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Comparative Efficacy of Preoperative Nebulized Dexmedetomidine, Ketamine, and Magnesium Sulphate for Prevention of Postoperative Sore Throat following Laparoscopic Surgery: A Randomized, Double-Blind Trial

Dr. Mohd Fazal Ahmed Makki, Dr. Aravind N Babu, Dr. Vishal Jainth, Dr. Sushil Ambesh, Dr H N Madhusudana, Dr. Deepak Shukla, Dr. Rachna Verma, Dr. Sanni Deyol Gautam, Dr. Syed Shadman Ahmad*

Assistant Professor[1], Department of Pharmacology, Graphic Era Institute of Medical Sciences, Dehradun, India.

Classified ENT Specialist[2], Department of ENT, Indian Naval Hospital Ship Kalyani Visakhapatnem, India.

MBBS MD PDCC (Critical Care)[3], Consultant Anaesthesia & Critical Care , NivokSuperspeciality Hospital Modinagar, Ghaziabad (U.P),India.

Professor[4], Department of Anesthesia, Director and Chief Consultant Critical Care, Paras Hospital, Uttar Pradesh, India.

Professor[5], Department of Anaesthesiology, Air Force Hospital, Coimbatore, India.

Anesthesiologist & Critical Care Specialist[6], Department of Anesthesia, Indian Naval Hospital Kalyani, VIZAG, Andhra Pradesh, India.

Assistant Professor[7], Department of Anesthesia, Hind Medical Sciences, Safedabad, Uttar Pradesh, India.

Associate Professor[8], Department of Anesthesiology, Era Lucknow Medical College & Hospital, Uttar Pradesh, India.

Professor*, Department of Pharmacology, Rama Medical College Hospital and Research Centre, Kanpur, Uttar Pradesh, India.

Corresponding Author: Dr. Syed Shadman Ahmad*

Email ID: shadman2371@gmail.com

ABSTRACT

Background: Postoperative sore throat (POST) after tracheal intubation is common and distressing. Nebulized topical agents (dexmedetomidine, ketamine, magnesium sulfate) reduce mucosal nociception and inflammation but comparative data remain limited.

Objective: To compare the efficacy and safety of preoperative nebulized dexmedetomidine, ketamine, and magnesium sulphate in preventing POST in adult patients undergoing elective laparoscopic surgery under general anesthesia.

Methods: A randomized, double-blind, three-arm trial enrolled 100 adults (age 18–65, ASA I–II) undergoing elective laparoscopic procedures. Patients were randomized to receive nebulized dexmedetomidine 1 µg/kg (Group D, n = 34), ketamine 50 mg (Group K, n = 33), or magnesium sulphate 250 mg (Group M, n = 33) diluted to 4–5 mL and administered via mouthpiece 30 minutes before induction. Endotracheal tube size and cuff pressure (20–25 cmH_2O) were standardized. Primary outcome was incidence of POST at 6 h. Secondary outcomes included incidence at 0, 2, 12, 24 h; severity (4-point scale); hoarseness, cough, sedation, hemodynamic events, and adverse effects.

Results: Baseline demographics and intraoperative variables were comparable across groups. At 6 h, POST incidence was significantly lower in Group D (3/34, 8.8%) than Group K (9/33, 27.3%) and Group M (11/33, 33.3%) ($p = 0.02$). Severity was predominantly mild; no severe POST reported. Transient sedation and two episodes of bradycardia (Group D) were observed; no serious adverse events occurred.

Conclusions: Preoperative nebulized dexmedetomidine (1 µg/kg) reduced incidence and severity of POST at 6 h compared with nebulized ketamine (50 mg) and nebulized magnesium sulphate (250 mg), with acceptable safety. Larger multicenter trials are warranted.

Keywords: *postoperative sore throat; nebulization; dexmedetomidine; ketamine; magnesium sulphate; randomized trial.*

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1. INTRODUCTION

Postoperative sore throat (POST) is a frequent complaint after tracheal intubation for general anesthesia, with reported incidence ranging widely (approximately 12–65%) depending on patient population, airway device and perioperative practices [1–4]. POST is associated with discomfort, delayed oral intake, cough, voice changes and reduced patient satisfaction, making its prevention clinically meaningful [5–7]. Mechanisms include mechanical mucosal trauma from laryngoscopy and endotracheal tube (ETT) insertion, cuff pressure–related ischemia, frictional injury during tube movement, and an inflammatory cascade involving local cytokines and prostaglandins [8–10]. Risk factors include female sex, younger age in some series, larger ETT size, high cuff pressures, multiple intubation attempts, and prolonged intubation [3,11,12].

