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EFFECT OF NEBULIZED KETAMINE AND MAGNESIUM SULPHATE IN THE PREVENTION OF POSTOPERATIVE SORE THROAT FOLLOWING GENERAL ANAESTHESIA WITH ENDOTRACHEAL INTUBATION - A COMPARATIVE STUDY"

Anaesthesiology

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ABSTRACT

Background: Postoperative sore throat (POST) is a frequent complication following endotracheal intubation, with incidences up to 70%. This study evaluates the efficacy of nebulized ketamine and magnesium sulphate in preventing POST compared to a normal saline control in patients undergoing general anaesthesia. **Methods:** This interventional study, conducted at Acharya Shri Chander College of Medical Sciences and Hospital, Jammu, from April 2024 to March 2025, included 150 patients (ASA I-II, aged 25–65 years) undergoing surgeries lasting less than 2 hours. Patients were randomized into three groups (n = 50 each): Group K (ketamine 50 mg in 5 mL of saline), Group M (magnesium sulphate 250 mg in 5 mL of saline), and Group C (5 mL of normal saline). Nebulization was administered pre-intubation. Cough reflex and sore throat were assessed at 1, 2, 4, and 24 hours post-extubation using a 0–3 scale. Statistical analysis was performed using IBM SPSS version 21, with significance set at $p \leq 0.05$. **Results:** The ketamine group showed significantly lower incidences of cough reflex and sore throat across all time points. At 1 hour, 64% of Group K had no cough (score 0) vs. 32% in Groups M and C ($p=0.021$); at 4 hours, 80% vs. 40% and 32% ($p<0.001$). For sore throat, 72% of Group K reported no symptoms at 1 hour vs. 34% (Group M) and 18% (Group C, $p<0.0001$), with similar trends at 2, 4, and 24 hours ($p<0.05$). No significant differences were noted in demographic or intubation parameters across groups. **Conclusion:** Nebulized ketamine significantly reduces the incidence and severity of POST and cough reflex compared to magnesium sulphate and normal saline, offering a promising preventive strategy for patients undergoing general anaesthesia with endotracheal intubation.

KEYWORDS

Postoperative sore throat, nebulized ketamine, magnesium sulphate

INTRODUCTION

Postoperative sore throat (POST) is a common complication following general anaesthesia with endotracheal intubation, with incidences up to 70% (1). It is ranked as the eighth most undesirable complaint by the American Society of Anesthesiologists and is the second most frequent complication after intubation (1-2). POST is mainly caused by mechanical irritation and airway mucosal injury, worsened by factors like smoking, difficult intubation, oversized endotracheal tubes, high cuff pressure, aggressive suctioning, and prolonged surgery. Symptoms peak 2 to 4 hours post-extubation and usually resolve within 24 hours (3). Pre-existing conditions such as asthma or chronic cough can increase the risk of POST, underscoring the importance of effective prevention strategies.

Ensuring high-quality anaesthesia with minimal postoperative complications is essential for patient-centred care. Complications like nausea, vomiting, pain, and POST can hinder recovery and elevate healthcare costs. While pain management has improved, POST remains a challenge. Non-pharmacological strategies include using supraglottic airway devices, smaller ET tubes, gentle laryngoscopy, and careful extubation. Pharmacological options such as corticosteroids, local anesthetics, NSAIDs, and ketamine have also been studied. Nebulization, known for its safety and ease, shows promise as an effective delivery method (4).

Ketamine, a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, offers analgesic and anti-inflammatory effects by inhibiting NMDA receptor activation and reducing glutamate release, mitigating spinal cord sensitization (5). It also suppresses inflammatory mediators, improves blood flow, and modulates cytokines, potentially alleviating POST-related discomfort.

Magnesium sulphate, an inorganic salt, antagonizes NMDA receptors less potently but inhibits calcium influx and inflammatory pathways, including NF-kappa B (6). Its smooth muscle relaxation and vasodilatory properties may reduce pharyngeal spasms and enhance mucosal recovery (7). Nebulized magnesium sulphate delivers ions directly to the airway, with effects lasting 1-3 hours, covering the acute POST window.

