Drug Design, Development and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CLINICAL TRIAL REPORT

Comparison of Preoperative Topical Magnesium Sulfate Spraying and Magnesium Sulfate Gargling for the Prevention of Postoperative Sore Throat after Tracheal Intubation: A Randomized, Double-Blind, Non-Inferiority Trial

Linxin Wang, Yuqing Liu, Fangfang Li, Qin Qiu, Xingyu Xiong, Guanglei Wang

Department of Anesthesiology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu, People's Republic of China

Correspondence: Guanglei Wang, Department of Anesthesiology, The Affiliated Hospital of Xuzhou Medical University, 99 huaihai Road West, Quanshan District, Xuzhou, Jiangsu, 221006, People's Republic of China, Tel +86 13852087156, Email 13852087156@163.com

Background and Aim: Postoperative sore throat is a common complication following endotracheal intubation, which can significantly affect patient comfort and recovery. The purpose of this study is that compares the efficacy of preoperative topical magnesium sulfate spraying with that of magnesium sulfate gargling aimed at preventing postoperative sore throat.

Patients and Methods: 236 Participants were randomly allocated to either the magnesium sulfate spray group (Group A) or the magnesium sulfate gargle group (Group B), with 118 patients in each group. In Group A, during intubation under direct laryngoscopy, 15 mg/kg of magnesium sulfate was sprayed using a single-use otorhinolaryngology anesthesia sprayer onto the pharyngeal mucosa and posterior pharyngeal wall near the glottis. In Group B, gargling with 20 mg/kg of magnesium sulfate for 30 seconds 15 minutes before surgery. The primary outcome measure was the total incidence of postoperative sore throat within 48 hours, with a non-inferiority margin of 0.15.

Results: The upper limit of the 95% confidence interval (CI) for the difference in the total incidence of POST between Group A and Group B was below the non-inferiority margin (0.15) (non-inferiority $P<0.001$). The upper limits of the 95% CI for the differences in the incidence rates of POST between Group A and Group B at time points T1- T6 were all below the non-inferiority margin (all non-inferiority $P<0.001$). The total incidence of POST ($P=0.046$) and the incidence of POST at T2-T4 (all $P<0.001$) in group A were lower than those in group B. The analysis of the individual effects between groups indicated significant differences in POST NRS scores at T1 ($P=0.034$) and T2-T4 (all $P<0.001$).

Conclusion: The local spray of magnesium sulfate on the throat before surgery to prevent postoperative sore throat is not inferior to, and may even be superior to, gargling with magnesium sulfate.

Keywords: postoperative sore throat, magnesium sulfate, endotracheal intubation, general anaesthesia

Introduction

Postoperative sore throat (POST) is a prevalent postoperative complication associated with general anesthesia, primarily associated with the placement of endotracheal tubes or supraglottic airway devices. Although POST is self-limiting, it can persist for 12 to 24 hours, causing significant postoperative swallowing discomfort that adversely affects feeding, thereby impeding recovery and diminishing patient satisfaction with the surgery.[1,2] The overall incidence of POST in the adult varies between 14.4% and 65%.[3,4]

Gynecological surgeries are often performed in the Trendelenburg position (a medical posture where the patient's head is lower than the abdomen and the feet are higher than the head), which facilitates exposure of the surgical field and aids in surgical manipulation. Prolonged use of the Trendelenburg position can lead to facial, conjunctival, laryngeal, and tongue

Received: 21 October 2024
Accepted: 28 February 2025
Published: 11 March 2025

swelling, increasing the likelihood of postoperative upper airway obstruction. Patients undergoing surgery in the Trendelenburg position for an extended duration may experience tracheal and pharyngeal mucosal edema, as well as Acidotic-shifted saliva, which increases the risk of POST.[5–8] Literature reports suggest that female sex is a pertinent risk factor for POST, as women generally have narrower tracheas and softer tracheal mucosa, making them more susceptible to POST.[9]

Anesthesia practitioners typically select appropriate endotracheal tubes, cuff pressures, insertion techniques, and angles, or utilize methods such as preheating the tube, acupuncture, visualized endotracheal intubation, and the application of medicines to reduce the incidence of POST.[10–17] Among these, the application of medications is relatively common and convenient, mainly including NSAIDs, local analgesics, corticosteroids, N-methyl-D-aspartate (NMDA) receptor antagonists, and opioid medications.[18–21]

Magnesium sulfate, which acts as an NMDA receptor antagonist, is currently recognized as one of the most effective agents for the prevention and management of POST.[22,23] The underlying mechanism includes the stimulating peripheral NMDA receptors, which can result in discomfort in the masticatory muscles, skin, and deeper tissues. Magnesium exerts its analgesic properties primarily by first preventing the activation of NMDA glutamate receptors through the inhibition of calcium entry into cells. The magnesium within the magnesium sulfate solution readily ionizes, enabling local absorption and use by the adjacent tissues. Since NMDA receptors exist both in the central and peripheral nervous systems, local application of magnesium can mitigate nociceptive stimuli caused by mucosal inflammation triggered by endotracheal intubation. Magnesium sulfate also exhibits astringent, anti-inflammatory, and anti-edema properties for traumatic edema and inflammation.[24–29] Conventional magnesium sulfate gargling has some shortcomings, such as bitter taste, inconvenient application, and low patient cooperation. To date, no studies have reported on the application of topical spray with magnesium sulfate in the throat. This research aims to perform a trial comparing the effects of a local throat spray with magnesium sulfate to magnesium sulfate mouthwash for the prevention of postoperative sore throat, with the hope of providing references for clinical medication practices.

Materials and Methods

Participants

This study is a prospective, single-center, randomized, double-blind controlled clinical trial, approved by the Medical Ethics Committee of Xuzhou Medical University Affiliated Hospital (XYFY2024-KL339-01) and registered with the Chinese Clinical Trial Registry (ChiCTR2400088661). This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline for randomized clinical trials and the CONSORT checklist is shown in Appendix 1. All participants provided written informed consent before enrollment. This clinical trial was conducted from July 2024 to November 2024.Inclusion criteria: (1) Patients scheduled for elective gynecological surgery; (2) ASA classification I–II; (3) Aged 18 to 64 years; (4) BMI 18–30 kg/m². Exclusion criteria: (1) Preoperative oral ulcers, sore throat, pharyngeal mucosal injury, or pharyngitis; (2) Preoperative nausea, vomiting, cough, or dysphagia; (3) History of pharyngeal surgery; (4) Mallampati classification ≥ II; (5) Preoperative hypermagnesemia or allergy to magnesium; (6) Recent respiratory system infectious diseases; (7) Preoperative hypoalbuminemia; (8) History of smoking; (9) Preoperative nasogastric tube placement; (10) Patients undergoing chronic treatment with calcium channel blockers or magnesium; (11) Contraindications to magnesium sulfate: acute gastrointestinal bleeding, acute abdomen, pregnancy, breastfeeding. Exclusion criteria during the study: (1) Cancellation of surgery; (2) Re-intubation postoperatively; (3) Repeated intubation two times or more; (4) Duration of intubation < 1 hour or > 5 hours; (5) Patients admitted to the ICU postoperatively.

