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A comparative study of preoperative nebulization of Magnesium sulphate and Ketamine HCL for attenuation of post operative sore throat, hoarseness of voice and cough.

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Abstract

Postoperative sore throat, hoarseness, and coughing are frequent and distressing complications following tracheal intubation. This study aimed to evaluate and compare the efficacy of preoperative nebulization with magnesium sulfate and ketamine hydrochloride in reducing these postoperative symptoms.

Patients and Methods: A prospective, randomized controlled trial was conducted involving 90 patients scheduled for general anesthesia with orotracheal intubation. The participants were divided randomly into three groups of 30 each:

- Group K received nebulization with 50 mg ketamine HCl,
- Group M received 500 mg magnesium sulfate, and
- Group S received 5 ml normal saline.

Postoperative assessments were conducted at 0, 2, 4, 12, and 24 hours to evaluate sore throat, hoarseness, and cough.

Results: Both ketamine and magnesium sulfate significantly reduced postoperative sore throat, hoarseness, and coughing compared to saline ($p < 0.05$). Ketamine demonstrated superior effectiveness in reducing sore throat and cough at 0, 2, and 4 hours compared to magnesium sulfate. Additionally, ketamine was more effective in alleviating hoarseness at 2, 4, and 12 hours ($p < 0.05$). No significant differences were observed in hemodynamic parameters before or after nebulization and intubation, and no adverse effects were reported in any of the groups.

Conclusion: Preoperative nebulization with ketamine HCl and magnesium sulfate effectively reduces postoperative sore throat, hoarseness, and cough, with ketamine showing greater efficacy than magnesium sulfate.

Keywords: Cough, hoarseness of voice, ketamine HCL, magnesium sulphate, nebulization, postoperative sore throat.

INTRODUCTION

Patient satisfaction is a fundamental aspect of perioperative care, and postoperative sore throat (POST) remains one of the most common complaints following general anesthesia with endotracheal intubation. This condition, though often self-limiting, can significantly impact a patient's comfort and overall postoperative experience, making its prevention an important goal in clinical practice. The reported incidence of POST ranges widely, from 14.4% to 62%, depending on various contributing factors. (1,2,3)

Several factors influence the development of POST, including patient age and sex, the diameter of the endotracheal tube, intracuff pressure, suctioning technique, the number of intubation attempts, intraoperative tube manipulation, coughing during emergence, duration of intubation, type of induction agents used, and the experience level of the anesthesiologist. (4,5,6,7) While the exact etiology of POST is not fully understood, it is generally attributed to mechanical trauma resulting in mucosal injury, inflammation, and erosion of the tracheal lining. These injuries may lead to the release of inflammatory mediators, such as mitochondrial DNA, which can activate TLR9-mediated responses via neutrophils and contribute to pain. (1,7,8,9)

Both non-pharmacological and pharmacological strategies have been explored to mitigate the incidence and severity of POST. Non-pharmacological measures include using smaller-sized endotracheal tubes, minimizing the number of laryngoscopy attempts, gentle airway manipulation, maintaining cuff pressure below 25 cm H_2O, and careful suctioning and extubation techniques. [10,11,12]

Pharmacological interventions involve a wide range of agents, such as corticosteroids, local anesthetics, NSAIDs, and NMDA receptor antagonists, administered via various routes—lubricants applied to the ETT, sprays, nebulization, gargles, lozenges, and intravenous preparations.[13-26] Among these methods, nebulization is considered particularly advantageous due to its ease of administration, uniform drug distribution over the mucosal surfaces, minimal invasiveness, high patient tolerance, and a lower likelihood of systemic side effects.

The NMDA receptor plays a critical role in nociception and inflammatory responses, and it is widely distributed throughout both the central and peripheral nervous systems. Magnesium sulfate and ketamine HCl are both NMDA receptor antagonists known for their antinociceptive and anti-inflammatory properties. [24,25]

Given this background, we aimed to compare the effects of preoperative nebulization with magnesium sulfate versus ketamine HCl on the incidence and severity of postoperative sore throat, cough, and hoarseness in patients undergoing general anesthesia with endotracheal intubation.

