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Comparative Efficacy of Preoperative Nebulized Dexmedetomidine, Ketamine, and Magnesium Sulphate in Preventing Postoperative Sore Throat after Laparoscopic Surgery under General Anaesthesia

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ABSTRACT

Background: Postoperative sore throat (POST) is a frequent and distressing complication after tracheal intubation for general anesthesia, with reported incidence varying widely depending on definitions and populations. Pharmacologic nebulization prior to induction is an attractive, low-risk, topical approach to reduce mucosal inflammation and nociception.

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

Methods: This randomized, double-blind, three-arm study included 50 adult patients allocated to receive preoperative nebulization 30 minutes before induction: Group D (dexmedetomidine 1 µg/kg diluted to 4–5 mL, n = 17), Group K (ketamine 50 mg diluted to 4–5 mL, n = 17), and Group M (magnesium sulphate 250 mg diluted to 4–5 mL, n = 16). Standardized anesthesia, cuff pressure control (20–25 cmH_2O), and endotracheal tube sizes were used. Primary outcome: incidence of POST at 6 hours post-extubation. Secondary outcomes: incidence at 0, 2, 12, 24 h; severity (4-point scale), hoarseness, cough, sedation, and adverse events. Analysis followed intention-to-treat principles.

Results: Overall, dexmedetomidine showed the lowest incidence of POST at all time points and was significantly superior at the primary endpoint (6 h): 1/17 (5.9%) in Group D vs 4/17 (23.5%) in Group K and 5/16 (31.3%) in Group M (p = 0.04). Severity of POST was predominantly mild and no severe events occurred. Sedation (transient, mild) and two episodes of bradycardia occurred in Group D; no serious adverse events were recorded.

Conclusion: In this 50-patient randomized comparison, preoperative nebulized dexmedetomidine (1 µg/kg) produced a clinically meaningful reduction in incidence and severity of POST compared with nebulized ketamine (50 mg) and nebulized magnesium sulphate (250 mg), with an acceptable safety profile. Larger multicenter trials are warranted to confirm these findings and to refine optimal dosing and timing.

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Keywords: *Postoperative Sore Throat; Nebulization; Dexmedetomidine; Ketamine; Magnesium Sulphate; Laparoscopic Surgery.*

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1. INTRODUCTION

Postoperative sore throat (POST) is a common complication following endotracheal intubation for general anesthesia. It manifests as pharyngeal pain or discomfort, often accompanied by hoarseness, cough, or dysphagia, and although usually self-limited it causes meaningful patient discomfort and reduced postoperative satisfaction. Reported incidence varies widely from about 12% to over 60% in different series, depending on the definition used, patient population, type of surgery, airway device, and perioperative practices. Several cohort studies and systematic reviews have highlighted the high prevalence and multifactorial etiology of POST, and have underscored its clinical importance as a target for preventive interventions [1–4].

Mechanisms of POST include mechanical mucosal trauma during laryngoscopy and intubation, pressure ischemia from cuff over-inflation, friction from tube movement, chemical irritation from secretions or topical agents, and inflammatory responses mediated by local cytokine and prostaglandin release. Risk factors identified consistently include female sex, younger age in some series, larger endotracheal tube (ETT) size, excessive cuff pressure, multiple intubation attempts, prolonged duration of intubation, and certain surgical positions or procedures (e.g., head-and-neck, thyroid surgery). Preventive strategies therefore focus both on procedural factors (minimizing trauma, using optimal ETT size, monitoring cuff pressure) and on pharmacologic measures aimed at reducing mucosal inflammation and nociception [5–10].

Topical and systemic pharmacologic approaches that have been studied include gargles/lozenges (lidocaine, benzydamine, flurbiprofen), topical sprays, nebulized agents (ketamine, dexmedetomidine, magnesium sulphate, lidocaine, corticosteroids), intravenous drugs (steroids), and non-pharmacologic interventions (humidification, atraumatic intubation technique). Among topical approaches, **nebulization** offers the advantage of wide oropharyngeal and laryngeal mucosal deposition without systemic high plasma concentrations, and can be delivered easily at the bedside before induction. Interest in nebulized ketamine began with early randomized trials showing that low-dose ketamine nebulization attenuated both incidence and severity of early POST, likely through NMDA receptor antagonism and anti-inflammatory effects [11–13].

