

Comparative Study to Evaluate the Incidence of Postoperative Sore Throat after Preinduction Nebulization with Ketamine and Magnesium Sulfate in Patients Undergoing General Anaesthesia with Endotracheal Intubation

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Abstract

Background: Postoperative sore throat (POST) is a common complication after general anaesthesia with endotracheal intubation, with a reported incidence of up to 62%, causing significant patient discomfort. Ketamine and magnesium sulfate, both N-methyl-D-aspartate (NMDA) receptor antagonists with anti-inflammatory and anti-nociceptive properties, have been used as preinduction nebulization to reduce POST, but comparative evidence on their relative efficacy is limited.

Objective: To compare the efficacy of preinduction nebulization with ketamine and magnesium sulfate in reducing the incidence and severity of postoperative sore throat in patients undergoing elective general surgery under general anaesthesia with endotracheal intubation.

Methods: This prospective, randomized, double-blinded study was conducted over one year at a tertiary care teaching hospital in 100 adult patients (18-50 years, ASA physical status I and II) undergoing elective general surgical procedures. Patients were randomized into two equal groups: Group A received nebulization with ketamine 50 mg and Group B received nebulization with magnesium sulfate 500 mg, both diluted to 5 mL and administered 15 minutes before induction. POST was assessed on a validated 4-point scale (0-3) at immediate post-extubation, and at 1, 6, 12 and 24 hours postoperatively. Hemodynamic parameters were recorded at standard intervals. Data were analyzed using SPSS version 28.0, with the unpaired t-test, Mann-Whitney U test and Chi-square test applied as appropriate; $p < 0.05$ was considered significant.

Results: The two groups were comparable for age, weight, gender, ASA-PS grade and duration of anaesthesia ($p > 0.05$ for all). The overall incidence of POST was significantly lower in Group A (26%) than Group B (52%, $p = 0.0005$). Incidence and severity of POST were significantly lower in Group A at immediate post-extubation, 1 hour, 6 hours and 24 hours ($p < 0.05$), although the difference at 12 hours was not statistically significant ($p = 0.1739$). Hemodynamic parameters remained comparable between groups at all time points.

Conclusion: Preinduction nebulization with ketamine is more effective than magnesium sulfate in reducing the incidence and severity of postoperative sore throat following endotracheal intubation, without adversely affecting hemodynamic stability.

Keywords: Postoperative Sore Throat; Ketamine; Magnesium Sulfate; Nebulization; Endotracheal Intubation; General Anaesthesia; NMDA Receptor Antagonist.

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Introduction

Postoperative sore throat (POST) is one of the most common and distressing complications following general anaesthesia with endotracheal intubation, with a reported incidence ranging up to 62% [1,2]. Patients typically describe pharyngeal discomfort, hoarseness of voice and dysphagia [2]. Although

often regarded as a minor postoperative complaint, POST is associated with patient dissatisfaction, prolonged hospital stay and increased healthcare costs, and it remains the second most common patient complaint after general anaesthesia despite continued advances in airway management [4]. The

pathophysiology of POST is multifactorial, involving mechanical trauma to the airway mucosa, cuff-related ischaemia, and inflammation mediated by activation of nociceptive type-C fibres [5]. Reported risk factors include younger age, female sex, pre-existing respiratory disease, larger endotracheal tube size, cuff pressures exceeding 20 cm H₂O, prolonged duration of intubation and traumatic or repeated laryngoscopy attempts [5,6,7,9]. A variety of pharmacological and non-pharmacological interventions - including topical anaesthetics, nebulized corticosteroids, lidocaine and humidification - have been evaluated for POST prophylaxis, but the optimal strategy remains undefined [10,11]. Ketamine and magnesium sulfate are both N-methyl-D-aspartate (NMDA) receptor antagonists possessing anti-inflammatory and anti-nociceptive properties, and both have shown promise in attenuating POST when delivered as gargles, lozenges or nebulization [3,14,16]. The benefit of ketamine appears to be predominantly a local mucosal effect, since systemic intravenous administration has not consistently reduced the incidence or severity of sore throat [3]. Given their shared mechanism of action, a head-to-head comparison of nebulized ketamine and magnesium sulfate is clinically relevant but has been reported in only a small number of trials [12,13,17,18], with variable conclusions regarding comparative efficacy.

Objective: This study was designed to compare the efficacy of preinduction nebulization with ketamine versus magnesium sulfate in reducing the incidence and severity of postoperative sore throat in adult patients undergoing elective general surgical procedures under general anaesthesia with endotracheal intubation, while also assessing their effect on perioperative haemodynamic parameters.