POST impacts patient satisfaction and healthcare resources, underscoring the need for better prevention strategies. Accordingly, this research will evaluate nebulized ketamine and magnesium sulphate to develop an evidence-based POST prevention protocol, improving patient outcomes.

Methodology

Study Design And Setting

This interventional study took place at Acharya Shri Chander College of Medical Sciences and Hospital in Jammu from April 2024 to March 2025, involving 150 patients divided into three groups of 50. It received ethical approval before starting.

Inclusion And Exclusion Criteria

Inclusion Criteria:

- American Society of Anesthesiologists (ASA) physical status I and II patients.
- Age 25–65 years.
- Patients undergoing general anesthesia with orotracheal intubation.
- Surgery duration less than 2 hours.

Exclusion Criteria:

- History of sore throat, respiratory infections, or reactive airway diseases.
- Ear, nose, and throat (ENT) surgeries.
- Pregnant or lactating women.
- Contraindications to study drugs (ketamine or magnesium sulphate).
- Anticipated difficult intubation.
- Surgery duration exceeding 2 hours.

Randomization And Group Allocation

Patients were randomly allocated into three groups (50 patients each) using a computer-generated randomization table:

- **Group K**: Received ketamine nebulization (50 mg in 5 ml normal

saline).
- **Group M**: Received magnesium sulphate nebulization (250 mg in 5 ml normal saline).
- **Group C**: Received 5 ml normal saline (control).

Preanesthetic Preparation And Premedication
A preanesthetic evaluation took place the day before surgery, involving a detailed history, physical examination, and airway assessment. Necessary investigations were conducted, and demographic data (age, sex, weight, height, BMI) were recorded. Informed consent was obtained after explaining the procedure. Patients fasted for 8 hours before surgery and received oral alprazolam 0.25 mg and pantoprazole 40 mg the night before.

Anaesthetic Protocol
Standard monitoring was initiated in the operating theater, including blood pressure, pulse, SpO2, ECG, and EtCO2. A 20G/18G IV cannula was placed, with premedication of tramadol (1 mg/kg IV) and ondansetron (0.1 mg/kg IV). Anesthesia was induced with propofol (2 mg/kg IV) and rocuronium (0.6 mg/kg IV), followed by intubation using suitable endotracheal tubes. Anesthesia maintenance included nitrous oxide and oxygen (66:33), 1% isoflurane, and intermittent rocuronium. Volume-controlled ventilation was set at a tidal volume of 6–8 ml/kg and respiratory rate of 10–12 breaths/min, with EtCO2 maintained between 35–45 mmHg.

Emergence From Anaesthesia
At surgery conclusion, muscle relaxation was reversed with neostigmine 0.05 mg/kg IV and glycopyrrolate 0.01 mg/kg IV. Patients were extubated after meeting criteria and following suctioning with a 14F soft catheter. Extubation occurred after cuff deflation, and patients were then transferred to the post-anesthesia care unit.

Outcome Assessment
Cough reflex was assessed within 10 seconds post-extubation on a 0–3 scale: 0 (no cough), 1 (single cough), 2 (multiple unsustained coughs), 3 (sustained coughing). Sore throat incidence and severity were evaluated at 1, 2, 4, and 24 hours post-extubation using the same scale. Postoperative airway complications (e.g., apnea, hypoxemia, airway spasm) were recorded within 30 minutes. Durations of surgery, anesthesia, and emergence were also noted.

Statistical Analysis
Data were analyzed using IBM SPSS version 21. Descriptive data were expressed as percentages and proportions, while continuous data were presented as means and standard deviations. Appropriate statistical tests were applied to compare outcomes across groups.

RESULTS AND OBSERVATIONS
The study compared three groups—Ketamine, Magnesium Sulphate, and Normal Saline (50 participants each)—across demographic parameters, baseline vitals, intubation characteristics, and post-intubation outcomes (cough reflex and sore throat).