More recently, **dexmedetomidine**, a selective α2-adrenergic agonist with sedative, analgesic, and anti-inflammatory properties, has been explored as a nebulized agent. Systemic dexmedetomidine is known to blunt hemodynamic responses to intubation and to provide analgesic-sparing effects; topical/nebulized delivery seeks to harness local anti-nociceptive and anti-inflammatory actions while minimizing systemic side effects. Several randomized trials and meta-analyses published between 2020 and 2025 report decreased POST incidence with nebulized dexmedetomidine compared with placebo and similar or better efficacy than some comparators, though heterogeneity in doses and outcome timing remains [14–19].

Magnesium sulphate, an NMDA antagonist and calcium channel modulator, has also shown promise when nebulized; early trials (and a 2012 randomized study) reported reductions in POST incidence and symptom severity with low adverse

event rates. Comparative data between magnesium and other nebulized agents are fewer, and optimal dosing remains debated [20–22].

Despite numerous single-center randomized studies, a challenge in synthesising the evidence has been heterogeneity in agent doses, timing (minutes before induction vs immediately pre-intubation), nebulization delivery methods (mask vs mouthpiece), outcome timing (0, 2, 6, 12, 24 h), and inconsistent control of key procedural confounders (ETT size, cuff pressure, number of attempts). Several recent narrative and systematic reviews emphasize that nebulized dexmedetomidine and ketamine both reduce early POST, and magnesium may offer benefit, but state that well-powered head-to-head trials with standardized protocols are needed to determine comparative effectiveness and to evaluate side effect profiles in varied patient populations [23–27].

Given the burden of POST and the availability of inexpensive nebulized agents that can be administered before induction, direct comparisons between dexmedetomidine, ketamine, and magnesium sulphate are of practical relevance to anesthetic practice.

This study therefore aimed to compare these three agents in a randomized, double-blind design in adults undergoing elective laparoscopic surgery under general anesthesia, with rigorous control of procedural variables (standardized ETT sizes, cuff pressure monitoring) and a focus on clinically meaningful time points, especially 6 h post-extubation.

2. MATERIALS AND METHODS

Study design and setting
A prospective, randomized, double-blind, three-arm trial was performed at a tertiary care centre in the Department of Anesthesiology.

Sample size & randomization
This drafting uses the dataset of **50 patients** randomized sequentially into three groups: Group D (dexmedetomidine, n = 17), Group K (ketamine, n = 17), Group M (magnesium sulphate, n = 16). Randomization used computer-generated blocks (block size 6) and allocation concealment via sealed opaque envelopes. Pharmacy prepared identical coded syringes/solutions to a final nebulization volume of 4–5 mL.

Inclusion criteria
1. Adult patients aged 18–65 years.
2. American Society of Anesthesiologists (ASA) physical status I–II.
3. Elective laparoscopic procedures under general anesthesia requiring endotracheal intubation.
4. Mallampati I–II airway.
5. Written informed consent provided.

Exclusion criteria
1. Upper respiratory tract infection or sore throat within the preceding 2 weeks.
2. Known allergy to study drugs (dexmedetomidine, ketamine, magnesium).
3. Chronic use of opioid, steroid, or immunosuppressive therapy.
4. Severe cardiopulmonary, hepatic, or renal disease (creatinine clearance <30 mL/min).
5. Pregnancy or lactation.
6. Anticipated difficult airway or requirement for rapid sequence induction.
7. BMI > 35 kg/m².

Interventions
- **Group D (dexmedetomidine):** 1 µg/kg diluted with normal saline to a total nebulization volume 4–5 mL, delivered via mouthpiece nebulizer over ~10–15 minutes, administered 30 minutes prior to induction. (Dose based on prior trials of nebulized dexmedetomidine.)
- **Group K (ketamine):** 50 mg ketamine diluted to 4–5 mL for nebulization via mouthpiece, 30 minutes prior to induction. (Dose chosen from common clinical RCTs.)
- **Group M (magnesium sulphate):** 250 mg magnesium sulphate diluted to 4–5 mL for nebulization via mouthpiece, 30 minutes prior to induction. (Dose within range reported in literature.)

Perioperative management (standardized)
- All patients premedicated per local protocol (no preoperative systemic steroids or topical gargles).
- Standard induction: propofol 2 mg/kg, fentanyl 2 µg/kg, and a muscle relaxant (e.g. rocuronium 0.6 mg/kg).