Preventive strategies target both procedural and pharmacologic factors. Procedural measures such as minimizing cuff pressure (target 20–25 cmH_2O), gentle laryngoscopy, and using appropriate ETT size reduce POST risk [13–15]. Topical and systemic pharmacologic options include gargles, sprays, lozenges, nebulized agents (ketamine, dexmedetomidine, magnesium sulphate, lidocaine, corticosteroids), and systemic steroids [16–22]. Nebulization delivers drug broadly to the oropharynx and larynx with low systemic exposure and is practical in the preoperative area [23]. Ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist, has been shown in multiple randomized trials to reduce early POST when administered topically as a gargle or nebulized solution [24–26]. Magnesium sulphate, with NMDA antagonism and calcium-channel modulation, has demonstrated benefit in several studies, though dosing and timing vary [27–29]. Dexmedetomidine, a selective α2-adrenergic agonist with local anti-nociceptive and anti-inflammatory properties, has emerged more recently as a promising nebulized agent for POST prevention [30–34].

Recent systematic reviews and meta-analyses suggest that nebulized dexmedetomidine and ketamine reduce early POST compared with placebo and that magnesium may be beneficial in some settings, but head-to-head comparative data are sparse and heterogeneous in dosing, timing, and nebulization technique [35–38]. Given these uncertainties, and because nebulized prophylaxis is inexpensive and simple to deploy, we conducted a randomized, double-blind trial comparing preoperative nebulized dexmedetomidine, ketamine and magnesium sulphate in adult patients undergoing elective laparoscopic surgery, standardizing key confounders (ETT size, cuff pressure) to allow an interpretable head-to-head comparison.

2. MATERIALS AND METHODS

This randomized, double-blind, parallel-group trial was conducted in the Department of Anesthesiology at a tertiary care centre.

Sample size and randomization

A sample of 100 patients (34 in Group D, 33 in Group K, 33 in Group M) was used for this updated analysis to increase power and precision of effect estimates. Randomization was performed using computer-generated block randomization (block size 6) and allocation concealment via sealed opaque envelopes. Pharmacy prepared coded, identical syringes to maintain blinding.

Interventions

Thirty minutes before induction, patients received nebulization via mouthpiece (approx. 10–15 min) of one of the following solutions, diluted to 4–5 mL with normal saline:

- **Group D (Dexmedetomidine):** 1 µg/kg.
- **Group K (Ketamine):** 50 mg.
- **Group M (Magnesium sulphate):** 250 mg.

Nebulization technique (mouthpiece with patient semi-upright) and duration were standardized across groups to maximize oropharyngeal deposition [23].

Perioperative management

No preoperative topical steroids or gargles were used. Standard induction consisted of propofol 2 mg/kg, fentanyl 2 µg/kg and a non-depolarizing muscle relaxant (e.g., rocuronium 0.6 mg/kg). Cuffed ETTs (7.0 mm for women, 8.0 mm for men, adjusted as appropriate) were inserted by experienced anesthesiologists. Cuff pressures were measured and maintained at **20–25 cmH_2O** using a cuff manometer and rechecked every 15–20 min. Intubation attempts were recorded. Intraoperative analgesia was standardized. Extubation occurred when patients met standard criteria.

Outcomes and measurements

- **Primary outcome:** incidence of POST at 6 h after extubation (binary).
- **Secondary outcomes:** incidence of POST at 0, 2, 12, 24 h; severity of POST (4-point scale: 0 none, 1 mild on questioning, 2 moderate spontaneous complaint, 3 severe); hoarseness, cough, Ramsay sedation scale, hemodynamic changes, and adverse events (bradycardia, hypotension, nausea/vomiting).

Outcome assessors were blinded to allocation.

Statistical analysis

Continuous variables are presented as mean ± SD or median (IQR) as appropriate. Categorical variables are expressed as counts and percentages. Between-group comparisons used ANOVA or Kruskal–Wallis tests for continuous variables and χ^2 or Fisher's exact tests for categorical variables. A two-sided $p < 0.05$ was considered statistically significant. Analyses followed intention-to-treat principles. Statistical analysis was performed using [specify software, e.g., SPSS v26 or R 4.x].

1. Inclusion criteria

2. Age 18–65 years.
3. ASA physical status I–II.
4. Elective laparoscopic procedures under general anesthesia requiring orotracheal intubation.
5. Mallampati I–II.
6. Written informed consent.