Table 1: Baseline Characteristics And Intubation Parameters

	Ketamine		Magnesium Sulphate		Normal Saline	
Parameter	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age (years)	48.66	10.24	46.38	11.76	48.64	9.73
Height (cm)	173.65	6.40	173.57	6.67	175.48	5.64
Weight (kg)	72.82	11.96	71.08	11.25	75.26	11.51
BMI (kg/m^2)	24.09	3.66	23.64	3.56	24.25	3.63
Heart Rate (bpm)	85.98	2.46	88.22	3.78	90.57	5.05
Systolic BP (mmHg)	133.60	3.20	127.02	3.76	126.98	5.91
Diastolic BP (mmHg)	82.26	4.10	79.44	4.80	80.72	5.20
Mean Arterial Pressure (mmHg)	99.37	2.81	95.30	3.51	96.14	3.90
SpO_2 (%)	98.04	0.97	98.02	1.00	98.04	0.88
Intubation Time (s)	13.18	2.19	12.86	2.15	12.78	2.68

Table-1 presents the mean and standard deviation (SD) of demographic and physiological parameters across the three groups. Parameters include age (years), height (cm), weight (kg), BMI (kg/m²), heart rate (bpm), systolic and diastolic blood pressure (mmHg), mean arterial pressure (mmHg), SpO_2 (%), and total intubation time (seconds). The Ketamine group showed the lowest heart rate (85.98 ± 2.46 bpm) but the highest blood pressure metrics, while intubation times were slightly longer (13.18 ± 2.19 seconds) compared to Magnesium Sulphate (12.86 ± 2.15 seconds) and Normal Saline (12.78 ± 2.68 seconds).

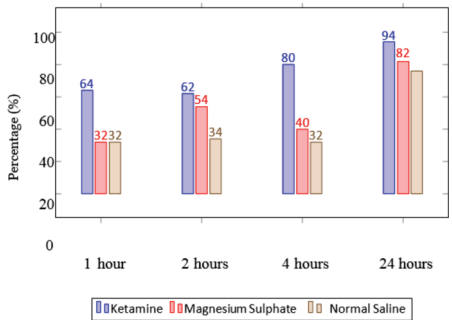

Figure 1: Cough Reflex (Score 0) Across Groups at 1, 2, 4, and 24 Hours

This bar diagram illustrates the percentage of participants with no cough reflex (score 0) at 1-, 2-, 4-, and 24 hours post-intubation. The Ketamine group consistently shows the highest percentage (64% at 1 hour to 94% at 24 hours), followed by Magnesium Sulphate (32–82%) and Normal Saline (32–76%). The bars highlight significant differences, particularly at 4 hours ($p < 0.001$).

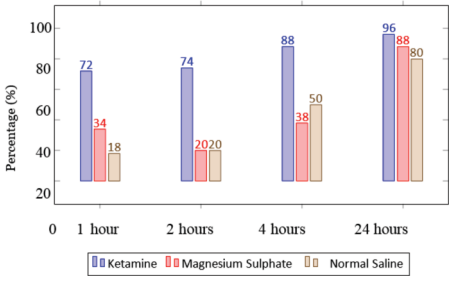

Figure 2: Sore Throat (Score 0) Across Groups at 1, 2, 4, and 24 Hours

This bar diagram displays the percentage of participants with no sore throat (score 0) at the same time points. The Ketamine group leads with 72% (1 hour) to 96% (24 hours) sore-throat-free participants, compared to Magnesium Sulphate (20–88%) and Normal Saline (18–80%). The most pronounced differences occur at 1, 2, and 4 hours ($p < 0.0001$).

