DOI: 10.35975/apic.v27i6.2348

### **AIRWAY MANAGEMENT**

# Nebulized dexmedetomidine for preventing postoperative sore throat after tracheal intubation: a randomized, double-blind clinical trial

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# ABSTRACT

**Background and Objective:** Endotracheal intubation is part of general anesthesia, and probably the most commonly performed airway related procedure in operating rooms as well as intensive care units. It may be a causative factor in about 74% of patients who experience postoperative sore throat (POST) due to airway mucosal injury. This doubleblind randomized clinical trial assessed the effectiveness of nebulized dexmedetomidine in preventing POST by comparing with a control group.

**Methodology:** In this randomized, double-blind clinical trial, we enrolled 56 patients, who were to undergo general anesthesia with endotracheal intubation. Patients were randomly divided into two groups of 28 each. Group A received dexmedetomidine nebulization, and Group B had normal saline nebulization, both for 15 min before induction. POST was assessed at 1, 2, 4, 6, 12, and 24 h after extubation using a POST scale. Data were collected and statistically analyzed

**Results:** The overall incidence of POST was 60.3%: Control group experienced POST by 28 (96.6%) patients, compared to 7 (24,1%) patients in dexmedetomidine group (P = 0.0001). Differences were significant at recording times post-operatively. The dexmedetomidine group had milder sore throats, less coughing, and lower heart rates/blood pressures compared to the control group.

**Conclusion:** Patients who were nebulized with dexmedetomidine, experienced lower rates and intensity of postoperative sore throat compared to the control group. Administering dexmedetomidine via nebulization before intubation can be considered a safe and effective method for reducing postoperative sore throat, with less postintubation hemodynamic derangement.

**Abbreviations:** ETT: Endotracheal Tube; GA: General Anesthesia; IL: Interleukin; MAC: Minimum Alveolar Concentration; N<sub>2</sub>O: Nitic Oxide; PACU: Post Anesthesia Care Unit; PONV- Postoperative Nausea and Vomiting; POST-Postoperative Sore Throat; TNF: Tumor Necrosis Factor

Key words: Dexmedetomidine; Endotracheal Intubation; Anaesthesia, General; Nebulization; Postoperative sore throat

**Citation:** Pradian E, Kestriani SS ND, Ritonga DZ. Nebulized dexmedetomidine for preventing postoperative sore throat after tracheal intubation: a randomized, double-blind clinical trial. Anaesth. pain intensive care 2023;27(6):737–744. **DOI:** 10.35975/apic.v27i6.2348

Received: Aug 28, 2023; Revised: Oct 21, 2023; Accepted: Oct 21, 2023

# **1. INTRODUCTION**

Following general anesthesia, postoperative sore throat (POST) can lead to patient discomfort and dissatisfaction, potentially delaying their return to regular activities. The prevalence of POST after tracheal intubation can range from 14.4% to 90%. Factors contributing to increased POST risk involve laryngoscopy-induced pathological changes, such as loss of mucosal epithelium, glottic hematoma, glottic edema, submucosal tears, and contact ulcer granulomas. Most injuries occur within the larynx, impacting the vocal cords or epiglottis, including issues like glottic congestion, vocal cord hematomas, and a minor number of submucosal tears.<sup>1,2</sup>

Factors that can increase the likelihood of POST include female gender, younger age, previous lung disease, prolonged anesthesia duration, not using neuromuscular blockade during tracheal intubation, use of a double lumen tube, and high ETT cuff pressure.<sup>3-7</sup>