MATERIAL AND METHODOLOGY

Following approval from the Institutional Ethics Committee and informed consent from participants, this prospective, randomized, controlled trial was conducted on 90 patients classified as ASA physical status I and II. Participants aged 18 to 90 years undergoing elective surgeries lasting less than three hours under general anesthesia with oral endotracheal intubation were included. Selection criteria included favorable airway anatomy: upper lip bite test grade I or II, thyromental distance >6.5 cm, and adequate neck mobility. Patients were excluded if they had ASA class >II, allergies to study medications, pre-existing sore throat or respiratory infection, were smokers, on chronic medications like NSAIDs or steroids, had difficult intubation (>3 attempts), or were undergoing head, neck, or oral surgeries. Patients with asthma, COPD, other respiratory or neurological conditions were also excluded.

A complete preoperative evaluation was conducted, including blood tests, ECG, chest X-ray, and coagulation profile. Patients fasted for 6–8 hours before surgery and received oral lorazepam 1 mg the night before. Randomization allocated patients into three groups of 30:

- Group K: Nebulized with 50 mg ketamine HCl (1 ml) + 4 ml normal saline
- Group M: Nebulized with 500 mg magnesium sulfate (1 ml) + 4 ml normal saline
- Group S: Nebulized with 5 ml normal saline

Nebulization was administered 15 minutes before anesthesia induction. Baseline vitals (pulse, SBP, DBP, MAP, SpO_2) were recorded pre- and post-nebulization and after intubation.

Upon arrival in the operating room, standard monitors were applied. Patients were preoxygenated for 3 minutes. Induction was done using glycopyrrolate (0.004 mg/kg), fentanyl (2 mcg/kg), and propofol (2 mg/kg), followed by suxamethonium (2 mg/kg) for muscle relaxation. Intubation was performed using a cuffed endotracheal tube of appropriate size with Macintosh blade (size 3 or 4), maintaining cuff pressure between 20–25 cm H_2O using a manometer.

Anesthesia was maintained with oxygen, 50% nitrous oxide, and sevoflurane (1–2%). Muscle relaxation was continued with vecuronium (0.1 mg/kg). Ondansetron (4 mg) was administered before surgery end. Reversal of neuromuscular blockade was done using glycopyrrolate (0.008 mg/kg) and neostigmine (0.05 mg/kg). Extubation was performed after gentle suctioning and recovery of spontaneous breathing.

Patients were then transferred to the recovery room and received humidified oxygen at 5 L/min via face mask. Vital signs were monitored, and sore throat, hoarseness, and cough were assessed at 0, 2, 4, 12, and 24 hours postoperatively using the following grading scales:[25]

Sore Throat:

- Grade 0: No sore throat
- Grade 1: Mild (only on inquiry)
- Grade 2: Moderate (patient reports spontaneously)
- Grade 3: Severe (obvious discomfort)

Cough:

- Grade 0: None
- Grade 1: Mild
- Grade 2: Moderate
- Grade 3: Severe

Hoarseness:

- Grade 0: No hoarseness
- Grade 1: Mild (noticed only upon inquiry)
- Grade 2: Moderate (spontaneous complaint)
- Grade 3: Severe (noticeable change in voice quality)

Side effects such as nausea, vomiting, hallucinations, hemodynamic changes, weakness, and headache were monitored. Rescue analgesia for sore throat (grade 3) was administered as intravenous tramadol HCl (1–2 mg/kg).

Statistical Analysis:
Data were documented using a predesigned format and analyzed using Microsoft Excel and tools from https://www.socscistatistics.com. Quantitative data were expressed as Mean ± SD. Intergroup comparisons were performed using ANOVA, while within-group analysis used the Student's t-test. A p-value of <0.05 was considered statistically significant.