Table 2: Cough Reflex And Sore Throat Distribution At 1, 2, 4, And 24 Hours

	Ketamine		Magnesium Sulphate		Normal Saline		
Time	**Score**	**No. (%)**	**Score**	**No. (%)**	**Score**	**No. (%)**	**p-value**
Cough Reflex							
1 hour	0	32 (64)	0	16 (32)	0	16 (32)	4*0.021*
	1	11 (22)	1	20 (40)	1	21 (42)	
	O	5 (10)	O	10 (20)	2	11 (22)	
	3	2 (4)	3	4 (8)	3	2 (4)	
2 hours	0	31 (62)	0	27 (54)	0	17 (34)	4*0.024*
	1	18 (36)	1	19 (38)	1	25 (50)	
	2	1 (2)	2	4 (8)	2	8 (16)	
	3	0 (0)	3	0 (0)	3	0 (0)	
4 hours	0	40 (80)	0	20 (40)	0	16 (32)	4*0.000**
	1	9 (18)	1	29 (58)	1	33 (66)	
	2	1 (2)	2	1 (2)	2	1 (2)	
	3	0 (0)	3	0 (0)	3	0 (0)	
24 hours	0	47 (94)	0	41 (82)	0	38 (76)	4*0.044*
	1	3 (6)	1	9 (18)	1	12 (24)	
	2	0 (0)	2	0 (0)	2	0 (0)	
	3	0 (0)	3	0 (0)	3	0 (0)	
Sore Throat							
1 hour	0	36 (72)	0	17 (34)	0	9 (18)	4*<0.000**
	1	9 (18)	1	17 (34)	1	22 (44)	
	2	4 (8)	2	15 (30)	2	16 (32)	
	3	1 (2)	3	1 (2)	3	3 (6)	
2 hours	0	37 (74)	0	10 (20)	0	10 (20)	4*<0.000**
	1	12 (24)	1	22 (44)	1	24 (48)	

	2	1 (2)	2	18 (36)	2	16 (32)	
	3	0 (0)	3	0 (0)	3	0 (0)	
4 hours	0	44 (88)	0	19 (38)	0	25 (50)	4*<0.000**
	1	5 (10)	1	30 (60)	1	24 (48)	
	2	1 (2)	2	1 (2)	2	1 (2)	
	3	0 (0)	3	0 (0)	3	0 (0)	
24 hours	0	48 (96)	0	44 (88)	0	40 (80)	4*0.048*
	1	2 (4)	1	6 (12)	1	10 (20)	
	2	0 (0)	2	0 (0)	2	0 (0)	
	3	0 (0)	3	0 (0)	3	0 (0)	

*P-value ≤ 0.05 Significant; **P-value ≤ 0.001 Highly Significant

Table 2: summarizes the frequency and percentage of cough reflex and sore throat scores (0–3) at four time points post-intubation. The Ketamine group consistently had the highest percentage of participants with no cough (64–94%) and no sore throat (72–96%) across all time points, with statistically significant differences ($p \leq 0.05$ to $p < 0.001$) compared to Magnesium Sulphate and Normal Saline groups, which showed higher incidences of mild to moderate symptoms.

Table 3: Demographic And Airway Characteristics

Parameter	Ketamine		Magnesium Sulphate		Normal Saline	
	No	%	No	%	No	%
Gender						
Male	27	54	27	54	28	56
Female	23	46	23	46	22	44
Age Groups (years)						
25-35	6	12	12	24	6	12
36-45	13	26	14	18	12	24
46-55	15	30	8	16	18	36
56-65	16	32	16	32	14	28
Intubation Attempts						
1	41	82	40	80	42	84
2	9	18	10	20	8	16
Mallampati Grading (MPG)						
Class 1	33	66	34	68	30	60
Class 2	9	18	12	24	13	26
Class 3	8	16	4	8	7	14
ASA Classification						
Class 1	25	50	25	50	24	48
Class 2	25	50	25	50	26	52
Upper Lip Bite Test						
Class 1	43	86	46	92	43	86
Class 2	7	14	4	8	7	14

Table 3 details the frequency distribution of gender, age groups (25–35, 36–45, 46–55, 56–65 years), intubation attempts (1 or 2), Mallampati Grading (MPG Classes 1–3), ASA classification (Classes 1–2), and Upper Lip Bite Test (ULBT Classes 1–2). Gender was balanced (54–56% male), and age distributions were comparable. Most participants required one intubation attempt (80–84%) and had favourable airway grades (MPG 1 or 2: 84–92%; ULBT Class 1: 86–92%).

DISCUSSION

Postoperative sore throat is a frequent and distressing complication following general anaesthesia with endotracheal intubation, impacting patient comfort and potentially delaying recovery. The primary objective of this study is to compare the effect of nebulized Ketamine and Magnesium sulphate in the prevention of postoperative sore throat following general anesthesia with endotracheal intubation.