Nebulized dexmedetomidine is employed as a method to avert POST. Dexmedetomidine is a potent alpha-2 receptor agonist recognized for its focused impact on these receptors, inducing sedation, pain alleviation, and diminished sympathetic activity. The local application of nebulized dexmedetomidine yields analgesic and antiinflammatory effects by lowering postoperative serum levels of IL-6, IL-8, and TNF- $\alpha$ . Administering

dexmedetomidine through nebulization is well tolerated and represents a promising new administration approach that has minimal effects on the cardiovascular and the respiratory systems. Experiments on animals have demonstrated that applying dexmedetomidine directly to the airway can relax tracheal smooth muscles and inhibit the cough reflex. Hence, the significant decrease in both the occurrence and severity of POST in the dexmedetomidine group may be attributed to the reduction of inflammatory mediators resulting from preoperative dexmedetomidine nebulization, along with its pain-relieving action.6-10

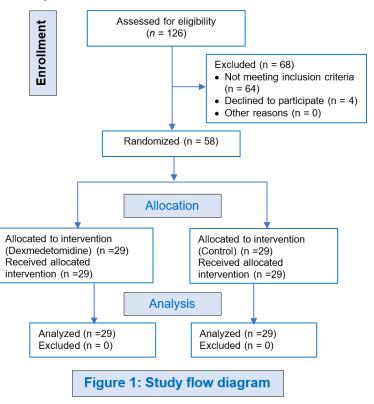
The distribution half-life of nebulized dexmedetomidine is 6 min, while its elimination half-life is 2 h. Unlike intravenous administration, it does not lead adverse hemodynamic effects. to Dexmedetomidine's direct influence on peripheral alpha-2 adrenoceptors induces relaxation of bronchial smooth muscles, resulting in bronchial dilation. Additionally, this medication has the advantageous ability to prevent bronchospasm. Nebulized dexmedetomidine demonstrates a 65% bioavailability through the nasal mucosa and an even higher 82% via the buccal mucosa.<sup>9-11</sup>

The objective of this research was to assess the efficacy of nebulized dexmedetomidine in reducing POST among patients undergoing intubation under general anesthesia (GA). This was achieved by comparing the occurrence and intensity of POST between the group receiving nebulized dexmedetomidine and the control group.

# 2. METHODOLOGY

This study employed a prospective, double-blind, randomized, comparative analytical approach involving two distinct study groups. Ethical approval was granted by the Research Ethics Committee of Dr. Hasan Sadikin General Hospital on August 15th, 2022 (COA Number: LB.02.01/X.6.5/260/2022). All patients gave informed written consent prior to the research to participate in the trial. The study followed the principles outlined in the Declaration of Helsinki.

The sample size was determined using statistical calculations, considering a 95% confidence level, 90% power test, and a 10% buffer for potential subject exclusions. This yielded a required 29 participants in each group.



Inclusion criteria were female patients undergoing elective surgery under GA with intubation, American Society of Anesthesiologists (ASA) physical status (PS) 1-2, aged 18 to 65 y. Exclusion criteria included contraindications to dexmedetomidine based on preoperative assessments, presence of difficult airway conditions, nasogastric tube insertion, first-trimester pregnancy, chronic obstructive pulmonary disease, respiratory tract infections, dexamethasone use, and preoperative sore throat. Additional exclusion criteria involved multiple intubation attempts, intraoperative deterioration preventing extubation, and anesthesia lasting over three hours.

Consecutive sampling was employed for research subject selection, while the permutation block randomization method was used to assign samples to either group A (treatment group) or group B (control group). Randomly selected samples were divided into Group A received two groups. nebulized dexmedetomidine 50 µg or 0.5 ml in 5 ml normal saline solution. Group B was nebulized with 5 ml normal saline solution. The randomization procedure was conducted by an uninvolved assistant, with the results sealed in envelopes. Another research assistant, who remained separate from subsequent analysis, prepared the nebulization solutions following the assigned group. Patients were unaware of their treatment as the nebulized substances were colorless and tasteless.