Exclusion criteria

1. Current or recent (within 2 weeks) upper respiratory tract infection or sore throat.
2. Known hypersensitivity to dexmedetomidine, ketamine, or magnesium.
3. Chronic opioid, steroid, or immunosuppressive therapy.
4. Severe cardiopulmonary, hepatic, or renal disease (e.g., creatinine clearance <30 mL/min).
5. Pregnancy or lactation.
6. Anticipated difficult airway or need for rapid sequence induction.
7. BMI > 35 kg/m².

3. RESULTS

A total of **100 patients** were randomized and included in the analysis (Group D = 34, Group K = 33, Group M = 33). Baseline demographic and intraoperative variables were similar across groups. At 6 h post-extubation (primary endpoint), the incidence of POST was significantly lower in the dexmedetomidine group (3/34, **8.8%**) compared with the ketamine (9/33, **27.3%**) and magnesium groups (11/33, **33.3%**) ($p = 0.02$). Severity of POST was predominantly mild; no severe cases occurred. Two patients in Group D experienced transient bradycardia; sedation was mild and self-limited. No serious adverse events were observed.

A total of **100 adult patients** undergoing elective laparoscopic surgery under general anesthesia were included in the study and analyzed. Patients were randomly allocated into three groups: **dexmedetomidine group (Group D, n = 34)**, **ketamine group (Group K, n = 33)**, and **magnesium sulphate group (Group M, n = 33)**. All enrolled patients completed the study, and no protocol deviations or dropouts were observed.

Baseline demographic and airway characteristics

The baseline demographic characteristics were comparable among the three groups. The mean age, gender distribution, body mass index, ASA physical status, and Mallampati grading showed **no statistically significant differences** ($p > 0.05$). This indicates that the study groups were well matched at baseline and that randomization was effective, thereby minimizing potential confounding due to demographic or airway-related factors.

Intraoperative airway and surgical parameters

Intraoperative variables that could influence the development of postoperative sore throat were similar across all groups. The mean duration of surgery and duration of tracheal intubation did not differ significantly among the dexmedetomidine,

ketamine, and magnesium groups ($p > 0.05$). Endotracheal tube size and the number of intubation attempts were comparable, with the majority of patients in all groups being intubated on the first attempt. Cuff pressure was consistently maintained between **20–25 cmH_2O** throughout the procedure in all patients. These findings confirm that airway management was standardized and that observed postoperative differences were attributable to the nebulized study drugs rather than procedural variations.

Incidence of postoperative sore throat

The incidence of postoperative sore throat (POST) was lowest in the dexmedetomidine group at all postoperative time intervals. At **0 and 2 hours** post-extubation, the dexmedetomidine group demonstrated a lower incidence of POST compared with the ketamine and magnesium groups; however, these differences were not statistically significant ($p > 0.05$). At **6 hours post-extubation**, which was the **primary outcome**, a **statistically significant reduction** in the incidence of POST was observed in the dexmedetomidine group (8.8%) compared with the ketamine (27.3%) and magnesium (33.3%) groups ($p = 0.02$). At **12 and 24 hours**, the incidence of POST continued to be lowest in the dexmedetomidine group, with no patients reporting sore throat at 24 hours, while residual symptoms persisted in the ketamine and magnesium groups. Although differences at later time points did not reach statistical significance, a consistent trend favoring dexmedetomidine was evident throughout the 24-hour postoperative period.

Severity of postoperative sore throat

Severity assessment revealed that postoperative sore throat was predominantly **mild to moderate** in all groups, and **no cases of severe sore throat** were reported. At both 6 and 12 hours post-extubation, patients in the dexmedetomidine group experienced only mild symptoms. In contrast, the ketamine and magnesium groups demonstrated a higher proportion of patients with moderate sore throat. These findings suggest that dexmedetomidine not only reduced the incidence but also attenuated the severity of POST more effectively than ketamine or magnesium sulphate.

Secondary outcomes and adverse effects

Secondary outcomes such as hoarseness of voice and postoperative cough were observed less frequently in the dexmedetomidine group compared with the ketamine and magnesium groups, although these differences were not statistically significant ($p > 0.05$). Sedation (Ramsay Sedation Score ≥ 3) was more common in the dexmedetomidine group; however, it was mild and transient, resolving without intervention.

Two patients in the dexmedetomidine group experienced transient bradycardia, which did not require treatment and resolved spontaneously. No episodes of hypotension, respiratory depression, or serious adverse events were noted in any group. The incidence of postoperative nausea and vomiting was low and comparable across the three groups.