Randomization and Masking

Subjects were randomly divided into two groups: the magnesium sulfate spray group (Group A) and the magnesium sulfate gargle group (Group B), using a random number table for allocation. The randomization process was performed by personnel not involved in this study, and the results of group allocation were securely enclosed in opaque envelopes. Upon entering the operating room, a nurse anesthetist unsealed the envelope and prepared the respective medications based on the group allocation. The prepared medications were sealed in identical syringes without any identifying labels. The drug intervention and endotracheal intubation were performed by the same senior anesthesiologist. Intraoperative metrics were documented, and postoperative follow-up was performed by another anesthesiologist, who remained blind to the group allocations. Patients were also kept

unaware of their group assignments. Data analysis of the trial outcomes was performed by a statistician who was not informed of the group allocations.

Intervention

Patients were routinely instructed to refrain from eating and drinking. Upon entering the operating room, basic anesthesia tests such as oxygenation, ventilation, circulation, and temperature were performed.[30] An intravenous access was established in the upper limb, and anesthesia depth was monitored using an AI anesthesia depth monitor, while neuromuscular blockade was assessed using a train-of-four (TOF) monitor. Anesthesia induction involved Preoxygenation was performed for 5 minutes, followed by administration of midazolam (0.05 mg/kg), etomidate (0.3 mg/kg), sufentanil (0.5 μg/kg), and rocuronium (0.6 mg/kg) prior to endotracheal intubation. And all patients in this study used a size 6.5 tracheal tube. In Group A, patients gargled with 30 mL of placebo for 30 seconds 15 minutes before intubation; during intubation, 25% magnesium sulfate (15 mg/kg) was sprayed onto the mucosa of the oropharynx and the posterior pharyngeal wall using a single-use ear, nose, and throat anesthesia spray device (hereafter referred to as the throat spray) under direct visualization with a laryngoscope (administration should be completed within 10 seconds before intubation). In Group B, patients gargled with magnesium sulfate (20 mg/kg dissolved in saline to a total volume of 30 mL) for 30 seconds 15 minutes prior to intubation; during intubation, a placebo was sprayed onto the mucosa of the oropharynx and the posterior pharyngeal wall using the throat spray under direct visualization with a laryngoscope. The pressure of the endotracheal tube cuff was kept within the range of 20 to 26 cmH_2O. Anesthesia maintenance involved administering propofol at a rate of 4–12 mg/kg/h and remifentanil at 0.2–0.3 μg/kg/min, while sevoflurane was maintained at 1.3 MAC. The dosage was adjusted to maintain the AI value between 40 and 60, and blood pressure and heart rate were maintained within ±20% of their baseline values. Additional rocuronium was administered based on neuromuscular monitoring results to maintain a TOF ratio of 0. Mechanical ventilation was implemented utilizing volume-controlled modes, characterized by a tidal volume of 6 to 8 mL/kg, an inspiratory-to-expiratory (I:E) ratio of 1:1.5, an inspired oxygen fraction (FiO_2) of 60%, and an oxygen flow rate of 2 L/min, with the respiratory rate adjusted to maintain $P_{ET}CO_2$ levels between 35 and 45 mmHg. Twenty minutes prior to the conclusion of the procedure, administration of sevoflurane was ceased, and a dose of 50 mg of flurbiprofen was given. At the conclusion of surgery, propofol and remifentanil were stopped, and after reaching the extubation criteria, the endotracheal tube was removed. Upon entry into the Post-Anesthesia Care Unit (PACU), patients received supplemental oxygen via face mask and were transferred back to the ward once they fulfilled the discharge criteria from the PACU.

Outcomes

The main outcome measure is the total occurrence of POST within 48 hours. The secondary outcome measures include the incidence and severity of POST at extubation (T1), 2 hours postoperatively (T2), 6 hours (T3), 12 hours (T4), 24 hours (T5), and 48 hours (T6), throat pain scores at T1-T6. The severity was assessed using the Numeric Rating Scale (NRS)[25] [ranging from 0 (no pain) to 10 (worst pain)], and the score for postoperative sore throat generally does not exceed 3. Therefore, we subdivided the scores according to the characteristics of postoperative sore throat: 0=none, 1= slight pain when swallowing but does not affect eating and drinking, 2= pain when swallowing significantly affects eating and drinking, 3= pain can still be felt without swallowing.[31] Other secondary outcome measures included the incidence of coughing at extubation; the occurrence of nausea and vomiting after surgery; the occurrence of dysphagia after surgery; the occurrence of hoarseness at T1-T6; and the scores on the 15-item Quality of Recovery Scale (QoR-15)[32] at 48 hours postoperatively.

Statistical Analysis

Sample size was calculated using PASS 15. And sample size estimations were performed using preliminary experiment and pertinent literature. The incidence of magnesium sulfate spray group was 40%, the incidence of magnesium sulfate gargle group was 44% in the preliminary experiment. For the non-inferiority analysis between the spray group and the gargle group, the non-inferiority margin was set at 15%[18,33] (Combined with previous studies, the fixed boundary value method was used for calculation), with an actual difference of −4% (Incidence in the magnesium sulfate spray group minus incidence in the magnesium sulfate gargle group). The significance threshold (α) was established at 0.025, with a power (1-β) of 80%. Taking into account a 10% dropout rate, the determined sample size was 118 participants per group, leading to a total of 236 participants (n=236).

Statistical analysis was conducted using SPSS version 26.0 and R version 4.4.1. For quantitative continuous data, the distribution's normality was evaluated with the Kolmogorov–Smirnov test, while Levene's test was used to assess the homogeneity of variances. Continuous variables exhibiting a normal distribution are presented as mean ± standard deviation; group comparisons were performed using the independent samples *t*-test; repeated measures ANOVA was used to compare groups at different time points within the same group. Continuous data not following normal distribution were presented as median (M) and interquartile range (IQR); the generalized estimating equations (GEE) were used to first assess the interaction between group and time. If significant, differences between treatments and within treatments at each time point were examined, with Bonferroni correction applied for multiple comparisons. If not significant, only the main effect of treatment was assessed without Bonferroni correction for evaluating treatment effects at each time point. Categorical variables were represented as percentages (%) and analyzed with either the chi-squared test or Fisher's exact test. The non-inferiority test for the primary outcome was conducted by comparing the 95% confidence interval (CI) for the difference in incidence rates between the two groups to the pre-defined non-inferiority margin. A p-value of less than 0.025 compared to the non-inferiority margin was considered statistically significant.

