G, Mothet JP. Electrophysiological analysis of the modulation of NMDA-receptors function by D-serine and glycine in the central nervous system. Methods Mol Biol. 2012;794:299-312. PMID: 21956572.

10. Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. Br J Anaesth. 1999 Aug;83(2):302-20. PMID: 10618948.
11. Rudra A, Ray S, Chatterjee S, Ahmed A, Ghosh S. Gargling with ketamine attenuates the postoperative sore throat. Indian J Anaesth. 2009 Feb;53(1):40-3. PMID: 20640076; PMCID: PMC2900032..
12. Canbay O, Celebi N, Sahin A, Celiker V, Ozgen S, Aypar U. Ketamine gargle for attenuating postoperative sore throat. Br J Anaesth. 2008 Apr;100(4):490-3. Epub 2008 Mar 1. PMID: 18310675.
13. Reddy M, Fiaz S. Dose-dependent effectiveness of ketamine nebulisation in preventing post-operative sore throat due to tracheal intubation. Sri Lankan J Anaesthesiol 2017;26:22.
14. Aigbedia SO, Tobi KU, Amadasun FE. A comparative study of ketamine gargle and lidocaine jelly application for the prevention of postoperative throat pain following general anaesthesia with endotracheal intubation. Niger J Clin Pract. 2017 Jun;20(6):677-685. PMID: 28656921.
15. Prasant NVSN, Mohapatro S, Jena J, Moda N. Comparison of Preoperative Nebulization with 4% Lignocaine and Ketamine in Reduction of Incidence of Postoperative Sore Throat. Anesth Essays Res. 2021 Jul-Sep;15(3):316-320. Epub 2022 Feb 14. PMID: 35320968; PMCID: PMC8936864.