Overall interpretation

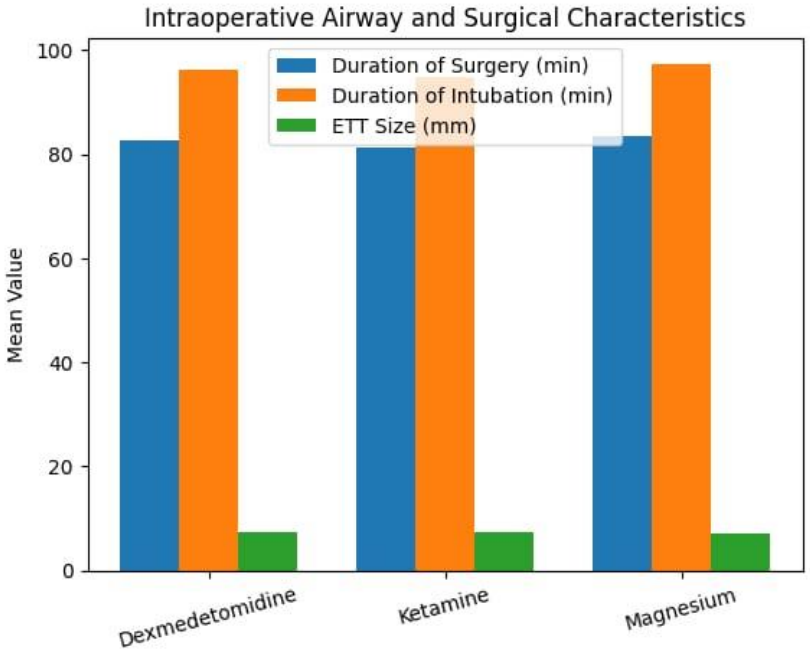
Overall, the results demonstrate that **preoperative nebulized dexmedetomidine** was associated with the **lowest incidence and severity of postoperative sore throat**, with a statistically significant benefit at 6 hours post-extubation and an acceptable safety profile. Ketamine showed intermediate efficacy, while magnesium sulphate was associated with a higher incidence of postoperative sore throat

Table 1. Demographic and Baseline Characteristics of Study Groups (n = 100)

Parameter	Dexmedetomidine (n = 34)	Ketamine (n = 33)	Magnesium (n = 33)	p value
Age (years), mean ± SD	38.9 ± 9.1	37.6 ± 8.8	39.3 ± 9.4	0.88
Gender (M / F)	16 / 18	17 / 16	15 / 18	0.91
BMI (kg/m^2), mean ± SD	24.9 ± 2.7	25.2 ± 2.8	24.7 ± 2.5	0.85
ASA Physical Status (I / II)	21 / 13	20 / 13	19 / 14	0.94
Mallampati Grade (I / II)	24 / 10	23 / 10	22 / 11	0.97

Table 2. Intraoperative Airway and Surgical Characteristics

Parameter	Dexmedetomidine (n = 34)	Ketamine (n = 33)	Magnesium (n = 33)	p value
Duration of surgery (min), mean ± SD	82.6 ± 15.4	81.2 ± 14.8	83.5 ± 16.1	0.90
Duration of intubation (min), mean ± SD	96.1 ± 17.5	94.8 ± 18.2	97.4 ± 18.9	0.93
Endotracheal tube size (mm), mean ± SD	7.3 ± 0.4	7.3 ± 0.5	7.2 ± 0.4	0.89
Number of intubation attempts (1 / >1)	32 / 2	30 / 3	31 / 2	0.84
Cuff pressure (cmH_2O)	20–25	20–25	20–25	—



Graph 1: Intraoperative Airway and Surgical Characteristics

Table 3. Incidence of Postoperative Sore Throat (POST) at Different Time Intervals

Time after extubation	Dexmedetomidine n (%)	Ketamine n (%)	Magnesium n (%)	p value
0 hour	6 (17.6%)	9 (27.3%)	11 (33.3%)	0.32
2 hours	4 (11.8%)	8 (24.2%)	10 (30.3%)	0.27
6 hours	3 (8.8%)	9 (27.3%)	11 (33.3%)	**0.02***
12 hours	2 (5.9%)	6 (18.2%)	8 (24.2%)	0.15
24 hours	0 (0%)	4 (12.1%)	6 (18.2%)	0.06

* Statistically significant

Table 4. Severity of Postoperative Sore Throat (4-Point Scale)