Results

Among 289 patients, a total of 236 participants who fulfilled the inclusion criteria and consented to take part in this study were recruited between July 2024 and November 2024 (Figure 1). All 236 patients completed the study; therefore, no patients were excluded from the statistical analysis. There were no statistical differences in the characteristics and clinical information of the patients among the groups (Table 1).

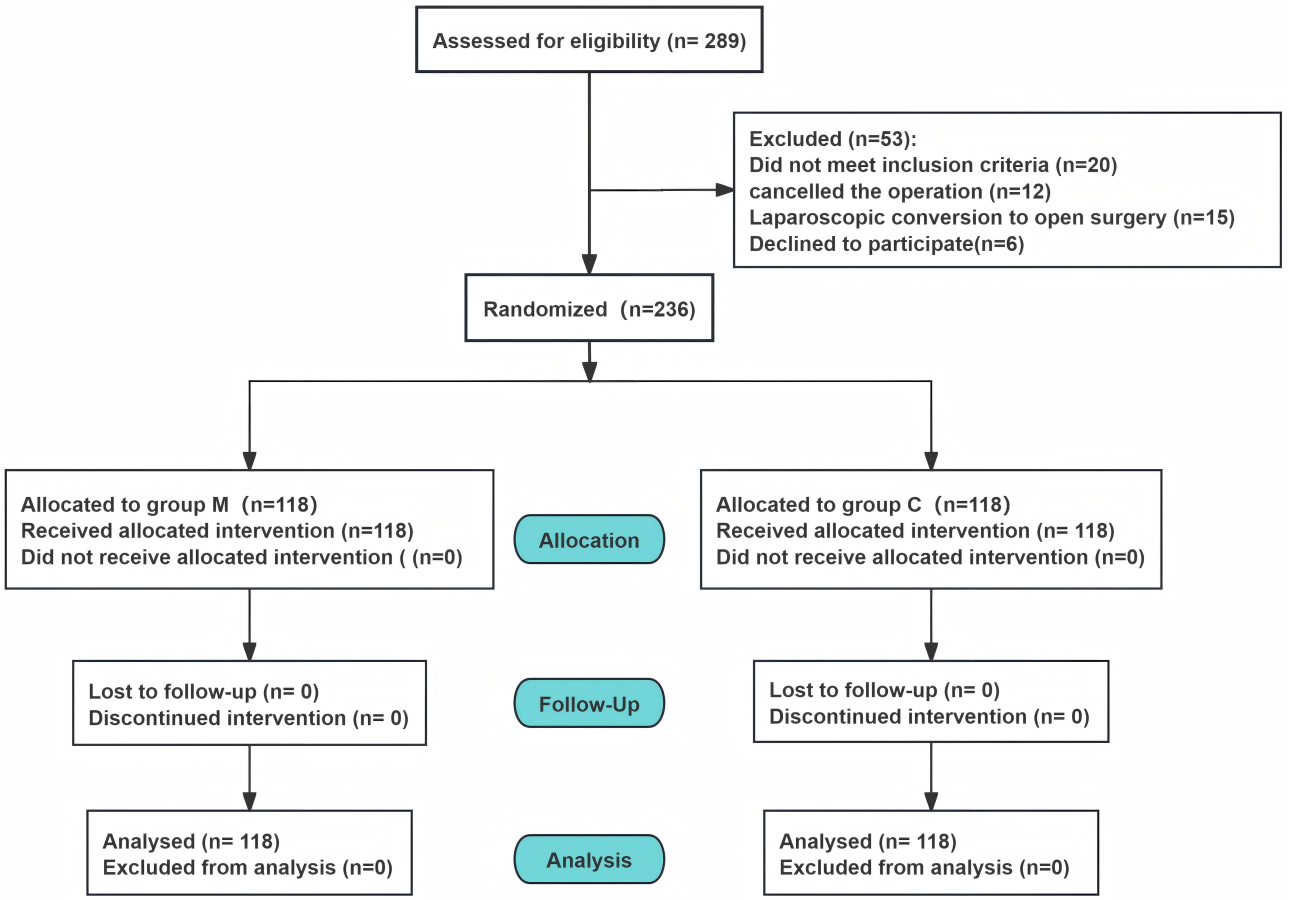

Figure 1 Study flow diagram.

Table 1 Cohort Characteristics

Variables	Group A (n=118)	Group B (n=118)	*P*
Age (years)	43(32,51)	45(36,45)	0.274
Height (cm)	1.61(1.58,1.65)	1.60(1.58,1.65)	0.628
Weight (kg)	62(56,70)	60(55,65)	0.268
BMI (kg/m^2)	23.93±3.12	23.71±3.30	0.602
Duration of tracheal intubation (min)	125(100,158)	119(105,140)	0.330
Preoperative serum albumin levels (g/dl)	46.15(43.63,48.40)	45.60(43.78,47.70)	0.270
Preoperative serum magnesium level (mmol/L)	0.81(0.77,0.85)	0.82(0.79,0.86)	0.448
Postoperative serum magnesium ion level (mmol/L)	0.80(0.75,0.82)	0.79(0.73,0.81)	0.849
The variation in serum magnesium ion levels before and after the surgical procedure (mmol/L)	−0.02(−0.05,0.00)	−0.03(−0.04,-0.02)	0.075
Intraoperative fluid volume infusion (mL)	1000(1000,1250)	1250(1000,1750)	0.077
Intraoperative urine volume (mL)	100(75,100)	100(75,150)	0.076
Remifentanil (mg)	1.75(1.5,2.10)	1.88(1.73,2.14)	0.051
Atropine (mg)	0(0,0)	0(0,0)	0.101
Postoperative rescue flurbiprofen ester (mg)	0(0,0)	0(0,0)	0.680
Indomethacin suppository (mg)	0(0,0)	0(0,0)	0.326
Cuff pressure (mmHg)			
5 min after intubation	24(22,24)	24(22,24)	0.167
30 min after intubation	24(24,24)	24(22,24)	0.108
1h after intubation	24(24,24)	24(22,24)	0.066
90 min after intubation	24(24,24)	24(22,24)	0.100
Surgery type			0.929
Laparoscopic Hysterectomy	27(22.9%)	31(26.3)	
Laparoscopic Myomectomy	38(32.2%)	38(32.2%)	
Laparoscopic Ovarian-cystectomy	31(26.3%)	28(23.7%)	
Laparoscopic Adnexectomy	22(18.6%)	21(17.8%)	

Notes: Values are shown as percentages, mean ± standard deviation, or median (interquartile range).
Abbreviation: BMI, body mass index.