OBSERV ATION AND RESULT:-

In this study, a total of 90 patients scheduled for elective surgeries requiring orotracheal intubation were enrolled. The participants were randomly assigned into three groups, with 30 patients in each group. Nebulization was administered to all patients 15 minutes prior to the induction of anesthesia as follows:

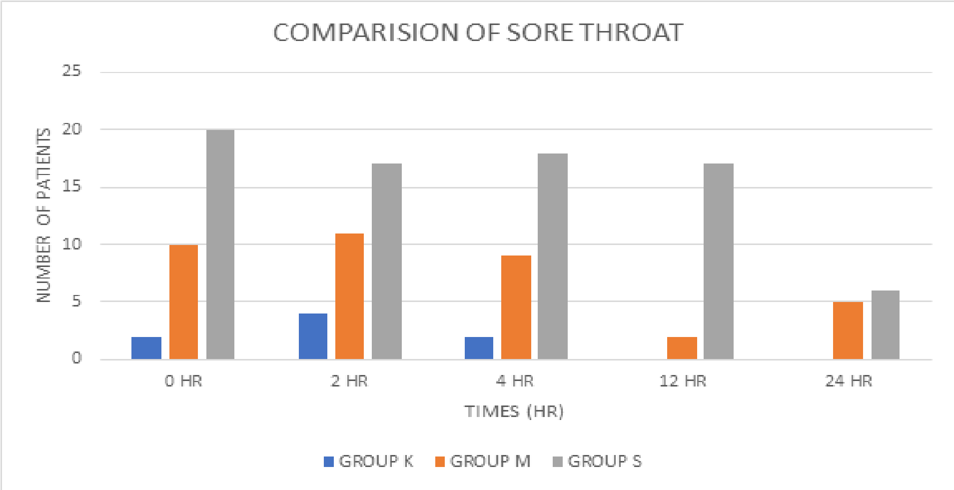
- Group K: Received nebulization with 50 mg ketamine HCl (1 ml) diluted in 4 ml of normal saline.
- Group M: Received nebulization with 500 mg magnesium sulfate (1 ml) mixed with 4 ml of normal saline.
- Group S: Received nebulization with 5 ml of normal saline alone.

Table-1 demographic data

	GROUP K	**GROUP M**	**GROUP S**	**P VALUE**	**SIGNIFICANCE**
Age (YRS)	49.4±10.7	43.4±12.8	44.8±0.5	0.117	NS
Weight (Kgs)	58±7.49	57.8±11.2 0	59.3±11.8	0.84	NS
Duration of Surgery (Min)	165.05±8.4	163.2±13.16	170±13.16	0.15	NS
SEX(M/F)	7/23	8/22	9/21	0.58	NS

The table shows there is no significant difference in all three groups in terms of age, sex, body weight and duration of surgery (p>0.005)

Fig -1



The incidence of sore throat is least in Group K at all time interval as compared to Group M and Group S(p<0.00001)

Table 2: Intergroup comparison of postoperative sore throat between two groups ketamine and magnesium group.

TIME	**GROUP K Mean± SD**	**GROUP M Mean ± SD**	**P VALUE**
O HR	0.1±0.40	0.36±0.55	0.037
2 HR	0.13±0.34	0.43±0.62	0.025
4 HR	0.06±0.25	0.3±0.46	0.01
12 HR	0±0	0.06±0.25	0.15
24 HR	0±0	0±0	1