Patients fasted for six hours before surgery. Upon arrival at the operating room's waiting area, patients underwent re-examination for identification, diagnosis, anesthesia plan, and intravenous access. Nebulization lasted 15-20 min according to the respective treatment group. Heart rate, blood pressure, and oxygen saturation were recorded before and every 3 min during nebulization. Presence of bradycardia, hypotension, respiratory depression, and sedation were also noted. In the operating room, monitoring devices were applied and hemodynamic data tracked. Induction comprised fentanyl 2 µg/kg, propofol 2 mg/kg, and atracurium 0.5 mg/kg. A senior anesthesiologist resident performed intubation via direct laryngoscopy. Endotracheal tube (ETT) size was determined using the formula ETT size = height (cm)/30 + 2.<sup>12</sup>

The ETT cuff was inflated to 20-25 cmH<sub>2</sub>O pressure, validated with a manometer, and connected to the anesthesia machine. ETT size, laryngoscopy duration, and blood on laryngoscope blade were documented. Intracuff pressure was monitored every 30 min to maintain 20-25 cmH2O pressure. Anesthesia relied on isoflurane (1-1.2 MAC), 50% oxygen in N<sub>2</sub>O, tidal volume 6-8 mL/kg, and respiratory rate 12 breaths/min. Ondansetron 4 mg was administered to prevent postoperative nausea and vomiting (PONV).

Hemodynamic data were assessed before intubation, 1 min after intubation, and every 3 min for the first 15 min post-intubation. During surgery, observations occurred every 15 min. Following surgery, subjects were monitored in the recovery room, with blood pressure, heart rate, oxygen saturation, nausea, cough, and emergence of delirium recorded. POST evaluation was conducted at 1, 2, 4, 6, 12, and 24 h after surgery, utilizing a four-point scale [0 for no sore throat, 1 for mild sore throat, 2 for moderate sore throat, and 3 for severe sore throat].

### **Statistical analysis**

Data analysis encompassed both descriptive examination and hypothesis testing. Data were documented in the research form and subsequently subjected to editing, verification, coding, data entry, and analysis using the SPSS version 25.0 software. The statistical analysis began with an assessment of the characteristics of the two groups. For numerical variables, a comparison of means was conducted between the two groups using an unpaired t-test in case of normal distribution, or alternatively, the Mann-Whitney U test for non-normally distributed data, preceded by a normality test.

For categorical data, the chi-square test was employed if conditions were met; otherwise, the Fisher's Exact test was applied for 2x2 tables, and the Kolmogorov-Smirnov test was used for tables other than 2x2. P  $\leq 0.05$ indicated statistical significance.

# 3. RESULTS

Patients were selected based on inclusion criteria. Among these patients, four declined participation, while a total of 58 individuals agreed to partake (Figure 1). No subjects were excluded from the study. Demographic characteristics, including age, sex, weight, height, BMI, ASA grading, anesthesia duration, laryngoscopy duration, cuff pressure, oropharyngeal airway usage, presence of blood on laryngoscope, blood presence during extubation, and type of surgery, were similar between both groups (Table 1). The incidence of sore throat in this study was observed in 35 patients (60.3%); out of which 28 (96.6%) were in group B and 7 (24.1%) patients in group A (P = 0.0001) (Table 2).

Severity of sore throat was consistently lower in the dexmedetomidine group across all time intervals (Table 2). Notably, no severe sore throats were reported within the dexmedetomidine group during the first hour postoperatively, whereas the control group had five cases.

Postoperative cough occurred in only one individual (3.4%) in the dexmedetomidine group compared to 19 (65.5%) in group B. Neither group experienced severe