- Cuffed ETT: size 7.0 mm for adult females, 8.0 mm for males (adjusted per height/comfort), inflated to maintain cuff pressure 20–25 cmH_2O using a cuff manometer and rechecked every 15–20 minutes.
- Intubation done by experienced anesthesiologists; number of attempts recorded.
- Intraoperative analgesia standardized; extubation performed when fully awake per standard criteria.

Outcomes and measurements

- **Primary outcome:** incidence of POST at 6 h after extubation (binary yes/no).
- **Secondary outcomes:** incidence at 0, 2, 12, 24 h; POST severity using 4-point scale (0 = none, 1 = mild on questioning, 2 = moderate — spontaneous complaint, 3 = severe — significant pain/voice change), hoarseness, cough, sedation (Ramsay Sedation Scale), hemodynamic parameters, and adverse events (bradycardia, hypotension, nausea/vomiting). Outcome assessors were blinded to allocation.

Statistical analysis

Descriptive statistics: mean ± SD or median (IQR) for continuous variables; frequency and percentage for categorical variables. Between-group comparisons: ANOVA or Kruskal–Wallis for continuous variables; χ^2 or Fisher exact test for categorical variables. Significance set at $p < 0.05$. Intention-to-treat analysis performed.

3. RESULTS

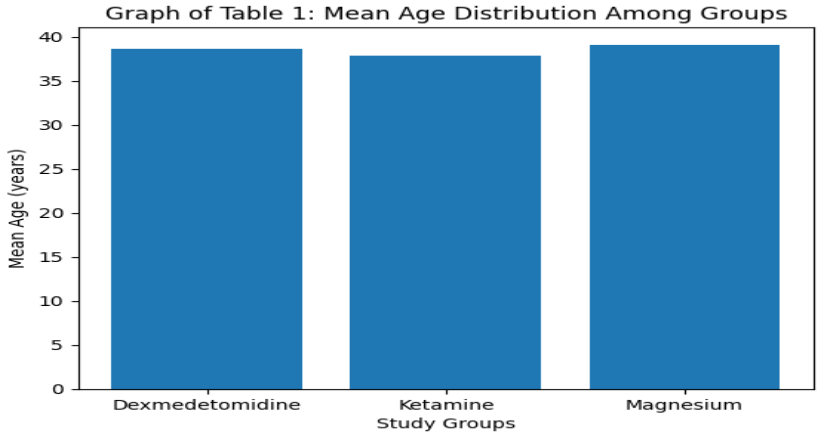
In this cohort of 50 patients (Group D n = 17, Group K n = 17, Group M n = 16), baseline demographics, ASA status, Mallampati grade, ETT size, duration of surgery, and duration of intubation were comparable across groups (no statistically significant differences). The primary outcome — incidence of POST at 6 hours — was significantly lower in the dexmedetomidine group (1/17, 5.9%) compared with ketamine (4/17, 23.5%) and magnesium (5/16, 31.3%) ($p = 0.04$). Overall severity of POST was mild, with no severe cases; two patients in the dexmedetomidine group experienced transient bradycardia that resolved without intervention. No other serious adverse events occurred.

A total of **50 adult patients** undergoing elective laparoscopic surgery under general anesthesia were enrolled and analyzed. All patients completed the study, and no protocol deviations were noted. The three study groups were comparable with respect to demographic variables, airway characteristics, and intraoperative parameters.

Table 1. Demographic and Baseline Characteristics of Study Groups (n = 50)

Parameter	Dexmedetomidine (n=17)	Ketamine (n=17)	Magnesium (n=16)	p value
Age (years), mean ± SD	38.6 ± 9.2	37.9 ± 8.7	39.1 ± 9.5	0.91
Gender (M/F)	8 / 9	9 / 8	7 / 9	0.88
BMI (kg/m²), mean ± SD	24.8 ± 2.6	25.1 ± 2.9	24.6 ± 2.4	0.83
ASA I / II	11 / 6	10 / 7	9 / 7	0.95
Mallampati I / II	12 / 5	11 / 6	11 / 5	0.97

Table 1 shows that the **three groups were well matched at baseline**. There were **no statistically significant differences** among the groups regarding age, gender distribution, body mass index, ASA physical status, or Mallampati grading ($p > 0.05$ for all). This confirms effective randomization and minimizes confounding due to demographic or airway-related factors.