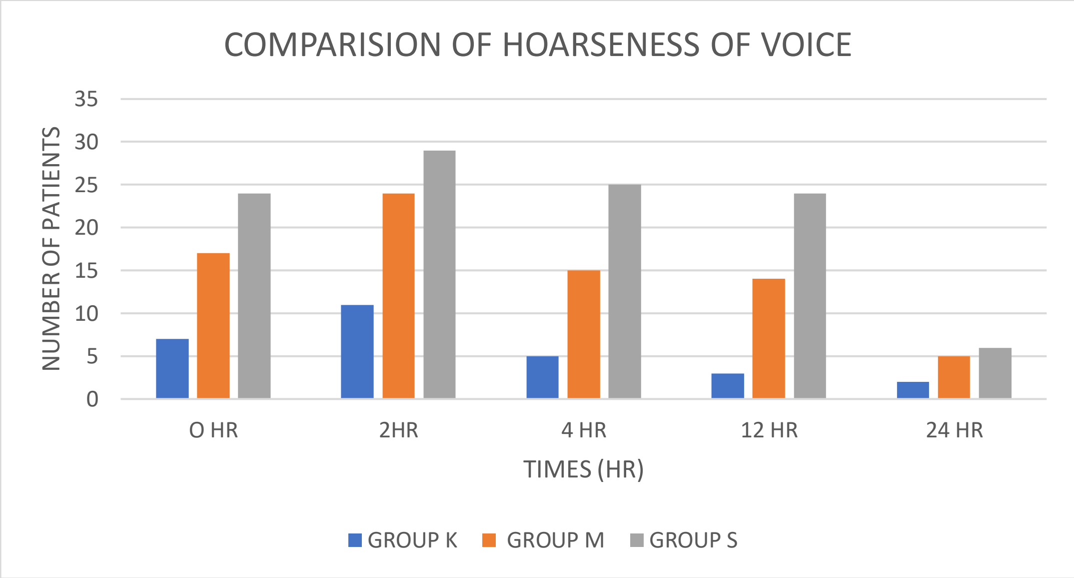
Data shows a statically significant difference in incidence of sore throat between in Group K as compared to M at 0,2,4 hour. At 12 and 24 hours there is no significant difference between Group K and Group M(p>0.05)

Table 3: Comparison of sore throat between three group.

TIME	**GROUP K Mean ± SD**	**GROUP M Mean ± SD**	**GROUP S Mean ± SD**	**P VALUE**
0 HR	0.133±0.433	0.366±0.55	1.13±1.04	0.00001
2 HR	0.13±0.34	0.433±0.62	1±1.08	0.00009
4 HR	0.066±0.23	0.3±0.46	1.066±1.088	0.00002
12 HR	0±0	0.06±0.25	0.733±0.739	0.00001
24 HR	0±0	0±0	0.26±0.52	0.00072

Data shows a statistically significant difference in the incidence of sore throat between Group K, Group M and Group S at all time intervals (p<0.05).

Fig :2



The data shows least incidence of hoarseness in the Ketamine group up to 24 hours in compared to the other two groups.

Table 4: Comparision of hoarseness of voice between two groups ketamine and magnesium group

TIME	**GROUP K**	**GROUP M**	**P VALUE**
0 HR	0.5±0.90	0.83±0.87	0.15
2 HR	0.4±0.56	0.96±0.61	0.0004
4 HR	0.2±0.48	0.5±0.56	0.02
12HR	0.1±0.30	0.46±0.50	0.01
24HR	0.06±0.24	0.16±0.37	0.2