Characteristic	Group A	Group B	P value
	(Dexmedetomidine)	(Normal saline)	
Age (y)	42.03 ± 13.303	39.76 ± 14.402	0.534
Weight (Kg)	56.07 ± 7.639	57.03 ± 14.446	0.858
Height (cm)	158.21 ± 6.091	157.41 ± 6.674	0.638
BMI (kg/m <sup>2</sup> )	22.48 ± 3.320	22.89 ± 4.901	0.711
ETT size (mm)	6.91 ± 0.234	$6.90 \pm 0.280$	0.950
Anesthetic duration (min)	152.59 ± 37.835	135.00 ± 40,883	0.084
Laryngoscopy duration (sec)	18.72 ± 9.486	19.66 ± 11.014	0.733
ASA PS			
Class 1	11 (37.9)	13 (44.8)	0.594
Class 2	18 (62.1)	16 (55.2)	
Operative area			
Mouth	3 (10.3)	2 (6.9)	1.000
• ENT	3 (10.3)	6 (20.7)	
Thyroid	7 (24.1)	5 (17.2)	
<ul> <li>Digestive tract</li> </ul>	5 (17.2)	3 (10.3)	
Breast	1 (3.4)	1 (3.4)	
<ul> <li>Gynecology</li> </ul>	10 (34.5)	10 (34.5)	
<ul> <li>Extremities</li> </ul>	0 (0.0)	2 (6.9)	
Mean intracuff pressure (cmH <sub>2</sub> O)	23.07 ± 1.193	23.28 ± 0.960	0.708
OPA usage	23 (79.3)	24 (82.8)	0.738

coughing (Table 3). No adverse effects like nausea, sedation, hypotension, bradycardia, bradypnea, or bitter taste were reported in either group.

In terms of intraoperative hemodynamic analysis, the dexmedetomidine group exhibited lower heart rates at 1 min post-intubation and lower mean arterial pressure (MAP) at 1- and 3-min post-intubation (Table 4 and Table 5). Both groups demonstrated stability in hemodynamics with no signs of instability.

# 4. DISCUSSION

Postoperative sore throat is frequently reported during the recovery phase after surgery. Earlier research indicated a POST incidence of 17%. We observed that out of the total samples, 35 (60.3%) experienced sore throats. These findings align with the earlier reported incidence documented in previous studies ranging from 12 to 65%.<sup>4,7,13</sup> Among adults undergoing tracheal intubation. factors such as female gender, younger age, previous lung disease, extended anesthesia duration. and encountering blood on the endotracheal tube (ETT) during extubation were linked to an increased risk of postoperative sore throat (POST). In this exclusively female study. patients were included. This selection aimed to mitigate potential biases, given that

postoperative sore throat incidence was higher among female patients. This difference is attributed to women having lower pain thresholds and tolerances, as well as heightened pain sensitivity, which likely contributes to the elevated sore throat rates observed in this study.

The underlying mechanism behind postoperative sore throat is primarily attributed to prolonged pressure exerted on airway structures. Extended pressure on the tracheal mucosa from the ETT cuff leads to ischemia and escalates the likelihood of postoperative sore throat. This study involved

subjects who received anesthesia for up to a maximum of 180 min, and no disparities in this aspect were noted between the two groups. When ETT cuff pressure surpasses the arteriolar capillary blood pressure (around 30 mmHg), tissue ischemia can trigger inflammation, ulceration, granulation, and stenosis. Maintaining ETT cuff pressure at the minimum level required to establish a seal during routine positive pressure ventilation typically around 20 mm Hg—results in a 75% reduction in tracheal blood flow at the cuff site. In this study, cuff pressure was upheld within the range of 20-25 cmH<sub>2</sub>O or approximately 15-20 mmHg, and no significant difference was discerned between the two groups.<sup>3,14</sup>

Within the dexmedetomidine group, none of the participants encountered severe POST. Moderate discomfort ceased to be evident at the 6-h postoperative mark. By the 12-h postoperative point, no instance of sore throat was observed. These findings are in agreement to prior research comparing ketamine and dexmedetomidine nebulization, which similarly