In this study, the mean ages were similar: 48.66 ± 10.24 years for Ketamine, 46.38 ± 11.76 years for Magnesium Sulphate, and 48.64 ± 9.73 years for Normal Saline. These findings align with previous studies on the effects of ketamine and magnesium sulphate on postoperative sore throat (8-9).

This study found the highest heart rate with Normal Saline, followed by Magnesium Sulphate, and the lowest with Ketamine, consistent with **Teymourian et al. (2015)(9)**. **Rajan et al. (2016)** reported no blood pressure changes with magnesium, indicating non-systemic effects (10). The highest systolic blood pressure was with Ketamine, then Magnesium Sulphate, due to ketamine's sympathetic stimulation (9,11). Ketamine's effects on blood pressure were confirmed across studies, while magnesium showed minimal systemic influence (12-14).

In our study, oxygen saturation (SpO_2) averaged 98%, with similar intubation times: Ketamine (13.18 ± 2.19 s), Magnesium Sulphate (12.86 ± 2.15 s), and Normal Saline (12.78 ± 2.68 s). **Teymourian et al. (2015)** found no significant difference in oxygen saturation (97.2%) between magnesium and ketamine groups (9). Gender distribution was balanced, with Ketamine (27M/23F), Magnesium Sulphate (27M/23F), and Normal Saline (28M/22F), suggesting gender did not affect outcomes—a finding echoed by **Hulakund et al. (2018)** and **Arianto et al. (2022) (4,8)**. Most patients were intubated successfully on the first attempt: Ketamine (82%), Magnesium Sulphate (80%), and Normal Saline (84%). Lin et al. (2017) noted success rates improved from 79% pre- to 93% post-intervention with standardized protocols, highlighting their significance. Similar standardization was noted in studies by **Thomas et al. (2018)** and **Mehta et al. (2022) (12-13)**.

In the Ketamine group, 66% were Mallampati grade 1, compared to 68% in the Magnesium Sulphate group and 60% in the Normal Saline group. Most patients had favorable airway grades (MPG 1 or 2), though this grading system is subjective. Studies show similar trends, with Mallampati grades 3-4 indicating potential intubation difficulties.

In the ASA Classification, both the Ketamine and Magnesium Sulphate groups had 50% (25 participants each) in Class I and II, while the Normal Saline group had 48% in Class I and 52% in Class II. The study by **Gauchan et al. (2024)** included patients with ASA Classes I, II, and III, providing a broader classification range than ours, which focused only on Classes I and II (1).

The Upper Lip Bite Test (ULBT) showed that most participants in all groups were Class 1, indicating easier airway access: 86% in the Ketamine group, 92% in Magnesium Sulphate, and 86% in Normal Saline. The ULBT is a reliable predictor of difficult intubation (16-18).

Post-intubation cough reflex evaluations revealed significant differences among groups. At 1 hour, the Ketamine group had a 64% cough-free rate vs. 32% for both Magnesium Sulphate and Normal Saline ($p = 0.021$). This trend continued, with 80% of the Ketamine group cough-free after 4 hours ($p < 0.001$) and 94% at 24 hours ($p = 0.044$).

The Ketamine group consistently showed lower cough incidence and severity than the other groups, aligning with findings by **Thomas et al. (2018)** and **Mehta et al. (2022) (12-13)**. In contrast, **Arianto et al. (2022)** found no significant differences between Ketamine and Magnesium Sulphate (4).

Regarding sore throat, 72% of the Ketamine group reported no sore throat at 1 hour compared to 34% (Magnesium Sulphate) and 18% (Normal Saline, $p < 0.0001$). This pattern continued at 2, 4, and 24 hours, with significant differences noted. A meta-analysis by **Tadesse et al. (2024)** supports Ketamine's effectiveness in reducing sore throat (19).

CONCLUSION:

The study concluded that the Ketamine group demonstrated significantly lower incidence and severity of both cough and sore throat compared to Magnesium Sulphate and Normal Saline across all time points.

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