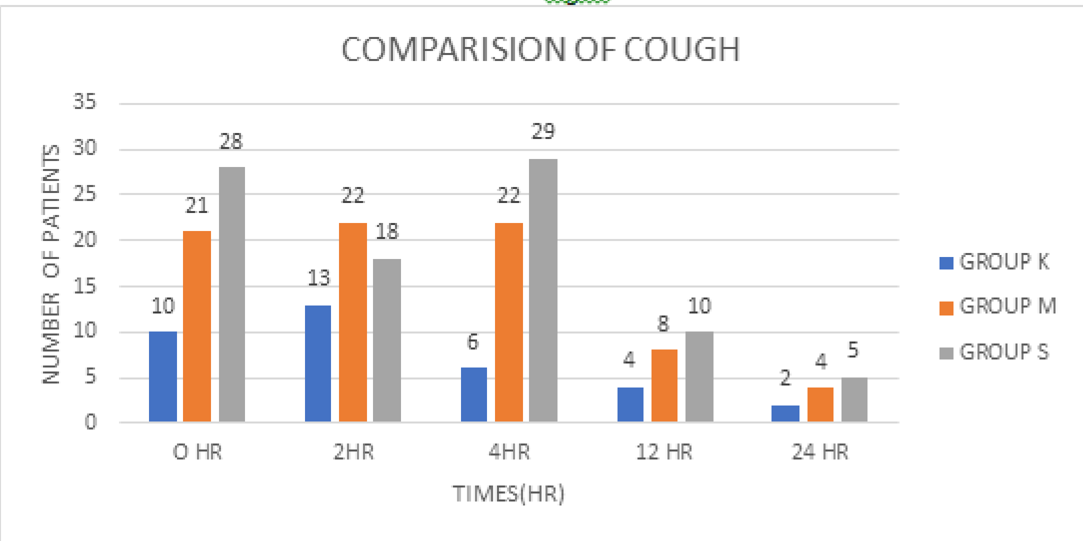
Data shows there is significant decrease in hoarseness in the Ketamine group at 2 and 4 hours compared to the Magnesium group. At 0,12 and 24 hours also reduce hoarseness but statistically insignificant. (p>0.05)

Table 5: Comparison of hoarseness in all three groups.

TIME	**GROUP K Mean ± SD**	**GROUP M Mean ± SD**	**GROUP S Mean ± SD**	**P VALUE**
0 HR	0.5±0.90	0.83±0.87	1.46±0.81	0.0001
2 HR	0.4±0.56	0.96±0.61	1.6±0.80	0.00001
4 HR	0.2±0.48	0.5±0.56	0.83±0.37	0.00001
12 HR	0.1±0.30	0.46±0.50	0.8±0.40	0.00001
24 HR	0.06±0.24	0.16±0.37	0.2±0.40	0.318

The table shows there is a statistically significant decrease in all three groups in the reduction of hoarseness up to 12 hours. (P<0.05) At 24 hours the result is insignificant. (p > 0.318).

Fig.:3



The graph demonstrates a significantly lower incidence of postoperative cough in Group K compared to both Group M and Group S.

Table 6: Comparision of cough between ketamine and magnesium group.

Time	Group K Mean±SD	Group M Mean±SD	P value
0 hr	0.4±0.62	1.03±0.88	0.002
2 HR	0.5±0.62	0.83±0.59	0.03
4 HR	0.2±0.40	0.8±0.40	0.00001
12 HR	0.13±0.34	0.26±0.44	0.20
24 HR	0.06±0.2	0.13±0.34	0.39

There is significant decrease in cough in the Ketamine group as compared to the Magnesium group at 0,2,4 hour($P<0.05$).But there is no significant difference in 12 and 24 hours.

Table 7: Comparision of cough between three group

TIME	Group K Mean ± SD	Group M Mean ± SD	Group S Mean ± SD	P Value
0 HR	0.4±0.62	1.03±0.88	1.7±0.83	0.00001
2 HR	0.5±0.62	0.83±0.59	1.13±0.50	0.00002
4 HR	0.2±0.40	0.8±0.40	0.96±0.18	0.00001
12 HR	0.13±0.34	0.26±0.44	0.33±0.47	0.19
24 HR	0.06±0.2	0.13±0.34	0.16±0.38	0.49

Data shows there is significant decrease in cough in both groups compared to saline at 0, 2, 4 hours.

