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Original Article

Comparison of Nebulized Ketamine with Nebulized Magnesium Sulfate for the Prevention of Postoperative Sore Throat

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ABSTRACT

Objective: To compare the effects of nebulized Ketamine versus nebulized Magnesium Sulfate to prevent post-operative sore throat.

Study Design: Quasi-Experimental Study.

Place and Duration of Study: Department of Anaesthesia, Combined Military Hospital, Rawalpindi Pakistan, from Sep 2020 to Feb 2021.

Methodology: A total of 154 patients who underwent general anaesthesia for elective procedures were randomly included in the study. These patients were divided into two equal Groups, i.e., Group-A (n=77), who received Magnesium Sulphate 250mg in 5ml saline and Group-B (n=77), who received Ketamine 50mg in 5ml saline, respectively. The effects of nebulized Ketamine versus nebulized Magnesium Sulfate to prevent post-operative sore throat, were observed in both the Groups.

Results: Both drugs were effective in the prevention of sore throat after extubation. Our study showed that Ketamine nebulization was more effective than Magnesium Sulfate nebulization in preventing sore throat. The frequency of sore throat in Group-A was 54.5% (42 out of 77 patients) as compared to 31.2% (24 out of 77 patients) in Group-B, which was statistically significant (p=0.003).

Conclusion: Post-operative sore throat is more effectively controlled with Ketamine as compared to Magnesium Sulfate

Keywords: Efficacy, Ketamine, Magnesium sulfate, Nebulization, Sore throat.

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INTRODUCTION

Post-operative sore throat (POST) is a very common complication seen in patients after general anaesthesia with endotracheal intubation. The primary cause of post-operative sore throat is airway irritation and inflammation or trauma caused by an endotracheal tube; however, the airway may be highly sensitive due to a preexisting comorbid condition.[1] In 30% to 70% of patients undergoing endotracheal intubation, post operative sore throat and hoarseness are comm-only seen soon after extubation.[1] This leads to an increase in morbidity and causes further complications in patients. Several techniques have been practised to decrease the incidence of post-operative sore throat after extubation.[2]

Numerous pharmacological and non-pharmacological techniques have been used to tackle post-operative sore throats. Non-pharmacological techniques aim to decrease the irritation of the airway by using small-size endotracheal tubes, decreasing the laryngoscopy and airway manipulation during intubation, preventing lighter states of anaesthesia, extuba-tion of a patient after completely deflating the cuff, keeping the cuff pressure up to 20cm of H2O etc.[3]

The pharmacological methods used for the prevention of post-operative sore throat are the use of inhalational, intravenous or topical agents that include inhalational Beclomethasone, gargles with Ketamine, Magnesium Sulfate, Aspirin Hydrochloride etc.[4]

The drugs, i.e., Magnesium Sulfate and Ketamine, are effective in treating post-operative sore throat by acting on N-methyl-D-aspartate receptors (NMDA). These receptors are present in the central nervous system and the peripheral nervous system. Both Magnesium Sulfate and Ketamine are antagonists at NMDA receptors which have a role in the control of nociception and reduction of inflammation.[5]

Post-operative sore throat remains the most frequent complaint experienced by patients in the post-operative ward at Combined Military Hospital, Rawalpindi Pakistan, after general anaesthesia. Non-pharmacological methods usually address this complaint. As no local protocol existed to date to counter this complaint, this study was conducted to develop a standard pharmacological method.

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METHODOLOGY

This was a quasi-experimental study conducted at the Department of Anaesthesia Combined Military Hospital, Rawalpindi Pakistan, from September 2020 to February 2021. After obtaining written informed consent and approval of the Ethical Committee Combined Military Hospital, Rawalpindi Pakistan, (71/05/20), the data collection was started.

WHO sample size calculator version 1.0 was used to calculate the sample size by keeping the level of significance (α) 5%, power of the test 90 % (1-β), anticipated population proportion-1 (p1) as 55% and anticipated population proportion-2 (p2) as 32%.[1] The calculated sample size of the study was 154. Using the Lottery method, patients were allocated to two Groups equally (Group-A and Group-B) 77 in each Group through consecutive non-probability sampling.

Inclusion Criteria: Patients of either gender, aged 18-65 years; undergoing any elective surgery under general anaesthesia requiring endotracheal intubation and having American Society of Anesthesiologists (ASA) physical status I & II were included in the study.