POST		Group A (Dexmedetomidi ne)	Group B (Normal saline)	P value
1 h	Scale 0	22 (75.9)	1 (3.4)	0.0001**
	Scale 1	3 (10,3)	5 (17.2)	
	Scale 2	4 (13.8)	18 (62.1)	
	Scale 3	0 (0.0)	5 (17.2)	
2 h	Scale 0	24 (82.8)	1 (3.4)	0.0001**
	Scale 1	2 (6.9)	7 (24.1)	
	Scale 2	3 (10,3)	20 (69.0)	
	Scale 3	0 (0.0)	1 (3.4)	
4 h	Scale 0	25 (86.2)	2 (6.9)	0.0001*
	Scale 1	3 (10,3)	16 (55.2)	
	Scale 2	1 (3.4)	10 (34.5)	
	Scale 3	0 (0.0)	1 (3.4)	
6 h	Scale 0	27 (93.1)	8 (27.6)	0.0001**
	Scale 1	2 (6.9)	15 (51.7)	
	Scale 2	0 (0.0)	6 (20.7)	
	Scale 3	0 (0.0)	0 (0.0)	
12 h	Scale 0	29 (100.0)	19 (65.5)	0.001*
	Scale 1	0 (0.0)	8 (27.6)	
	Scale 2	0 (0.0)	2 (6.9)	
	Scale 3	0 (0.0)	0 (0.0)	
24 h	Scale 0	29 (100.0)	24 (82.8)	0.020*
	Scale 1	0 (0.0)	5 (17.2)	
	Scale 2	0 (0.0)	0 (0.0)	
	Scale 3	0 (0.0)	0 (0.0)	

including  $\alpha 2A$ ,  $\alpha 2B$ , and  $\alpha 2C$ , and are widely distributed in the central nervous system, peripheral nervous system, ganglia. autonomic and diverse tissues like blood kidney, vessels, liver. platelets. pancreas. and Among them,  $\alpha 2A$  receptors serve as significant inhibitory presynaptic feedback receptors, regulating neurotransmitter release from adrenergic neurons. These receptors also contribute to sedation, analgesia, seizure control. and platelet aggregation. On the other hand,  $\alpha 2B$  receptors are mainly found in vascular muscles, inducing a brief surge in blood pressure followed by a decline upon activation. In the spinal cord, a2B receptors influence pain modulation, leading to analgesic effects. Bv suppressing catecholamine release at nerve endings and monoaminergic neurons in the brain, dexmedetomidine holds potential in mitigating neuronal damage by impeding neurotransmitter release. which could enhance blood perfusion to ischemic tissues. These mechanisms could contribute to the observed

Data given as n (%);  $P \le 0.05$  considered as significant. POST: Post-operative sore throat; \* significant P-values; \*\*Highly significant P-values

indicated a generally low level of pain across all examination time points.<sup>7</sup>

Dexmedetomidine's pain-relieving impact manifests centrally in the locus coeruleus, at the spinal substantia gelatinosa, as well as peripherally. It has the capacity to activate receptors both in the central and peripheral domains, leading to decreased sympathetic activity and lower levels of catecholamines release. This results in the attenuation of the perioperative stress response. The capacity of dexmedetomidine to diminish sympathetic activity while indirectly enhancing parasympathetic activity holds significant importance in curbing inflammation, restraining the release of inflammatory agents, and mitigating cell apoptosis.<sup>15</sup>

Dexmedetomidine is a notably specific  $\alpha 2$  receptor agonist. These  $\alpha 2$  receptors exist in various forms,

prevention of sore throats in patients receiving dexmedetomidine.<sup>16</sup>

The release of key catecholamines like dopamine, and noradrenaline can elicit adrenaline. а proinflammatory reaction from macrophages. Surgical stress prompts the release of inflammatory cytokines such as IL-1, IL-6, and TNF- $\alpha$ , while tissue damage activates small nociceptive nerve endings and local inflammatory cells like macrophages, mast cells, lymphocytes, and platelets in peripheral areas. Injured cells additionally release inflammatory mediators, including bradykinin, histamine, 5-hydroxytryptamine (5-HT), ATP, nitric oxide, and ions. Recruited immune cells also release various mediators like cytokines (TNFα, IL-1, IL-6, IL-8, and chemokines). These substances can either directly sensitize nociceptors or activate other cells that produce pain, such as histamine from mast