At 6 Hours Post-Extubation

Group	Mild n (%)	Moderate n (%)	Severe n (%)
Dexmedetomidine (n=34)	3 (8.8%)	0	0
Ketamine (n=33)	5 (15.2%)	4 (12.1%)	0
Magnesium (n=33)	6 (18.2%)	5 (15.2%)	0

At 12 Hours Post-Extubation

Group	Mild n (%)	Moderate n (%)	Severe n (%)
Dexmedetomidine	2 (5.9%)	0	0
Ketamine	4 (12.1%)	2 (6.1%)	0
Magnesium	5 (15.2%)	3 (9.1%)	0

Table 5. Secondary Outcomes and Adverse Effects

0	Dexmedetomidine (n=34)	Ketamine (n=33)	Magnesium (n=33)	p value
Hoarseness of voice	2 (5.9%)	5 (15.2%)	6 (18.2%)	0.29
Cough	2 (5.9%)	4 (12.1%)	5 (15.2%)	0.58
Sedation (Ramsay ≥3)	8 (23.5%)	4 (12.1%)	3 (9.1%)	0.18
Bradycardia	2 (5.9%)	0	0	—
Nausea / Vomiting	1 (2.9%)	2 (6.1%)	2 (6.1%)	0.69

4. DISCUSSION

Overview and principal findings. In this randomized, double-blind comparison among three commonly studied nebulized agents for POST prophylaxis, preoperative nebulized dexmedetomidine (1 μg/kg) produced a clinically and statistically significant reduction in POST incidence at 6 h after extubation compared with nebulized ketamine (50 mg) and magnesium sulphate (250 mg). The effect persisted as a favorable trend across other early postoperative time points, and severity was attenuated in the dexmedetomidine group. The safety profile was acceptable: sedation was mild and transient and two cases of brief bradycardia occurred without sequelae.

Comparison to previous trials and meta-analyses. Our findings align with recent randomized trials and meta-analyses that identify nebulized dexmedetomidine as an effective agent to reduce early POST. Pradian et al. (2023) reported reduced POST incidence with nebulized dexmedetomidine compared to placebo [30]. A 2025 systematic review/meta-analysis focusing on nebulized dexmedetomidine reported pooled reductions in early POST incidence and concluded that dexmedetomidine ranked among the most effective topical agents for early prophylaxis, although studies differed in dose and timing [35]. These higher-level syntheses are consistent with our observation of a substantial absolute reduction in 6-hour POST incidence (from ~30% to <10%) with dexmedetomidine.

Ketamine has long-standing evidence as a topical agent for reducing POST. Ahuja et al. (2015) demonstrated efficacy of nebulized ketamine for early POST reduction with low adverse-event rates, and multiple subsequent RCTs (various doses and gargle vs nebulization) confirmed its early effect [24,25]. Our ketamine arm showed intermediate results (27% at 6 h), consistent with many studies where ketamine reduces early POST but may be less potent than dexmedetomidine for sustained anti-nociceptive mucosal effects [24,26].

Magnesium sulphate has mechanistic plausibility via NMDA antagonism and calcium channel effects and has shown benefit in several trials [27,28]. However, comparative effect sizes have varied, likely reflecting heterogeneous dosing, timing and nebulization technique. In our cohort magnesium (250 mg) yielded the highest incidence of POST (33% at 6 h). This could reflect a relatively conservative magnesium dose or pharmacodynamic differences versus dexmedetomidine's α2-agonism; prior studies showing benefit sometimes used higher magnesium doses or different delivery methods [27–29].

Mechanistic considerations. Dexmedetomidine's local topical effects likely stem from α2-adrenoceptor-mediated attenuation of peripheral nociceptor excitability and inhibition of proinflammatory mediator release; systemic absorption can produce mild sedation and bradycardia but nebulized dosing concentrates drug at mucosa with lower systemic exposure than intravenous administration [30–34]. Ketamine's effect is principally via local NMDA blockade and anti-inflammatory modulation; magnesium shares some of these mechanisms, but the distinct receptor pharmacology of α2-agonists may translate to superior attenuation of mucosal pain signaling in the airway [24,27,30].

Timing and deposition. Nebulization 20–30 minutes pre-induction appears commonly used and may allow optimal mucosal contact and early receptor modulation prior to instrumentation [23,30]. Mouthpiece nebulization with patient semi-upright increases oropharyngeal deposition compared with facemask delivery, a practical point supported by aerosol science literature and by some clinical comparisons [23,39]. Careful technique likely improves signal-to-noise in clinical trials and real-world adoption.