Table 8: Comparision of hemodynamic parameter

	COMPARISON OF HEART RATE			P VALUE
	PRE NEBULIZATION	**POST NEBULIZATION**	**POST INTUBATION**	
GROUP K	82.2±11.2	82.13±11.62	83.8±11.98	0.82
GROUP M	74.86±9.17	72.3±9.18	76..26±8.53	0.22
GROUP S	81.3±11.78	79.93±11.23	83.06±11.88	0.58
	COMPARISON OF MEAN ARTERIAL PRESSURE			
GROUP K	95.76±7.77	94.41±7.92	92.7±7.98	0.31
GROUP M	94.51±6.34	93.05±6.16	92.36±5.56	0.41
GROUP S	92.16±8.80	91.1±8.69	93.68±8.42	0.51

Table shows that there is no significant difference in hemodynamic parameter in all three groups.
In both Group K and Group M, no patients required administration of rescue medication, whereas in Group S, 12 patients necessitated its use.

DISCUSSION

Postoperative sore throat, cough, and hoarseness of voice vary in incidence and severity among patients. These symptoms are among the most commonly reported complaints following tracheal intubation, though they are generally self-limiting. Non-pharmacological measures tend to offer only limited relief in terms of symptom severity.
Numerous studies have explored a wide range of interventions—including lubricants, sprays, gargles, lozenges, intravenous medications, and nebulization—using various pharmacological agents to minimize NMDA receptors play a significant role in mediating nociception and inflammation in the human body. These receptors are found throughout both the central and peripheral nervous systems. Ketamine HCl and magnesium sulfate possess NMDA receptor antagonistic properties. By acting on receptors in the pharyngeal wall, they exhibit antinociceptive, anti-inflammatory, anti-hyperalgesic, and anti-allodynic effects. Additionally, they help mitigate opioid tolerance through their synergistic interaction with opioids and by blocking postsynaptic NMDA receptors, which reduces central sensitization and the wind-up phenomenon.[24]

In our study, we selected nebulization as the route of administration. Unlike gargles—which have an unpleasant taste, require a larger volume (raising the risk of aspiration), and depend on patient cooperation—nebulization is non-invasive, better tolerated, and does not require active participation. This makes it a more practical and safer choice. B. Aminagad et al. [35] also concluded that ketamine nebulization is an effective alternative to ketamine gargles in reducing the incidence of postoperative sore throat (POST).

All demographic variables—such as age, sex, body weight, ASA physical status, and mean duration of surgery—were comparable across the three groups, with no statistically significant differences. According to a study by N.P. Edomwonayi et al. [3], the incidence of sore throat was 19.8% when intubation lasted less than 60 minutes, compared to 80.2% when it exceeded 60 minutes. Similarly, Srestha et al. [10] found that the incidence of sore throat increased with surgical durations over 120 minutes. Neepa Patel et al. [25] included patients undergoing surgeries shorter than 180 minutes. In our study, only patients undergoing surgeries lasting less than 180 minutes were included.

Endotracheal tube size is also a known factor influencing the incidence of postoperative sore throat and hoarseness. M. Jaensson [11] reported a higher incidence of sore throat with a 7.0 mm tube compared to a 6.0 mm tube (51.1% vs. 27.1%). The use of smaller ETTs was associated with reduced throat discomfort, especially among female patients in the post-anesthesia care unit. In our study, a 7.0 mm ETT was used for female patients and an 8.0 mm ETT for male patients.

Tracheal tube cuff pressure is a known contributing factor to the development of postoperative sore throat (POST). Excessive cuff inflation can compromise the blood supply to the tracheal mucosa, potentially leading to ischemia, ulceration, and even necrosis. Seegobin and Van Hasselt [36] reported that tracheal mucosal blood flow begins to diminish when endotracheal tube cuff (ETTC) pressure exceeds 30 cm H_2O. They further noted that maintaining cuff pressure at

50 cm H_2O for just 15 minutes can result in ischemic injury to the tracheal lining. In a study by Nagappan et al. [12], ETTC pressure was measured and adjusted to 25 cm H_2O, and the incidence of POST, hoarseness, and cough was significantly lower compared to the conventional method of assessing cuff pressure through pilot balloon palpation.In our study we use cuff pressure monitoring (respi cuff) and kept cuff pressure to 20-25cm H_2O. In our study, we used ketamine HCl 50 mg and magnesium sulfate 500 mg diluted in 4 ml of normal saline for nebulization, consistent with the dosing regimen used by Neepa et al. [25].