Comparison of POST Between the Two Groups

The 95% confidence interval (CI) for the difference in overall POST incidence rates between Group A and Group B was (−0.251 to −0.003), with the upper limit of the rate difference 95% CI being below the non-inferiority margin (0.15) (non-inferiority $P<0.001$). The upper limits of the 95% CI for the differences in the incidence rates of POST between Group A and Group B at time points T1 (95% CI −0.239 to 0.002), T2 (95% CI −0.329 to −0.111), T3 (95% CI −0.313 to −0.110), T4 (95% CI −0.288 to −0.101), T5 (95% CI −0.118 to 0.017), and T6 (95% CI −0.051 to 0.051) were all below the non-inferiority margin (0.15) (all non-inferiority $P<0.001$). In summary, it can be considered that the effect of magnesium sulfate spray is not inferior to that of magnesium sulfate gargle. Furthermore, the upper limits of the 95% CI for the overall incidence rates of POST and the

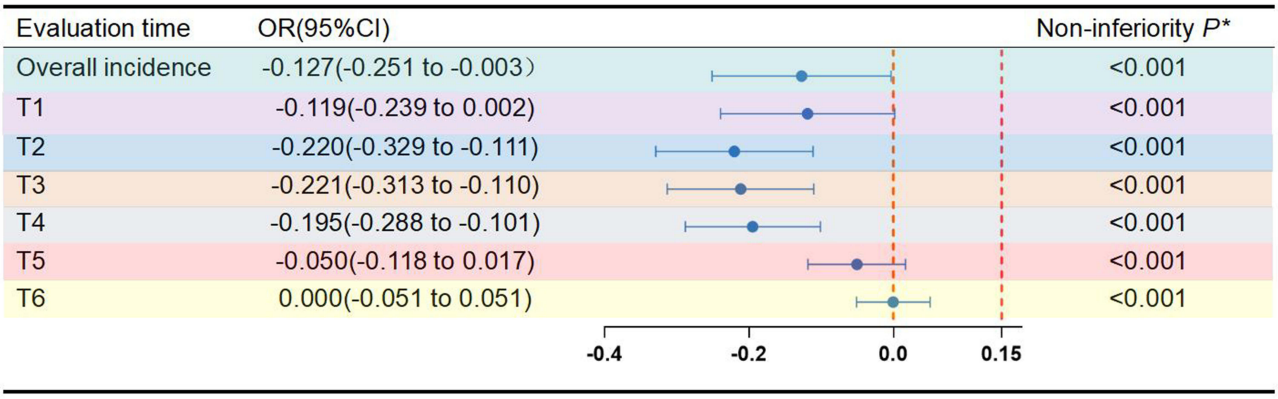

Figure 2 Difference in the incidence of postoperative sore throat. *The upper limit of the 95% confidence interval (CI) for the difference in the total incidence of POST between Group A and Group B was below the non-inferiority margin (0.15), non-inferiority P<0.05.
Notes: T1=0 h postoperatively, T2=2 h postoperatively, T3=6 h postoperatively, T4=12 h postoperatively, T5=24 h postoperatively, T6=48 h postoperatively.

differences in POST incidence rates at time points T2, T3, and T4 between Group A and Group B were all below the superiority margin (0), suggesting that the effect of magnesium sulfate spray is superior to that of magnesium sulfate gargle (Figure 2).

The overall occurrence rate of POST in Group A was lower than that observed in Group B (33.9% vs 46.6%, *P*=0.046). At time points T2 (15.3% vs 37.3%), T3 (11.0% vs 32.2%), and T4 (7.6% vs 27.6%), the incidence rates of POST in Group A were consistently lower than those observed in Group B at each of these time points (all *P*<0.001). No statistically significant differences were observed in the incidence rates of POST between the two groups at time points T1 (28.8% vs 40.7%, *P*=0.056), T5 (5.1% vs 10.2%, *P*= 0.141), and T6 (4.2% vs 4.2%, *P*=1.000) (Table 2).

Table 2 Incidence and Severity of Postoperative Sore Throat

Variables	Group A (n=118)	Group B (n=118)	χ^2/Z	*P*
Incidence of POST				
Overall incidence	40(33.9%)	55(46.6%)	3.964	0.046*
0 h postoperatively(T1)	34(28.8%)	48(40.7%)	3.663	0.056
2 h postoperatively(T2)	18(15.3%)	44(37.3%)	14.788	<0.001*
6 h postoperatively(T3)	13(11.0%)	38(32.2%)	15.633	<0.001*
12 h postoperatively(T4)	9(7.6%)	32(27.6%)	15.615	<0.001*
24 h postoperatively(T5)	6(5.1%)	12(10.2%)	2.165	0.141
48 h postoperatively(T6)	5(4.2%)	5(4.2%)	0.000	1.000
NRS of POST**				
0 h postoperatively(T1)	$0(0,1)^{b}$	$0(0,1)^{efg}$	−2.123	0.034*
2 h postoperatively(T2)	$0(0,0)^{a}$	$0(0,1)^{fg}$	−3.937	<0.001*
6 h postoperatively(T3)	$0(0,0)^{a}$	$0(0,1)^{cg}$	−3.970	<0.001*
12 h postoperatively(T4)	$0(0,0)^{ab}$	$0(0,1)^{cdg}$	−4.013	<0.001*
24 h postoperatively(T5)	$0(0,0)^{ab}$	$0(0,0)^{cdef}$	−1.481	0.139
48 h postoperatively(T6)	$0(0,0)^{ab}$	$0(0,0)^{cdef}$	0.000	1.000

Notes: *Compared Group A with Group B, P<0.05. **NRS of sore throat were compared in generalized estimating equations between and within groups (P for group<0.001, P for time<0.001, P for interaction=0.001; Waldχ^2 for groups=14.337, Waldχ^2 for time=81.569, Waldχ^2 for interaction=21.746). [a]In Group A, the comparison with T1, *P*<0.05. [b]In Group A, the comparison with T2, *P*<0.05. [c]In Group B, the comparison with T1, *P*<0.05. [d]In Group B, the comparison with T2, *P*<0.05. [e]In Group B, the comparison with T3, *P*<0.05. [f]In Group B, the comparison with T4, *P*<0.05. [g]In Group B, the comparison with T5, *P*<0.05.