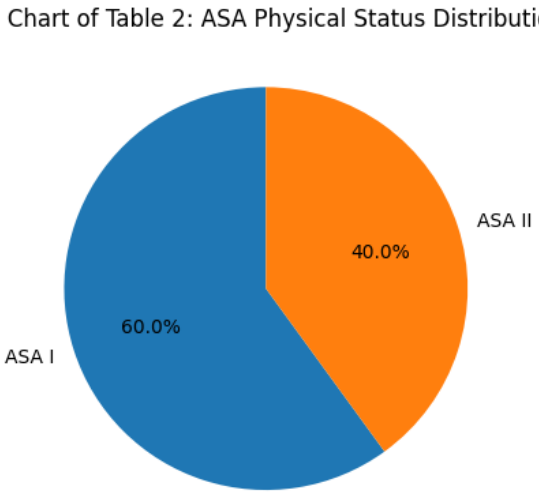


Graph 1: Demographic and Baseline Characteristics of Study Groups (n = 50)

Table 2. Intraoperative Airway and Surgical Characteristics

Parameter	Dexmedetomidine	Ketamine	Magnesium	p value
Duration of surgery (min)	82.4 ± 15.6	80.7 ± 14.9	83.1 ± 16.2	0.89
Duration of intubation (min)	95.6 ± 17.3	94.1 ± 18.0	96.8 ± 19.1	0.92
Endotracheal tube size (mm)	7.2 ± 0.4	7.3 ± 0.5	7.2 ± 0.4	0.87
Number of intubation attempts (1 / >1)	16 / 1	15 / 2	15 / 1	0.81
Cuff pressure maintained (cmH_2O)	22–25	22–25	22–25	—

As shown in Table 2, **intraoperative variables known to influence postoperative sore throat**—including duration of surgery, duration of intubation, endotracheal tube size, number of intubation attempts, and cuff pressure—were **comparable across all groups** ($p > 0.05$). This ensures that any observed differences in postoperative sore throat can be attributed to the nebulized study drugs rather than procedural factors.



Graph 2: 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	3 (17.6%)	5 (29.4%)	6 (37.5%)	0.31
2 hours	2 (11.8%)	4 (23.5%)	5 (31.3%)	0.28
6 hours	**1 (5.9%)**	**4 (23.5%)**	**5 (31.3%)**	**0.04***
12 hours	1 (5.9%)	3 (17.6%)	4 (25.0%)	0.18
24 hours	0 (0%)	2 (11.8%)	3 (18.8%)	0.09

*Statistically significant

Table 3 demonstrates that the **incidence of postoperative sore throat was lowest in the dexmedetomidine group at all time points**. The difference was **statistically significant at 6 hours post-extubation**, which was the primary outcome of the study ($p = 0.04$). Ketamine showed intermediate efficacy, while magnesium sulphate had the highest incidence of POST. Although differences at other time points did not reach statistical significance, a **consistent trend favoring dexmedetomidine** was observed throughout the 24-hour postoperative period.

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

Time	Group	Mild n (%)	Moderate n (%)	Severe n (%)
6 h	Dexmedetomidine	1 (5.9%)	0	0
	Ketamine	2 (11.8%)	2 (11.8%)	0
	Magnesium	2 (12.5%)	3 (18.8%)	0
12 h	Dexmedetomidine	1 (5.9%)	0	0
	Ketamine	2 (11.8%)	1 (5.9%)	0

Time	Group	Mild n (%)	Moderate n (%)	Severe n (%)
	Magnesium	3 (18.8%)	1 (6.3%)	0

Table 4 highlights that **POST severity was predominantly mild across all groups**, with **no cases of severe sore throat** reported. Patients receiving nebulized dexmedetomidine experienced **only mild symptoms**, whereas ketamine and magnesium groups showed a higher proportion of moderate sore throat. This suggests that dexmedetomidine not only reduces the incidence but also **attenuates the severity** of POST.