Materials and Methodology

Study Design and Setting: This was a prospective, randomized, double-blinded, controlled study conducted in the Department of Anaesthesiology over a period of one year in a tertiary care teaching hospital, following approval from the Institutional Ethics Committee and after obtaining written informed consent from all participants.

Study Population and Sample Size: One hundred adult patients aged 18-50 years, belonging to American Society of Anesthesiologists physical status (ASA-PS) class I or II and scheduled for elective general surgical procedures under general anaesthesia with endotracheal intubation lasting more than one hour, were enrolled. Sample size was calculated using G-power analysis with a study power of 80% and an alpha error of 5%, yielding a minimum requirement of 100 subjects (50 per

group). Patients with anticipated difficult airway, pregnancy, thyroid, oral or neck surgery, recent upper respiratory tract infection or asthma, ASA-PS class III/IV, or surgery of less than one hour duration were excluded.

Randomization and Blinding: Eligible patients were randomly allocated in a 1:1 ratio into two groups of 50 patients each using a computer-generated random number sequence: Group A (ketamine) and Group B (magnesium sulfate). The study drug was prepared by an independent anaesthesiologist not involved in perioperative care, and both the patient and the treating team performing nebulization and subsequent assessment were blinded to the group allocation.

Intervention: Group A received nebulization with ketamine 50 mg (1 mL) diluted to 5 mL with sterile water, and Group B received nebulization with magnesium sulfate 500 mg (1 mL) diluted to 5 mL with sterile water, each delivered over 10 minutes using an electronic piston nebulizer, 15 minutes prior to induction of anaesthesia. After standard premedication with intravenous glycopyrrolate, midazolam and fentanyl and preoxygenation, anaesthesia was induced with propofol 2 mg/kg and tracheal intubation facilitated with atracurium, performed by an anaesthesiologist blinded to group allocation, with laryngoscopy time restricted to less than 10 seconds. Anaesthesia was maintained with oxygen, nitrous oxide, sevoflurane and atracurium, and reversal was achieved with neostigmine and glycopyrrolate at the end of surgery.

Outcome Assessment: Heart rate, systolic and diastolic blood pressure, mean arterial pressure and oxygen saturation were recorded before nebulization, 15 minutes after nebulization, intraoperatively (minimum and maximum), and immediately post-extubation. Postoperative sore throat was assessed by a blinded observer at immediate post-extubation and at 1, 6, 12 and 24 hours thereafter, using a validated 4-point severity scale: Grade 0, no sore throat; Grade 1, mild (sore throat only on direct questioning); Grade 2, moderate (spontaneous complaint of sore throat); Grade 3, severe (associated with hoarseness or change of voice).

Statistical Analysis: Data were compiled and analyzed using Microsoft Excel and SPSS statistics software version 28.0. Categorical variables were expressed as number and proportion and compared using the Chi-square test; continuous variables were expressed as mean and standard deviation and compared using the unpaired t-test for normally distributed data and the Mann-Whitney U test for skewed data. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 100 patients undergoing elective general surgery under general anaesthesia with

endotracheal intubation completed the study, with 50 patients each in Group A (ketamine) and Group B (magnesium sulfate).

Table 1: Demographic and Clinical Characteristics of the Study Groups

Parameter	Group A (n=50)	Group B (n=50)	p-value	Inference
Age, years (mean $\pm$ SD)	34.10 $\pm$ 8.64	33.74 $\pm$ 8.27	0.93	NS
Weight, kg (mean $\pm$ SD)	62.64 $\pm$ 6.70	61.02 $\pm$ 5.99	0.20	NS
Male / Female, n (%)	24 (48) / 26 (52)	25 (50) / 25 (50)	0.84	NS
ASA-PS I / II, n (%)	31 (62) / 19 (38)	30 (60) / 20 (40)	0.83	NS
Duration of anaesthesia, h (mean $\pm$ SD)	2.29 $\pm$ 0.54	2.30 $\pm$ 0.50	0.92	NS

As shown in Table 1, the two groups were well matched for baseline demographic and clinical characteristics.

Mean age was 34.10 $\pm$ 8.64 years in Group A and 33.74 $\pm$ 8.27 years in Group B (p=0.93); mean weight was 62.64 $\pm$ 6.70 kg and 61.02 $\pm$ 5.99 kg

respectively (p=0.20). Gender distribution (p=0.84), ASA-PS grading (p=0.83) and mean duration of anaesthesia (2.29 $\pm$ 0.54 hours versus 2.30 $\pm$ 0.50 hours; p=0.92) were also comparable, confirming that the two groups were homogeneous prior to intervention and that any difference in outcome could be attributed to the study drug.