Generalized estimating equations were employed, revealing an interaction between group and time. Therefore, separate effect analyses were conducted. The analysis of the individual effect of time demonstrated a downward trend in the POST NRS scores for both two groups. In Group A, statistically significant differences in POST NRS scores were noted between T1 and T2 (P=0.005), T3 (P=0.002),as well as T4-T6 (all P<0.001); there were also significant differences in POST NRS scores between T2 and T1 (P=0.005), T4 (P=0.027), T5 (P=0.009), and T6 (P=0.016). In Group B, significant differences in POST NRS scores were identified between T1 and T3 (P=0.010), T4 (P=0.001), as well as T5-T6 (all P<0.001); additionally, significant differences in POST NRS scores were found between T2 and T4 (P=0.002), as well as T5-T6 (all P<0.001); significant differences were also found between T3 and T1 (P=0.010), as well as T5-T6 (all P<0.001); there were also significant differences between T4 and T1 (P=0.001), T2 (P=0.002), as well as T5-T6 (all P<0.001), and between T5 and T1-T4 (all P<0.001). The analysis of the individual effects between groups indicated significant differences in POST NRS scores at T1 (P=0.034) and T2-T4 (all P<0.001) (Table 2).

Comparison of Other Conditions Across the Two Groups

The frequency of coughing episodes following extubation did not differ significantly between the two groups (P=0.235). The incidence of postoperative nausea and vomiting was not significantly different between the two groups (P=0.434). No significant difference was observed in the incidence of postoperative dysphagia between the two groups (P=0.098). In Group A, the incidence of postoperative hoarseness at T3 (P=0.037) and T4 (P=0.006) was significantly lower compared to Group B; however, no statistically significant differences in hoarseness incidence were found between the two groups at T1 (P=0.185), T2 (P=0.343), T5 (P=0.762), and T6 (P=0.790). There were no statistically significant differences in the peak airway pressures at 5 minutes post-intubation (P=0.415), 30 minutes post-intubation (P=0.055), 1-hour post-intubation (P=0.179), and 90 minutes post-intubation (P=0.109) between the two groups. The QoR-15 scores at 48 hours after surgery did not reveal a statistically significant difference between the two groups (P=0.052) (Table 3).

Table 3 Other Secondary Outcome Measures

Variables	Group A (n=118)	Group B (n=118)	*p*
Coughing during extubation	0(0,1)	0(0,1)	0.235
Postoperative nausea and vomiting (%)	60(50.8%)	66(55.9%)	0.434
Postoperative dysphagia (%)	5(4.2%)	1(0.8%)	0.098
Postoperative hoarseness (%)			
0 h postoperatively (T1)	91(77.1%)	82(69.5%)	0.185
2 h postoperatively (T2)	72(61.0%)	79(66.9%)	0.343
6 h postoperatively (T3)	56(47.5%)	72(61.0%)*	0.037
12 h postoperatively (T4)	39(33.1%)	60(50.8%)*	0.006
24 h postoperatively (T5)	28(23.7%)	30(25.4%)	0.762
48 h postoperatively (T6)	7(5.9%)	8(6.8%)	0.790
Peak airway pressure (cmH_2O)			
5 min after intubation	14(13,17)	13(14,16)	0.415
30 min after intubation	17(15,21)	16(14,20)	0.055
1h after intubation	21(18,25.25)	17(17,23)	0.179
90 min after intubation	15(13,19)	15(13,17.25)	0.109
The QoR-15 score at 48 hours post-surgery	126(118,137)	131(124,139)	0.052

Notes: Values are shown as percentages, mean ± standard deviation, or median (interquartile range). *Compared Group A with Group B, P < 0.05.

https://doi.org/10.2147/DDDT.S502081

Risk Factors for the Overall Incidence of POST

Univariate logistic analysis revealed that the *P* values for age, preoperative serum magnesium levels, intraoperative remifentanil, and mean cuff pressure were all less than 0.1; thus, these variables were included in the multivariate logistic model. The Hosmer–Lemeshow test showed χ^2=3.352, df=8, p=0.91, indicating a good fit of the model. Both age and mean cuff pressure were recognized as independent risk factors for postoperative sore throat (Table 4).

Comparison of Adverse Reaction Incidence Between Two Groups

No adverse reactions (weakened or absent tendon reflexes, decreased respiratory rate, facial flushing, sweating, dry mouth, diarrhea, allergic reactions) were observed in either group of patients (Table 5).

Table 4 Binary Logistic Regression Analysis to Identify the Total Incidence of Postoperative Sore Throat

Variable	Univariate Analysis		Multivariate Analysis	
	p	OR (95% CI)	*p*	OR (95% CI)
Age (yr)	<0.001	0.955(0.932–0.978)	0.002	0.961(0.937–0.986)
BMI (kg/m^2)	0.675	0.983(0.906–1.066)	NA	NA
Preoperative serum albumin levels (g/dl)	0.343	0.969(0.909–1.034)	NA	NA
Preoperative serum magnesium level (mmol/L)	0.069	0.021(0.000–1.352)	0.146	0.036(0.000–3.186)
Intraoperative fluid volume infusion (mL)	0.613	1.000(1.000–1.001)	NA	NA
Remifentanil (mg)	0.054	0.512(0.258–1.012)	0.190	0.623(0.308–1.263)
Supplementary administration of flurbiprofen axetil postoperatively (mg)	0.812	0.998(0.984–1.012)	NA	NA
Indomethacin (mg)	0.363	0.985(0.955–1.017)	NA	NA
Duration of tracheal intubation (min)	0.442	0.998(0.992–1.004)	NA	NA
Mean cuff pressure (mmHg)	0.003	1.373(1.113–1.694)	0.005	1.363(1.097–1.694)

Note: The multivariable section in the model only used variables with P value in univariable analysis<0.1.
Abbreviation: NA, not applicable.

Table 5 The Incidence of Adverse Reactions in the Two Groups

Adverse Reactions	Group A (n=118)	Group B (n=118)	*p*
Tendon reflexes were reduced or absent	0	0	1.00
Decreased respiratory rate	0	0	1.00
Facial flushing	0	0	1.00
Sweat out	0	0	1.00
Xerostomia	0	0	1.00
Diarrhea	0	0	1.00
Allergic reaction	0	0	1.00

Discussion

Postoperative sore throat is primarily caused by mechanical injury due to the placement and displacement of the endotracheal tube, leading to an aseptic inflammatory process.[34] Currently, the prevention and treatment of POST mainly utilize pharmacological therapies. Magnesium sulfate is an NMDA receptor antagonist that exhibits anti-inflammatory properties. A systematic review indicated that the administration of magnesium was linked to the lowest occurrence of postoperative sore throat, with evidence suggesting that localized magnesium treatment is likely to alleviate postoperative throat pain within the first 24 hours (low-quality evidence).[22]

Currently, the methods for administering magnesium sulfate for the prevention and treatment of POST mainly include intravenous infusion, gargling, and nebulized inhalation, with a significant amount of research focused on magnesium sulfate gargling. However, considering that magnesium sulfate used for gargling primarily targets the oral vestibule and does not fully facilitate contact between magnesium sulfate and the areas of the endotracheal tube and mucosa. This study employed a direct topical spraying method to apply magnesium sulfate to the throat region. We did a study before that showed that preoperative spraying of 25% magnesium sulfate in the throat reduced the overall incidence and severity of POST after surgery.[35] The aim of this study was to compare the effectiveness of topical magnesium sulfate spraying versus gargling in the prevention and treatment of POST. Local drug spraying to the throat is a common preoperative approach for preventing POST, often using devices to aerosolize the medication in the oropharynx, close to the vocal cords.[36–40] Research by Jingyi Niu et al demonstrated that pre-intubation topical spraying of ropivacaine combined with dexmedetomidine primarily targeted the tracheal mucosa and glottic area, significantly reducing the incidence and severity of POST within 24 hours.[37] This study confirms that topical spraying of magnesium sulfate is superior to gargling with magnesium sulfate in the prevention and treatment of POST.