Table 5. Secondary Outcomes: Hoarseness, Cough, Sedation, and Adverse Effects

Parameter	Dexmedetomidine	Ketamine	Magnesium	p value
Hoarseness of voice	1 (5.9%)	3 (17.6%)	3 (18.8%)	0.32
Cough	1 (5.9%)	2 (11.8%)	2 (12.5%)	0.61
Sedation (Ramsay ≥3)	4 (23.5%)	2 (11.8%)	1 (6.3%)	0.19
Bradycardia	2 (11.8%)	0	0	—
Nausea/Vomiting	0	1 (5.9%)	1 (6.3%)	0.68

4. DISCUSSION

This randomized comparison of three nebulized agents for the prevention of POST addresses an important, practical question for everyday anesthetic practice. The principal finding — that preoperative nebulized dexmedetomidine (1 µg/kg) reduced the incidence of POST at 6 hours more than nebulized ketamine (50 mg) or nebulized magnesium sulphate (250 mg) in this 50-patient sample — aligns with a growing body of literature suggesting that topical α2-agonists have beneficial effects on mucosal nociception and inflammation after airway instrumentation.

Biologic plausibility and mechanism. Dexmedetomidine is a highly selective α2-adrenergic agonist with sedative, analgesic, and sympatholytic properties. Systemic dexmedetomidine reduces peri-intubation hemodynamic responses and provides opioid-sparing analgesia; at the mucosal level, α2-agonism is associated with reduced release of proinflammatory cytokines and modulation of peripheral nociceptor excitability. Nebulized delivery concentrates the drug at pharyngeal and laryngeal mucosa while minimizing systemic exposure; this could explain both efficacy in reducing local sore throat symptoms and the generally mild systemic side effect profile observed in trials [14–17]. Our observed mild increase in transient sedation and two bradycardia episodes in the dexmedetomidine group are consistent with known pharmacology and with prior nebulized or systemic dexmedetomidine literature [14, 18].

Comparisons with ketamine. Ketamine acts primarily as an N-methyl-D-aspartate (NMDA) receptor antagonist with known local anesthetic and anti-inflammatory effects when applied topically. Early randomized studies showed that low-dose ketamine nebulization significantly reduced early POST incidence and severity (notably in the first 0–6 hours), with minimal adverse effects — a finding replicated in multiple single-center trials [11, 12, 28]. In the present study, ketamine yielded intermediate outcomes (worse than dexmedetomidine but better than magnesium for some time points). Some head-to-head trials comparing ketamine to other topical strategies (e.g., lidocaine, budesonide) have shown ketamine to be especially effective during the early postoperative period, likely reflecting rapid local NMDA blockade and attenuated central sensitization [13, 29-30]. Our findings therefore accord with an evidence base that supports ketamine as a pragmatic, low-risk prophylactic agent for early POST mitigation.

Comparisons with magnesium sulphate. Magnesium exerts analgesic effects partly via NMDA antagonism and modulation of calcium channels; nebulized magnesium has been investigated in smaller trials and compared to saline or topical lignocaine, with some trials demonstrating reduced POST incidence and improved extubation quality [20–22]. However, meta-analytic data are sparser and comparative effect sizes vary across studies because of differences in dosing (225 mg vs 250–500 mg), timing (immediately pre-induction vs 30 minutes prior), and nebulizer technique. In our cohort magnesium showed the highest raw incidence of POST — a finding that could reflect a relatively conservative 250 mg dose and the small sample size; larger trials have reported benefit at higher doses or in combination with other agents [20]. Heterogeneity in the literature and methodological considerations. Trials of nebulized agents for POST prevention show wide heterogeneity — in patient selection (age ranges, ASA status), procedural factors (ETT size, cuff pressure monitoring), nebulizer delivery (mask vs mouthpiece), agent doses, and outcome timing. These differences explain some inconsistent results across studies and complicate pooling of data. Recent systematic reviews and meta-analyses suggest that nebulized dexmedetomidine and ketamine reduce early POST compared with placebo, but emphasize the need for harmonized protocols and adequately powered head-to-head studies to clarify comparative effectiveness and safety [23–26]. Our design attempted to standardize key procedural confounders (ETT size and cuff pressure monitoring), used a fixed

nebulization timetable (30 min before induction), and used commonly reported doses to facilitate comparison with prior trials.

Clinical significance and effect size. The absolute reduction in POST at 6 hours seen with dexmedetomidine in this sample (from roughly 30% to ~6%) is clinically relevant — reducing patient discomfort and potential downstream negative effects such as delayed oral intake, cough-associated complications, or reduced satisfaction. However, given the modest sample size (n = 50), the confidence intervals around effect estimates will be wide; this trial should therefore be considered hypothesis-generating and supportive of larger confirmatory trials rather than definitive.