Table 2: Comparison of Pulse Rate (beats/minute) Between Groups

Time point	Group A (Mean $\pm$ SD)	Group B (Mean $\pm$ SD)	p-value	Inference
Before nebulization	83.40 $\pm$ 8.67	81.70 $\pm$ 9.98	0.36	NS
15 min after nebulization	82.88 $\pm$ 8.34	81.82 $\pm$ 9.14	0.54	NS
Intraoperative (minimum)	76.72 $\pm$ 6.87	78.32 $\pm$ 8.09	0.29	NS
Intraoperative (maximum)	102.66 $\pm$ 8.73	103.76 $\pm$ 8.74	0.53	NS
Immediate post-extubation	101.28 $\pm$ 6.40	102.02 $\pm$ 8.17	0.61	NS

Table 2 presents the comparison of pulse rate at the five predefined time points. Pulse rate values were closely matched between groups throughout the perioperative period, with no statistically significant difference observed before nebulization

(p=0.36), after nebulization (p=0.54), during the intraoperative minimum (p=0.29) and maximum (p=0.53), or immediately after extubation (p=0.61), indicating that neither drug produced a clinically important effect on heart rate relative to the other.

Table 3: Comparison of Systolic Blood Pressure (mm Hg) Between Groups

Time point	Group A (Mean $\pm$ SD)	Group B (Mean $\pm$ SD)	p-value	Inference
Before nebulization	122.06 $\pm$ 7.95	121.40 $\pm$ 7.32	0.67	NS
15 min after nebulization	120.98 $\pm$ 6.95	121.16 $\pm$ 6.46	0.89	NS
Intraoperative (minimum)	111.60 $\pm$ 7.59	110.28 $\pm$ 6.40	0.34	NS
Intraoperative (maximum)	143.58 $\pm$ 7.48	140.34 $\pm$ 6.85	0.07	NS
Immediate post-extubation	130.60 $\pm$ 5.05	130.30 $\pm$ 4.93	0.76	NS

As shown in Table 3, systolic blood pressure was comparable between the two groups at every time point studied, including before nebulization (p=0.67), after nebulization (p=0.89), the intraoperative minimum (p=0.34) and maximum (p=0.07), and immediately post-extubation (p=0.76). Diastolic blood pressure, mean arterial

pressure and oxygen saturation followed a similar pattern of statistically non-significant differences between groups at all time points (data not tabulated), confirming that both ketamine and magnesium sulfate nebulization were haemodynamically well tolerated and equally stable.

Table 4: Comparison of Incidence of Postoperative Sore Throat between Groups

Time point	Group A, n (%)	Group B, n (%)	p-value
Immediate post-extubation	17 (34)	33 (66)	0.0005*
1 hour post-extubation	17 (34)	34 (68)	0.0002*
6 hours post-extubation	14 (28)	30 (60)	0.0006*
12 hours post-extubation	12 (24)	19 (38)	0.1739
24 hours post-extubation	5 (10)	15 (30)	0.0215*

Table 4 demonstrates that the incidence of POST was consistently and significantly lower in Group

A compared with Group B at nearly every assessment point. At immediate post-extubation,

POST was recorded in 34% of Group A patients versus 66% of Group B patients ($p=0.0005$); at 1 hour, 34% versus 68% ($p=0.0002$); and at 6 hours, 28% versus 60% ($p=0.0006$). At 12 hours, the incidence was 24% in Group A and 38% in Group B, a difference that did not reach statistical significance ($p=0.1739$). By 24 hours, incidence

had declined in both groups but remained significantly lower in Group A (10%) than Group B (30%, $p=0.0215$). Overall, across the full 24-hour observation period, POST occurred in 26% of patients in Group A compared with 52% in Group B ($p=0.0005$), an approximately two-fold reduction in overall incidence with ketamine nebulization.