Table 3: Comparative post-operative complications			
Group A (Dexmedetomidine)	Group B (NaCl 0.9)	P value	
Post-operative Cough			
28 (96.6)	10 (34.5)	0.0001**	
1 (3.4)	17 (58.6)		
0 (0.0)	2 (6.9)		
0 (0.0)	0 (0.0)		
1 (3.4)	0 (0,0)	1.000	
2 (6.9)	2 (6.9)	1.000	
7 (24.1)	28 (96.6)	0.0001**	
	Group A (Dexmedetomidine) 28 (96.6) 1 (3.4) 0 (0.0) 0 (0.0) 1 (3.4) 2 (6.9)	Group A (Dexmedetomidine)Group B (NaCl 0.9)28 (96.6)10 (34.5)1 (3.4)17 (58.6)0 (0.0)2 (6.9)0 (0.0)0 (0.0)1 (3.4)0 (0,0)2 (6.9)2 (6.9)	

 $P \le 0.05$  was considered as significant; \*\*Highly significant P-values; Absent = no cough, Mild = light or single cough, Moderate = more than one episode of un-sustained (65 sec) cough, Severe = sustained (65s) and repetitive cough with head tilt

Time	Heart Rate (Beats/min)		P value
	Group A (Dexmedetomidin e)	Group B (Normal saline)	
Before intubation	85.41 ± 10.322	81.34 ± 8.965	0.115
1 min after intubation	82.55 ± 10.179	97.14 ± 11.488	0.0001**
3 min after intubation	82.55 ± 11.828	83.76 ± 11.044	0.689
6 min after intubation	80.17 ± 10.043	79.21 ± 8.015	0.901
9 min after intubation	80.03 ± 8.415	77.48 ± 9.144	0.274
12 min after intubation	77.69 ± 9.831	77.48 ± 10.812	0.870
15 min after intubation	77.59 ± 10.894	76.52 ± 9.583	0.697

Table 5: Comparative mean arterial p	pressure between two groups
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Time	Mean Arterial Pressure (mmHg)		P value	
	Group A	Group B (Normal saline)		
	(Dexmedetomidine)	(Normal Same)		
Before intubation	97.11 ± 11.064	96.09 ± 11.960	0.737	
1 min after intubation	86.59 ± 10.844	96.84 ± 12.327	0.006*	
3 min after intubation	84.63 ± 9.263	90.06 ± 10.861	0.045*	
6 min after intubation	83.55 ± 9.225	86.56 ± 11.195	0.509	
9 min after intubation	84.31 ± 8.477	83.95 ± 10.751	0.889	
12 min after intubation	83.97 ± 7.922	85.28 ± 8.780	0.577	
15 min after intubation	83.87 ± 9.621	83.87 ± 8.506	1.000	
P value significant at the 0.05 level: *significant P-value				

P value significant at the 0.05 level; \*significant P-value

cells, basophils, and platelets, alongside serotonin released by mast cells and platelets, and prostaglandins due to tissue damage.

respiratory mucosa. The noteworthy decrease in the occurrence and intensity of POST within the

A subset of these agents (like bradvkinin. protons. prostaglandin E2, purines, directly and cytokines) stimulate nociceptors or trigger sensitization of nociceptors to pain stimuli. Conversely, others (such as serotonin. histamine. arachidonic acid metabolites, cytokines) activate and inflammatory cells, leading to the release of cytokines that induce sensitization pain.<sup>17-20</sup> and