Exclusion Criteria: Patients requiring surgery in the prone position, surgery of the oral cavity, pharynx or larynx and neck regions, surgery requiring more than 3 hours, previous history of sore throat, common cold, anticipated difficult airway, allergies to study drugs, recent use of non-steroidal anti-inflammatory drugs and pregnant patients, difficult or traumatic airway patients were excluded from the study.

As per the study protocol, counselling and briefing were done before the procedure. Patients were kept nil per oral overnight. Before the procedure, patient history, clinical examination and investigations were reviewed, and the vital signs of all the patients were recorded. Patients were shifted to the operation theatre on the day of the procedure, and an intra-venous line and non-invasive standard monitoring were ensured before the procedure. Patients from Group-A were nebulized with 250mg Magnesium Sulfate in 5ml Normal Saline, and patients from Group-B were nebulized with 50mg Ketamine in 5ml Normal Saline. After 15mins of nebulization, premedication with the injection of Nalbuphine 0.1 mg/kg IV, Dexamethasone 8mg IV, and injection of Ondansetron 8mg IV stat was given. Induction was done after pre-oxygenation for 3 minutes, with an injection of Propofol 2.0 mg/kg IV and Atracurium 0.5 mg/kg IV to facilitate tracheal intubation according to the stan-dard protocol.

Laryngoscopy followed by tracheal intubation using endotracheal tube size of 7.0mm ID for females and 7.5-8mm ID for males was performed. The endotracheal tube cuff was inflated with air. The time taken by laryngoscopy and the number of attempts of laryngoscopy were recorded. More than two attempts of traumatic intubation ended in excluding such patients from the study. Maintenance of anaesthesia was done with Isoflurane 1.2% to 1.5% and Oxygen. Muscle relaxant injection Atracurium 0.1mg/kg IV was given as maintenance dose. A tidal volume of 8–10 mL/kg was given to maintain endtidal CO^2 within the normal range.

At the end of the surgery, neuromuscular blockade was reversed with an injection of Neostigmine 2.5mg IV and Glycopyrrolate 0.5 mg IV, followed by gentle suctioning. After the return of muscle activity, the inhalational agent was stopped, and 100% Oxygen was given. Extubation was done when the adductor policis muscle showed three twitches with a nerve stimulator. However, if the patient experienced bucking at the time of extubation, Lignocaine at 1.5mg/kg was given as a rescue drug, and these patients were excluded from the study. The severity of post-operative sore throat was assessed by a four-point scale (0–3), i.e., 0=no sore throat, 1=mild sore throat (complains of sore throat only on asking), 2= moderate sore throat (complains of sore throat on his/her own), 3=severe sore throat (change of voice or hoarseness, associated with throat pain).[6] Afterwards, patients were assessed for frequency and severity of post-operative sore throat at 0, 2 and 4 hours. Patients with a scale of 1, 2 or 3 on the post-operative sore throat severity scale were taken as *YES* while those with a score of 0 were taken as *NO* for sore throat. Any side effects, such as a cough, nau-sea, and vomiting, were also noted.

Computer software Statistical Package for Social Sciences (SPSS) version 25.0 was used to manage and analyze the data. Using descriptive studies, the mean and standard deviation was calculated for quantitative variable, while frequencies and percentages were for qualitative variables and chi-square was app-lied. The *p*-value ≤0.05 was considered significant.

RESULTS

A total of 154 patients were included in this study and divided into two equal Groups (n=77). The comparison of age and weight was shown in Table-I. There were 48(62.3%) males and 29(37.7%) females in Group-A, while 42(54.5%) males and 35(45.4%) female patients were included in Group-B respectively (*p*=0.327).

In Group-A, 65 patients (84.4%) while in Group-B, 69 patients (89.6%) were found to be in ASA Class-I. The difference between the Groups was non-significant (p=0.338). The response rate was found to be highest in the Group-A as POST was noted at zero, two and four hours after extubation in both the Groups. In Group-A (Magnesium Sulfate) 42 patients (54.5%) developed POST while in Group-B (Ketamine) 24 patients (31.2%) had symptoms as shown in Table-II.