Non-inferiority analysis indicates that topical spraying of magnesium sulfate is not less effective than gargling with magnesium sulfate for the prevention and treatment of POST. It is even the case that the efficacy of topical magnesium sulfate spraying surpasses that of gargling with magnesium sulfate in terms of overall POST incidence as well as the incidence rates at 2 hours, 6 hours, and 12 hours postoperatively. Both groups exhibited a declining trend in POST incidence; however, the decrease in the magnesium sulfate spraying group was steeper compared to the gargling group (Figure 3). The NRS scores at postoperative time points of 0 hours, 2 hours, 6 hours, and 12 hours were lower in the

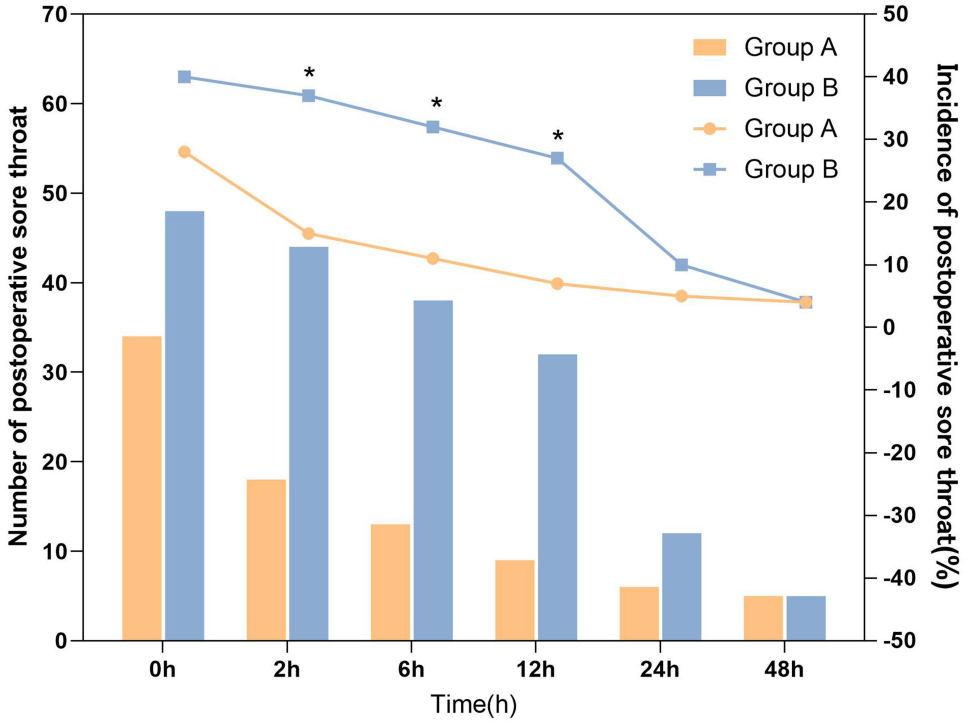

Figure 3 The trend of the number and incidence of postoperative sore throat. *Compared Group A with Group B, $P<0.05$.

https://doi.org/10.2147/DDDT.S502081

magnesium sulfate spraying group than in the gargling group, with a more significant gradient of decline observed within the spraying group. The advantages of topical magnesium sulfate spraying lie not only in reducing the incidence of POST but also in alleviating its severity. Gargling with magnesium sulfate requires a high level of patient compliance, as well as adequate gargling duration and depth. Given that magnesium sulfate has a notably bitter taste, achieving satisfactory gargling by patients presents a challenge. By directly spraying magnesium sulfate onto the patient's throat after anesthesia induction, discomfort from the bitter taste is alleviated, and the application site is more accurately targeted, surpassing the tongue root. The typical dosage for magnesium sulfate gargling is generally 20 mg/kg,[11,26,28,41–43] whereas this study utilized a reduced dosage to 15 mg/kg without compromising efficacy. The mechanism by which local spraying of magnesium sulfate reduces the incidence and severity of postoperative sore throat may include that tracheal intubation may cause mechanical damage to the throat mucosa and activate peripheral NMDA receptors, leading to inflammation and local pain. Magnesium sulfate can antagonize NMDA receptors through local absorption to reduce inflammation and pain. Magnesium sulfate itself has a deswelling effect, which directly and continuously acts on the throat mucosa, thereby antagonizing throat edema caused by trendelenburg position and reducing the incidence of sore throat.[27–29]

The study also demonstrated that the occurrence of hoarseness at 6 and 12 hours postoperatively in the spraying group was significantly less than in the gargling group. A systematic review revealed that magnesium administration is correlated with the lowest occurrence of hoarseness, with a 73.63% probability of being the most effective agent for preventing postoperative hoarseness.[22] Furthermore, no significant difference in intraoperative airway pressure was observed between the two groups. Both application methods of magnesium sulfate did not result in any adverse reactions during and after the procedure. Among the factors included in this study, Age and the average cuff pressure of the endotracheal tube were recognized as independent risk factors. The results indicated that younger age and higher average cuff pressure were associated with an increased likelihood of developing postoperative throat pain.

This study is subject to several limitations. Firstly, it is a single-center randomized controlled trial with a relatively small sample size, which limits the generalizability and external validity of the findings; therefore, further extensive research is necessary. Second, This study is limited to gynecological laparoscopic surgery, and the application effect of this method in other surgeries and groups needs to be further studied.

Conclusion

In conclusion, this study confirms that in gynecological laparoscopic surgery, the preoperative local spraying of magnesium sulfate for the prevention and treatment of POST is not inferior to magnesium sulfate gargling and may even be superior. Additionally, it demonstrates greater effectiveness in reducing the incidence of postoperative hoarseness compared to magnesium sulfate gargling. This implies that magnesium sulfate spraying may be a more novel, convenient and effective form of action for the prevention and control of POST.

Data Sharing Statement

The raw data are available upon reasonable requests to the corresponding author.