Dexmedetomidine diminishes levels of intraoperative catecholamines and notably curtails inflammatory responses, leading to lowered serum concentrations of inflammatory mediators like TNF- $\alpha$ , IL-6, and S100 $\beta$ . Other investigations have also demonstrated that dexmedetomidine reduces IL-1. IL-6. IL-10. TNF-α. and CRP levels in patients undergoing intestinal surgery. This decline in inflammatory substances might play a role in

pain prevention, particularly in the transduction process occurring at the periphery. nebulized The dexmedetomidine circulates systemically, influencing both the central nervous system and the course of pain. Dexmedetomidine's peripheral analgesic effect thwarts the sensitization of Aδ and C-type fibers, coupled with its central analgesic impact and the depolarization of descending noradrenergic pathways in the spinal cord toward the presynaptic

Following nebulization, drug deposition takes place within the nasal, buccal, and

membrane.7,9,16

dexmedetomidine group can be attributed to the considerable reduction in inflammatory mediators due to preoperative administration of nebulized dexmedetomidine, coupled with its analgesic properties.<sup>7,9,16</sup>

Animal studies have consistently indicated that the local application of dexmedetomidine leads to the dilation of tracheal smooth muscle and the inhibition of cough response. This is due to the positive impact of dexmedetomidine on bronchial dilation through relaxation of smooth muscles, facilitated by its direct influence on peripheral alpha-2 adrenoceptors.<sup>9,10,21</sup>

No adverse effects were identified in this investigation, including sedation, bradycardia, or hypotension, as well as nausea, bradypnea, hallucinations, or an unpleasant taste. This outcome is supported by prior studies involving nebulized dexmedetomidine administration. underscores the safetv This of nebulized dexmedetomidine administration, which exhibits favorable absorption and fewer cardiovascular side effects. As such, nebulized dexmedetomidine holds promise as a novel and secure approach for perioperative administration.7,22,23

The findings of this study revealed significant discrepancies in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) within the first minute after intubation, and mean arterial pressure (MAP) in the initial and third minutes post-intubation. These differences underscored an enhanced state of hemodynamic stability in the group receiving treatment. These results mirror prior investigations that explored the influence of nebulized dexmedetomidine on promoting improved hemodynamics compared to control groups. In our study, the control group exhibited an elevation in SBP, DBP, MAP, and HR at the 1st, 5th, and 10th minutes after intubation, exhibiting a P < 0.005across all assessment intervals. In a similar vein, another study documented that the administration of nebulized dexmedetomidine at a dosage of 1 µg/kg restrained the rise in HR during the initial 5 min following intubation. This effect can be attributed to dexmedetomidine's interaction with diverse  $\alpha 2$  receptors, including  $\alpha 2B$ receptors which impact vascular smooth muscle. The observed hemodynamic stability in the treated group post-intubation is likely a result of the diminished release of catecholamines and the mitigation of pain signals initiated during laryngoscopy and intubation.9,19,24,25

### **5. LIMITATION**

Our study had several limitations. The dosages of both drugs were fixed and not adjusted based on individual factors. We were unable to measure the serum levels of the administered drugs, and our follow-up analysis only extended up to 24 h. Inflammatory mediator levels were not assessed in either group. The total amount of analgesic and anesthetic agents used during surgery was not recorded. Moreover, data on overall patient satisfaction and the length of hospital stays were not collected.

# 6. CONCLUSION

The preoperative application of nebulized dexmedetomidine effectively reduces postoperative sore throat (POST) and cough, accompanied by fewer disturbances in hemodynamics. Consequently, nebulized dexmedetomidine may be considered for a safe and routine use for decreasing postoperative sore throat.

### 7. Data availability

The numerical data generated during this research is available with the authors.

### 8. Conflict of interests

There are no conflicts of interest concerning research, authorship, and/or publication of this article

### 9. Ethical considerations

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics committee of Hasan Sadikin Hospital. Informed consent was obtained from all individual participants included in the study.

#### **10. Funding**

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors concerning research, authorship, and/or publication of this article

### 11. Authors' contribution

<sup>®</sup>All authors contributed equally to this work, as well as data analysis, literature search and manuscript preparation. All authors have read this manuscript and approve for publishing.

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