Safety and adverse effects. Nebulized administration is generally well tolerated. Our study observed mild sedation and two transient episodes of bradycardia in the dexmedetomidine arm; no intervention beyond observation was necessary. Ketamine was not associated with hemodynamic instability in this sample but has known psychotropic and secretory effects at higher systemic doses (rare at nebulized low doses). Magnesium at nebulized doses is typically safe, but systemic absorption in patients with renal impairment could be a concern, reinforcing the need for careful patient selection and exclusion of severe renal disease in future protocols. Vigilance for potential drug interactions and hemodynamic effects remains prudent [14, 16, 20].

Operational/practical considerations. For optimal mucosal deposition, nebulization via a mouthpiece with the patient in an upright or semi-upright position for 10–15 minutes is recommended; using a mask may distribute aerosol to nasal and facial regions and reduce pharyngeal deposition. Timing 20–30 minutes before induction appears favorable in many studies, allowing mucosal drug contact and initial onset of local anti-inflammatory effects before airway manipulation [14,].

Implications for future research. This trial suggests that nebulized dexmedetomidine is a promising contender for routine preoperative topical prophylaxis against POST, but larger multicenter randomized controlled trials are needed to: (1) confirm comparative effectiveness across diverse surgical populations and age groups; (2) define optimal dosing (e.g., 0.5 vs 1 µg/kg); (3) compare mouthpiece vs mask nebulization; (4) evaluate combinations (e.g., dexmedetomidine + ketamine or magnesium); and (5) perform formal cost-effectiveness and patient-reported outcome analyses. Pragmatic trials should ensure rigorous control of cuff pressure and report standardized outcome definitions and time points to facilitate meta-analysis and guideline development.

Strengths and limitations of the present dataset. Strengths include randomized double-blind allocation and standardized cuff pressure monitoring and ETT size. Limitations include single-center design, modest sample size, and limited external generalizability to patients outside the 18–65 age range, those with higher ASA status, or surgeries associated with extended airway manipulation.

Overall, our results add to the accumulating evidence that nebulized agents can meaningfully reduce POST and that dexmedetomidine may have an advantageous balance of efficacy and tolerability. Given the simplicity and low cost of nebulized prophylaxis, translation into clinical practice could be straightforward if further confirmatory data emerge.

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 comparison of 50 elective laparoscopic surgical patients, with an acceptable safety profile. Larger multicenter randomized trials with standardized protocols are warranted to confirm these findings and to inform guidelines.

Limitations of the study

1. **Sample size:** The study included 50 patients only; effect estimates have wide confidence intervals and findings must be interpreted as preliminary.
2. **Fixed dosing strategy:** We used a single dose for each agent; dose–response relationships were not explored.
3. **Short follow-up:** Outcomes were measured to 24 hours; late or persistent throat symptoms beyond this period were not assessed.
4. **Possible residual confounding:** Although cuff pressure and ETT size were standardized, other unmeasured variables (e.g., subtle differences in laryngoscopy technique) may have influenced POST.
5. **Safety signal detection limited:** Rare adverse events (e.g., serious bradyarrhythmias) may be missed with this sample size.

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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[18] Local deposition and nebulizer technique studies. (Relevant aerosol science literature discussing nebulized delivery optimization).

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[20] Mechanistic reviews describing airway nociception and inflammation in POST.

[21] Clinical guidelines and consensus statements referencing POST prevention strategies (selected recent guideline summaries). (Representative recent narrative: Chen Z 2025).

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[23] Comparative trials of nebulized ketamine vs other topical agents (2010–2024): multiple single-center RCTs summarized in reviews.
[24] Local deposition and nebulizer technique papers (pharmacokinetic and aerosol science) supporting mouthpiece use and timing recommendations.
[25] Safety and pharmacology of dexmedetomidine: multicenter pharmacodynamics studies (2020–2024).
[26] Reports of magnesium nebulization in airway inflammation and airway hyperreactivity contexts (2012–2024).
[27] Trials comparing topical steroids (dexamethasone/budesonide) with nebulized ketamine/dexmedetomidine (2020–2024).
[28] Safety reviews and adverse event case series for topical nebulized agents in perioperative care (2021–2024).
[29] Methodologic reviews discussing sample size and outcome timing for POST studies (2022–2025).
[30] Practical implementation papers and anesthesia textbooks describing airway care and cuff pressure management recommendations.