Ethics Approval Statement

The Medical Ethics Committee of the Affiliated Hospital of Xuzhou Medical University approved this study protocol (XYFY2024-KL339-01), which was also registered with the Chinese Clinical Trial Registry (ChiCTR2400087240). The trial is being carried out in compliance with the ethical principles of the Declaration of Helsinki.

Acknowledgment

The authors express their gratitude to the Department of Anesthesiology at the Affiliated Hospital of Xuzhou Medical University for their assistance and support.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that there are no conflicts of interest associated with this work.

References

1. Yhim HB, Yoon SH, Jang YE, et al. Effects of benzydamine hydrochloride on postoperative sore throat after extubation in children: a randomized controlled trial. *BMC Anesthesiol*. 2020;20(1):77. doi:10.1186/s12871-020-00995-y
2. Huang WC, Tan EC, Huang SS, et al. Postoperative Sore Throat Helps Predict Swallowing Disturbance on Postoperative Day 30 of Anterior Cervical Spine Surgery: a Secondary Exploratory Analysis of a Randomized Clinical Trial of Tracheal Intubation Modes. *Dysphagia*. 2022;37(1):37–47. doi:10.1007/s00455-021-10247-x
3. Zou S, Guo L, Xu C, et al. Effect of Chewing Gum of Different Weights before Surgery on Sore Throat after Total Thyroidectomy: a Randomized Controlled Trial. *World J Surg*. 2024;48(1):130–137. doi:10.1002/wjs.12025
4. Chen Z, Jin Y, Lu G, et al. Preoperative Ultrasound-Guided Internal Branch Block of Superior Laryngeal Nerve Reduces Postoperative Sore Throat Caused by Double Lumen Endotracheal Intubation: a Randomized Trial. *Anesth Analg*. 2023;137(6):1270–1278. doi:10.1213/ANE.0000000000006534
5. Siktas O, Gulec E, Turktan M, et al. A comparative analysis of elevated endotracheal tube cuff pressure incidence in laparoscopic abdominal surgery: saline versus air inflation. *Minerva Anestesiol*. 2024;90(9):739–747. doi:10.23736/S0375-9393.24.18078-9
6. Geng G, Hu J, Huang S. The effect of endotracheal tube cuff pressure change during gynecological laparoscopic surgery on postoperative sore throat: a control study. *J Clin Monit Comput*. 2015;29(1):141–144. doi:10.1007/s10877-014-9578-2
7. Yildirim ZB, Uzunkoy A, Cigdem A, et al. Changes in cuff pressure of endotracheal tube during laparoscopic and open abdominal surgery. *Surg Endosc*. 2012;26(2):398–401. doi:10.1007/s00464-011-1886-8
8. Koike M, Abukawa Y, Kaji K, et al. Does salivary pH affect postoperative sore throat in the head-down position of general anesthesia? *J Oral Rehabil*. 2024;51(7):1202–1206. doi:10.1111/joor.13694
9. Murugaiyan A, Sahoo AK, Rao PB, et al. Effect of 5% EMLA Cream on Postoperative Sore Throat in Adults Following General Endotracheal Anesthesia: a Randomized Placebo-Controlled Study. *Anesthesia Analg*. 2023;136(2):338–345. doi:10.1213/ANE.0000000000006269
10. Cui G, Zhao L, Chi C, et al. The feasibility and accuracy of the method for selecting the optimal size of double-lumen tube in thoracic surgery: a prospective, randomized controlled trial. *Sci Rep*. 2024;14(1):17539. doi:10.1038/s41598-024-68349-z
11. Mondal AK, Maiti AK, Chattopadhyay S, et al. A Randomised, Double-Blind, Comparative Study of Preoperative Magnesium Sulphate versus Zinc Sulphate Gargle for Prevention of Postoperative Sore Throat Following Endotracheal Intubation. *Indian J Anaesth*. 2023;67(Suppl 4):S261–S267. doi:10.4103/ija.ija_975_22
12. Bi X, Wen J, Chen Q, Zhang X. Effects of Thermal Softening of Double-Lumen Endobronchial Tubes on the Prevention of Postoperative Sore Throat in Smokers: a Randomized Controlled Trial. *J Cardiothor Vascul Anesthesia*. 2022;36(8 Pt B):3109–3113. doi:10.1053/j.jvca.2022.04.017
13. Wang D, Ma T, Li G, et al. The preventive and therapeutic effects of acupoint electrical stimulation on postoperative sore throat following tracheal intubation under general anesthesia. *Chin Acupunct*. 2017;37(7):701–704.
14. Luo D, Su Y, Pang Y. Effects of ultrasound-guided stellate ganglion block on postoperative sore throat and postoperative sleep disturbance after lumbar spine surgery: a randomized controlled trial. *BMC Anesthesiol*. 2023;23(1):343. doi:10.1186/s12871-023-02301-y
15. Wang C, Yan X, Gao C, et al. Effect of continuous measurement and adjustment of endotracheal tube cuff pressure on postoperative sore throat in patients undergoing gynecological laparoscopic surgery: a randomized controlled trial. *J Clin Monit Comput*. 2024;38(6):1379–1386. doi:10.1007/s10877-024-01173-y
16. Yu JH, Paik HS, Ryu HG, et al. Effects of thermal softening of endotracheal tubes on postoperative sore throat: a randomized double-blinded trial. *Acta Anaesthesiol Scand*. 2021;65(2):213–219. doi:10.1111/aas.13705
17. Dutta A, Sethi N, Choudhary P, et al. The impact of tracheal-tube introducer guided intubation in anticipated non-difficult airway on postoperative sore throat: a randomized controlled trial. *Minerva Anestesiol*. 2020;86(9):913–921. doi:10.23736/S0375-9393.20.14257-3
18. Liang J, Liu J, Qiu Z, et al. Effect of Esketamine Gargle on Postoperative Sore Throat in Patients Undergoing Double-Lumen Endobronchial Intubation: a Randomised Controlled Trial. *Drug Des Devel Ther*. 2023;17:3139–3149. doi:10.2147/DDDT.S430077
19. Ayalew SB, Daniel T, Samuel H, et al. Comparison between intravenous lidocaine and dexamethasone in reducing postoperative sore throat after endotracheal extubation at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia; a prospective cohort study. *BMC Anesthesiol*. 2024;24(1):259. doi:10.1186/s12871-024-02634-2
20. Muderris T, Tezcan G, Sancak M, et al. Oral flurbiprofen spray for postoperative sore throat and hoarseness: a prospective, randomized, double-blind, placebo-controlled study. *Minerva Anestesiol*. 2019;85(1):21–27. doi:10.23736/S0375-9393.18.12703-9
21. Hintong T, Chongvisal S, Pipanmekaporn T, et al. A Randomized Comparison of Effects of Budesonide Spray and K-Y Gel as an Endotracheal Tube Cuff Lubricant on Incidence of Postoperative Sore Throat. *J Perianesth Nurs*. 2023;38(4):585–589. doi:10.1016/j.jopan.2022.10.003
22. Singh NP, Makkar JK, Cappellani RB, et al. Efficacy of topical agents for prevention of postoperative sore throat after single lumen tracheal intubation: a Bayesian network meta-analysis. *Can J Anaesthesia*. 2020;67(11):1624–1642.
23. Kuriyama A, Maeda H, Sun R. Topical application of magnesium to prevent intubation-related sore throat in adult surgical patients: a systematic review and meta-analysis. *Can J Anaesthesia*. 2019;66(9):1082–1094. doi:10.1007/s12630-019-01396-7
24. Oh TK, Chung SH, Park J, et al. Effects of Perioperative Magnesium Sulfate Administration on Postoperative Chronic Knee Pain in Patients Undergoing Total Knee Arthroplasty: a Retrospective Evaluation. *J Clin Med*. 2019;8(12):2231. doi:10.3390/jcm8122231
25. Bhanwra A, Palta S, Saroa R, Saxena P, Bhanwra S, Jain A. Role of preoperative zinc, magnesium and budesonide gargles in Postoperative Sore Throat (POST) - a randomised control trial. *BMC Anesthesiol*. 2024;24(1):164. doi:10.1186/s12871-024-02534-5