Sunil Rajan et al [24] used ketamine 50 mg and 2 doses of magnesium sulphate, 225mg and 500mg and concluded that 500 mg magnesium and ketamine 50 mg have better effect. Ketamine 50mg and magnesium sulphate 250 mg dose used by M.O. Orji et al[31], C R Ranjha et al[34], Chandrakala et al[32].

In our study, sore throat incidence was 6.6 %, 3.3%, 6.7%, 0%, 0% in ketamine group, magnesium group it was 33.3%, 36.6%, 30%, 6.7%, 16.6% and in saline group it was 66.6%, 56.6%, 60%, 56.6%, and 20%, at 0, 2, 4, 12 and 24hours respectively. In comparison with ketamine and magnesium group ketamine significantly reduced sore throat at 0, 2, and 4 hours compared to the magnesium group and at 12 and 24 hr ketamine group had no sore throat incidence but not significant compared to the magnesium group Our observations indicated that ketamine was more effective than magnesium sulfate in reducing the incidence of postoperative sore throat. However, both ketamine and magnesium sulfate significantly lowered the occurrence of sore throat compared to the saline group.Study done with nebulization of magnesium sulphate 225mg and ketamine 50mg by Shalini Jain and Swapnil Kumar [28] reported overall incidence of sore throat was 37.3%, 60% in group GS group, 30% in GM, and 22% in GK. Suggestive that GK was least incidence than GM and GS. Both GK and GM incidence of ST was significantly less. Also, M.O. Orji [31]reported a lower incidence of sore throat in the magnesium group (18.2%, 12.1%, 0%, 0%) and the ketamine group (24.2%, 12.1%, 6.1%, 0%) compared to the saline group, which showed higher rates at all time intervals (48.5%, 42.2%, 39.4%, 24.2%). Similarly, Dr. Chandrakala [32] found the overall incidence of sore throat to be 37.5%. In her study, the saline group (GS) had an incidence of 60%, while the magnesium (GM) and ketamine (GK) groups showed significantly lower incidences at 30% and 20%, respectively.

Neepa Patel et al [25] found that incidence of sore throat was significantly less in ketamine group at 0,2 and 4 hours but not significant at 12 and 24 hours than magnesium group.

Essam Ali Mustafa et al [37] found magnesium sulphate significantly reduce sore throat compare to ketamine group. Teymourianetal.[23] studied magnesium sulphate and ketamine gargle in attenuating the incidence of postoperative sore throat. They found ketamine is more effective than magnesium.

In our study, ketamine and magnesium significantly reduced hoarseness of voice at 0, 2, 4 and 12 hr compared to the saline group. (P value < 0.05) At 0 hour and 24hours there is no significant difference between ketamine and magnesium group. Ketamine is best at 2, 4, and 12 hrs for reduction of hoarseness of voice than magnesium. At 24 hours there is no significant difference between the three groups.

Postoperative cough incidence was 33.3%, 70% and 93.3% at 0 hr in the ketamine, magnesium and saline group respectively. At 2 hour 43.3%, 73.3% and 60 % in ketamine, magnesium and saline group respectively. The Incidence of cough was significantly reduced in group K and group M than the saline group at 0, 2, 4 hour, but ketamine is superior to magnesium. In their study, Neepa Patel et al. [25]observed that at the 0-hour mark, the frequency of postoperative cough was notably lower in patients who received ketamine nebulization (30%) compared to those in the magnesium group (70%). A similar pattern was seen at 2 hours, with incidences of 40% in the ketamine group and 74% in the magnesium group. Furthermore, the ketamine group experienced significantly less hoarseness of voice than the magnesium group, with statistical significance ($p < 0.05$).