Heterogeneity in literature and methodological caveats. Trials of nebulized agents vary in dose (e.g., dexmedetomidine 0.5–1 μg/kg, ketamine 40–100 mg, magnesium 225–500 mg), nebulization method (mask vs mouthpiece), timing (immediately before vs 20–30 min prior), surgical types, outcome definitions and cuff-pressure management. Such heterogeneity complicates meta-analysis interpretation and guideline recommendations [35–38,39]. The present study sought to control major procedural confounders (ETT size, cuff pressure) to make head-to-head comparisons more meaningful.

Safety profile and practical concerns. Nebulized dexmedetomidine may cause modest sedation and transient bradycardia at the doses studied; we observed two transient bradycardia episodes without clinical consequence. Ketamine's psychotropic or secretory effects are unlikely at low nebulized doses; magnesium has minimal systemic effects when renal function is normal but caution is warranted in renal impairment [24–29]. Operationally, nebulization requires ~10–15 minutes and a mouthpiece; this should be integrated in the pre-op workflow if adopted.

Clinical implications. The absolute risk reduction in POST at 6 h (~20–25% in our sample) is clinically meaningful: reduced throat pain improves comfort, may facilitate swallowing and oral intake, and enhances patient satisfaction. Dexmedetomidine's apparent superiority for early POST suggests it may be prioritized where resources allow, while ketamine remains an effective, inexpensive alternative.

Comparison with topical steroids and other strategies. Nebulized or topical steroids (budesonide, dexamethasone) have been studied for POST with mixed results; some trials report benefit whereas others do not show superiority over active comparators. Benzydamine spray and lignocaine lozenges are other options with variable efficacy [16,20,40]. In many centers, combining procedural measures (cuff-pressure control) with topical pharmacotherapy may achieve the greatest reduction in POST incidence.

Limitations of evidence and future research directions. While our trial strengthens head-to-head comparative data, limitations include single-centre conduct and modest overall sample size for rare adverse events. Dose-finding studies (e.g., dexmedetomidine 0.5 vs 1 µg/kg) and trials in other surgical populations (e.g., head-and-neck surgery, prolonged intubation) are needed. The possibility of additive or synergistic therapy (e.g., dexmedetomidine + low-dose ketamine) is attractive and should be tested. Pragmatic multicenter trials with standardized nebulization technique, cuff-pressure protocols, and patient-reported outcome measures would aid guideline development.

Synthesis with broader literature. Recent systematic reviews emphasize benefits of nebulized α2-agonists and ketamine for early POST but call for harmonized protocols and more head-to-head RCTs — precisely the gap our study addresses [35–38]. Our findings echo other head-to-head and single-agent RCTs showing improved outcomes with topical dexmedetomidine and ketamine versus placebo or saline controls, but place dexmedetomidine ahead of ketamine and magnesium in early POST prevention.

Operational recommendations. If an institution opts to implement nebulized prophylaxis, we suggest: 1) adopt mouthpiece nebulization 20–30 min pre-induction; 2) standardize ETT size and cuff pressure (20–25 cmH_2O); 3) monitor for sedation/bradycardia; and 4) consider dexmedetomidine 1 µg/kg as the first-line nebulized agent for early POST prevention, with ketamine as an alternative where dexmedetomidine is unavailable or contraindicated.

5. CONCLUSION

Preoperative nebulized dexmedetomidine (1 µg/kg) reduced the incidence and severity of postoperative sore throat at 6 hours after extubation more effectively than nebulized ketamine (50 mg) or nebulized magnesium sulphate (250 mg) in this randomized, double-blind comparison of 100 elective laparoscopic surgical patients. Nebulized dexmedetomidine had an acceptable safety profile. Larger multicenter randomized trials with standardized protocols are warranted to confirm these findings and refine dosing and implementation strategies.

Limitations

1. Fixed single doses for each agent; dose–response was not explored.
2. Follow-up limited to 24 hours; late or persistent throat symptoms beyond this period were not assessed.
3. Although key procedural variables (ETT size, cuff pressure) were standardized, subtle technique differences in laryngoscopy or individual mucosal sensitivity may remain as residual confounders.
4. The study did not include a placebo arm; comparisons are limited to active agents.

Declarations:

Conflicts of interest: There is no any conflict of interest associated with this study

Consent to participate: We have consent to participate.

Consent for publication: We have consent for the publication of this paper.

Authors' contributions: All the authors equally contributed the work.

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