26. Abedzadeh E, Modir H, Pazooki S, Barsari FZ, Almasi-Hashiani A. Comparison of adding magnesium sulfate, dexmedetomidine and ondansetron to lidocaine for gargling before laryngoscopy and endotracheal intubation to prevent sore throat: a randomized clinical trial. *Med Gas Res*. 2024;14 (2):54–60. doi:10.4103/2045-9912.372664
27. Rajan S, Malayil GJ, Varghese R, et al. Comparison of Usefulness of Ketamine and Magnesium Sulfate Nebulizations for Attenuating Postoperative Sore Throat, Hoarseness of Voice, and Cough. *Anesth Essays Res*. 2017;11(2):287–293.
28. Borazan H, Kececioglu A, Okesli S, et al. Oral magnesium lozenge reduces postoperative sore throat: a randomized, prospective, placebo-controlled study. *Anesthesiology*. 2012;117(3):512–518. doi:10.1097/ALN.0b013e3182639d5f
29. Rana V, Ghosh S, Bhatt A, Bisht D, Joshi G, Purohit P. N-Methyl-D-Aspartate (NMDA) Receptor Antagonists and their Pharmacological Implication: a Medicinal Chemistry-oriented Perspective Outline. *Curr Med Chem*. 2024;31(29):4725–4744.
30. Committee on Standards and Practice Parameters (CSPP). Standards for Basic Anesthetic Monitoring. American Society of Anesthesiologists (ASA). Available from: https://www.asahq.org/standards-and-practice-parameters/standards-for-basic-anesthetic-monitoring. Accessed January 16, 2025.
31. Chinese Society of Anesthesiology Task Force on Management of Artificial Intelligent Patient-Controlled Analgesia. Expert consensus on management of artificial intelligent patientcontrolled analgesia. *Chin J Anesthe*. 2018;38(10):1161–1165.
32. Choi JY, Lee HS, Kim JY, et al. Comparison of remimazolam-based and propofol-based total intravenous anesthesia on postoperative quality of recovery: a randomized non-inferiority trial. *J Clin Anesth*. 2022;82:110955. doi:10.1016/j.jclinane.2022.110955
33. Park JH, Shim J-K, Song J-W, Jang J, Kim JH, Kwak Y-L. A Randomized, Double-blind, Non-inferiority Trial of Magnesium Sulphate versus Dexamethasone for Prevention of Postoperative Sore Throat after Lumbar Spinal Surgery in the Prone Position. *Int J Med Sci*. 2015;12 (10):797–804. doi:10.7150/ijms.12831
34. Calabrese M, Arlotta G, Antoniucci ME. Flurbiprofen in the Subglottic Space to Prevent Postoperative Sore Throat after Cardiac Surgery: a Randomized Double-Blind Study. *J Clin Anesth*. 2024;95:111418. doi:10.1016/j.jclinane.2024.111418
35. Wang L, Li F, Liu Y, et al. The effect of preoperative topical magnesium sulfate spraying in the oropharyngeal region on postoperative sore throat following gynecological laparoscopic surgery: a randomized clinical trial. *BMC Anesthesiol*. 2025;25(1):16.
36. Altinsoy S, Ütebey G, Kavak AF, et al. The effects of topical chlorhexidine-benzydamine spray on laryngeal mask airway application. *Minerva Anestesiol*. 2020;86(3):277–285. doi:10.23736/S0375-9393.19.13970-3
37. Niu J, Hu R, Yang N, et al. Effect of Intratracheal Dexmedetomidine Combined with Ropivacaine on Postoperative Sore Throat: a Prospective Randomised Double-Blinded Controlled Trial. *BMC Anesthesiol*. 2022;22(1):144.
38. Fang P, Zong Z, Lu Y, Han X, Liu X. Effect of topical ropivacaine on the response to endotracheal tube during emergence from general anesthesia: a prospective randomized double-blind controlled study. *BMC Anesthesiol*. 2018;18(1):134. doi:10.1186/s12871-018-0601-x
39. Looze F, Shephard A, Smith AB. Locally Delivered Flurbiprofen 8.75 mg for Treatment and Prevention of Sore Throat: a Narrative Review of Clinical Studies. *J Pain Res*. 2019;12:3477–3509. doi:10.2147/JPR.S221706
40. Lin J, Wang WD, Wen YL, et al. Effect of intravenous and topical laryngeal lidocaine on sore throat after extubation: a prospective randomized controlled study. *Eur Rev Med Pharmacal Sci*. 2024;28(6):2493–2500. doi:10.26355/eurrev_202403_35756
41. Teymourian H, Mohajerani SA, Farahbod A, et al. Magnesium and Ketamine Gargle and Postoperative Sore Throat. *Anesthesiol Pain Med*. 2015;5 (3):e22367. doi:10.5812/aapm.5(3)2015.22367
42. Wang M, Chen X, Bai Z, et al. The effect of isotonic magnesium sulfate aerosol inhalation on airway pressure during operation and postoperative sore throat. *J Ningxia Med Univ*. 2013;2013(3):3.
43. Yadav M, Chalumuru N, Gopinath R. Effect of magnesium sulfate nebulization on the incidence of postoperative sore throat. *J Anaesthesiol Clin Pharmacol*. 2016;32(2):168–171. doi:10.4103/0970-9185.173367