Ranjana et al. [30] found that hoarseness of voice was consistently lower in patients receiving ketamine, lignocaine, or magnesium compared to those given saline, across all time intervals. Their study also showed a statistically significant reduction in cough in both the ketamine and magnesium groups when compared to saline, with no reports of coughing in any group beyond 8 hours postoperatively. Among the interventions, ketamine was most effective in minimizing postoperative sore throat (POST), followed by magnesium sulfate and then lignocaine. However, lignocaine demonstrated better efficacy in reducing cough than ketamine and magnesium. Similarly, Sunil Rajan et al. [24] observed a reduction in hoarseness in patients treated with ketamine, magnesium 250 mg (Group M1), and magnesium 500 mg (Group M2) at 0, 2, 4, and 12 hours compared to the saline group. A statistically significant improvement in voice quality was noted in Group K and Group M2 at 0 hours. While a decrease in cough was observed in Groups K, M1, and M2 at 0, 2, and 4 hours, it did not reach statistical significance. By 12 and 24 hours, no cough was reported in any of the groups.

Dr. Chandrakala et al. [32] concluded that both ketamine at a dose of 50 mg and magnesium sulfate at 250 mg were effective in reducing postoperative cough when compared to saline. Among the two, ketamine was more effective in lowering the incidence of sore throat and cough. Similarly, Jaya Lalwani et al. [38] demonstrated that using ketamine as a gargle significantly decreased postoperative sore throat, cough, and hoarseness for up to 24 hours when compared to the saline group. In our study, there were no statistically significant changes observed in heart rate or blood pressure at any point—before nebulization, after nebulization, or following intubation ($p > 0.05$). These findings are consistent with those of Neepa et al. [25], who also reported no significant variations in hemodynamic parameters pre- and post-nebulization. Similarly, Shalini Jain et al. [29] found that mean arterial pressure (MAP) remained stable during induction across all groups. While heart rate changes in the ketamine group (Group K) were not significant, they were statistically significant in both the magnesium group (Group M) ($p = 0.002$) and the saline group (Group S) ($p = 0.004$). Supporting this, Sunilrajan et al. (24) reported no notable changes in MAP across groups when comparing baseline, pre-nebulization, and post-intubation values. However, a significant rise in heart rate was recorded in the group receiving 500 mg of magnesium sulfate (Group M2) ($p = 0.003$ and $p = 0.012$ when comparing to baseline and pre-nebulization values, respectively).

No postoperative adverse effects were observed in any patient group, likely due to minimal systemic absorption associated with nebulization. Previous studies by Neepa et al. [25], Chaudhary Reheel Ranjha [34], Delrin Thomas et al. [29], and Ranjana et al. [30] have also reported a lack of side effects with the use of nebulized ketamine and magnesium sulfate for preventing postoperative sore throat (POST). Additionally, none of the patients in the ketamine or magnesium groups required rescue analgesia, whereas 12 patients in the saline group did. A limitation of our study is that we did not assess serum concentrations of ketamine or magnesium sulfate. Furthermore, the use of a subjective grading scale for POST may introduce some degree of bias.

CONCLUSION

From this study we concluded that, nebulization with ketamine HCl and magnesium sulphate preoperatively effectively reduce postoperative sore throat, hoarseness of voice and cough. Ketamine HCL nebulization seems to be more effective than magnesium sulphate for prevention of postoperative sore throat, hoarseness of voice and cough. Haemodynamic parameter remains stable in all three groups. Ketamine HCl and magnesium sulphate nebulization does not have any side effects. **Hence, we concluded that preoperative ketamine HCL 50 mg nebulization decreased incidence of post operative sore throat, hoarseness of voice and cough compared to the magnesium sulphate 500mg nebulization.**

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