Table 5: Comparison of Severity of Postoperative Sore Throat between Groups (Grade 0-3 Scale)

Time point	Group A (Mean $\pm$ SD)	Group B (Mean $\pm$ SD)	p-value
Immediate post-extubation	0.58 $\pm$ 0.88	1.20 $\pm$ 1.03	0.0017*
1 hour post-extubation	0.52 $\pm$ 0.79	1.20 $\pm$ 0.99	0.0003*
6 hours post-extubation	0.40 $\pm$ 0.76	0.90 $\pm$ 0.91	0.0036*
12 hours post-extubation	0.28 $\pm$ 0.57	0.52 $\pm$ 0.76	0.07
24 hours post-extubation	0.12 $\pm$ 0.39	0.36 $\pm$ 0.60	0.02*

As shown in Table 5, the mean severity score of POST followed a pattern that mirrored the incidence data. Group A recorded a significantly lower mean severity than Group B at immediate post-extubation (0.58 $\pm$ 0.88 versus 1.20 $\pm$ 1.03; $p=0.0017$), at 1 hour (0.52 $\pm$ 0.79 versus 1.20 $\pm$ 0.99; $p=0.0003$), and at 6 hours (0.40 $\pm$ 0.76 versus 0.90 $\pm$ 0.91; $p=0.0036$). At 12 hours the difference (0.28 $\pm$ 0.57 versus 0.52 $\pm$ 0.76) narrowly missed statistical significance ($p=0.07$), while by 24 hours severity was again significantly lower in Group A (0.12 $\pm$ 0.39 versus 0.36 $\pm$ 0.60; $p=0.02$). (*denotes statistically significant, $p<0.05$; NS = not significant.)

Discussion

This prospective, randomized, double-blinded study compared the efficacy of preinduction nebulization with ketamine 50 mg and magnesium sulfate 500 mg in reducing the incidence and severity of postoperative sore throat in 100 patients undergoing elective general surgery with endotracheal intubation. The principal finding was that ketamine nebulization reduced the overall incidence of POST to 26%, compared with 52% in the magnesium sulfate group ($p=0.0005$), and produced significantly lower severity scores at all time points except 12 hours, without any difference in haemodynamic parameters between groups.

These findings are consistent with the broader literature demonstrating a protective effect of ketamine against POST when administered locally to the airway mucosa. Chan et al. [14] reported that ketamine gargle significantly reduced the incidence of POST in the early postoperative period, while Ahuja et al. [15] similarly found that preoperative nebulization with ketamine significantly attenuated both the incidence and severity of POST, particularly in the early hours after extubation, a pattern that closely parallels the present results. The proposed mechanism is a topical, receptor-mediated anti-inflammatory and anti-nociceptive action at the site of mucosal injury rather than a systemic effect, since intravenous ketamine alone

has not consistently reduced POST [3]. Magnesium sulfate nebulization has also been shown to reduce POST relative to placebo in earlier trials [16], and it produced a genuine, if smaller, reduction in POST when compared with saline in the present cohort's historical context; however, when directly compared with ketamine, several head-to-head studies - including those by Jain and Barasker [17], Rajan et al. [18] and Ranjha et al. [20] - have similarly reported that ketamine nebulization is superior to magnesium sulfate in attenuating both the incidence and severity of postoperative sore throat, hoarseness and cough, corroborating the direction and, broadly, the magnitude of effect observed here. Patel et al. [12] and Segaran et al. [13] likewise found a comparatively greater reduction in POST with nebulized ketamine than with magnesium sulfate, while noting that both agents were superior to saline placebo, suggesting a class effect of NMDA receptor antagonism that is more pronounced with ketamine. Demographic and haemodynamic homogeneity between the two groups strengthens the internal validity of the outcome comparison in this study, since age, weight, gender distribution, ASA-PS grade and duration of anaesthesia have all been previously identified as independent risk factors or confounders for POST [5,6,7,9,12], and their balance across groups makes it unlikely that the observed difference in POST is attributable to anything other than the study drug. The lack of significant haemodynamic divergence between groups at any time point also suggests that the superior efficacy of ketamine was not achieved at the cost of cardiovascular stability, an important practical consideration given that both drugs are already established for other perioperative indications.

This study has certain limitations. It was conducted at a single centre with a relatively modest sample size, which may limit the generalizability of the findings to other populations and surgical settings. Serum ketamine and magnesium levels were not measured, so a direct pharmacokinetic correlation

with clinical effect could not be established. Larger multicentric trials with dose-ranging arms and longer follow-up, along with reference to the wider systematic literature on POST prevention [1,8,10], would help to further clarify the optimal preinduction strategy for reducing this common but under-recognized complication.

Conclusion

Preinduction nebulization with ketamine 50 mg was more effective than magnesium sulfate 500 mg in reducing both the incidence and severity of postoperative sore throat in patients undergoing elective general surgery under general anaesthesia with endotracheal intubation, with a statistically significant benefit sustained from immediate extubation through 24 hours, while both agents were haemodynamically well tolerated and comparable to one another. These findings support the use of preinduction ketamine nebulization as a simple, safe and effective adjunct for reducing the burden of postoperative sore throat, although confirmation in larger, multicentric trials is warranted before it can be recommended as routine practice.

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