Table-I: Demographic Characteristics of the Study Groups (n=154)

Variable	Group-A (n=77) (Mean±SD)	Group-B (n=77) (Mean±SD)	*p*-value
Age (years)	36.92±14.6	39.23±15.03	0.335
Weight (Kg)	65.57±8.75	66.49±11.24	0.571

Table-II: Comparison of Type of Magnesium Sulfate versus Ketamine in terms of Postoperative Sore Throat (n=154)

Time	Group-A (n=77) Frequency (%)	Group-B (n=77) Frequency (%)	*p*-value
At 0 hours	42(54.5)	24(31.2)	0.003
At 2 hours	8(10.4)	4(5.2)	0.009
At 4 hours	20(26.0)	10(13.0)	0.04

DISCUSSION

One of the common complications of general anaesthesia requiring the placement of an endotracheal tube is a post-operative sore throat, reported in 21% to 65% of patients.[1] This is the eighth most common complication following endotracheal intubation, leading to various pharmacological and non pharmacological techniques.

A study done by Yadav *et al*. compared the use of preoperative nebulization; Normal Saline versus Magnesium Sulfate for the prevention of post-operative sore throat. The results showed that Magnesium Sulphate is superior in decreasing the incidence of post-operative sore throat compared to Normal Saline.[2] Ahuja *et al*. used Ketamine nebuli-zation preoperatively to attenuate post-operative sore throat in patients. Gargles were used in several studies, but Ketamine nebulization has an advantage over Ketamine gargles as it prevents aspiration, spares the patient from its bitter taste and requires less dosage than when used for gargles. This study showed that Ketamine nebulization preoperatively significantly reduced post-operative sore throat with no adverse effects, and the frequency of post-operative sore throat was 20% compared with patients not receiving nebulized Ketamine to be 33%.[3]

Our results are comparable to the study by Rajan *et al*.[4] They also used Ketamine and Magnesium Sulfate 15 minutes preoperatively to attenuate the incidence of post-operative sore throat and hoarseness.[4] Teymourian *et al*. compared Magnesium Sulfate and Ketamine gargles in attenuating the incidence of post-operative sore throat. The results, however, revealed that Magnesium Sulfate is more effective than Ketamine if used in the form of gargles for the prevention of post-operative sore throat.[5] Mayhood *et al*. studied gargles of Ketamine preoperatively and found a reduction of post-operative sore throat at all-time intervals.[6] Shehkar *et al*. found out that when Ketamine and Clonidine were used in a combination for nebulization preoperatively, it reduced the frequency of post-operative sore throat significantly compared to when only Ketamine nebulization was used was done.[7] Apart from these, various lubricants have been applied to the endotracheal tube (ETT) to attenuate post-operative sore throat. Charan *et al*. studied two doses of Ketamine nebulization and found that both low (25mg) and high doses (50mg) effectively reduce post-operative sore throat.[8] Mekhemar *et al*. revealed that Benzydamine Hydrochloride gel, when applied to ETT, was more effective than 5% Lidocaine Hydrochloride, 10% Lidocaine Hydrochloride or Normal Saline.[9]

Intravenous agents have also been used to tackle post-operative sore throat. Kajal *et al*. used intravenous Dexamethasone 0.2mg/kg before the induction of anaesthesia to decrease the frequency of post-operative sore throat. The results were highly significant, i.e., they decreased from 48% in the Control Group to 20% in the Dexamethasone Group.[10] Cirilla *et al*. found out that replacing ETT with a flexible laryngeal mask airway reduced the incidence of post-operative sore throat significantly.[11] Gong *et al*. found that in thyroid surgeries, sore throat postoperatively was significantly reduced when a flexible laryngeal mask airway was used compared to ETT.[12]

Chattopadhyay *et al*. and Safavi *et al*. compared other anti-inflammatories with Magnesium Sulphate and Ketamine, respectively, and found a significant reduction in post-operative sore throat in Magnesium Sulphate and Ketamine Groups.[13,14] Strepsils lozenges, with the advantage of cost-effectiveness, have also been used in smokers to prevent post-operative sore throat. In the study by Gupta *et al*. Strepsils were given to smokers before general anaesthesia. Postoperatively, these patients were evaluated for sore throat, and the incidence of sore throat was significantly less at

intervals of 0 minutes, 30 minutes, 12 hours and 24 hours, with a *p*-value of <0.05 at these intervals.[15] Topical application of Magnesium Sulphate also proved to be effective in reducing post-operative sore throat in a study by Kuriyama *et al*.[16] In 2020, Kuriyama *et al*. also found that topical application of Ketamine was effective in reducing POST.[17] Faiz *et al*. compared Ketamine with Benzydamine gargling and found Ketamine to be superior in reducing postoperative sore throat. However, systemic effects due to the absorption of both drugs were a limitation of the study.[18] Puthenveettil *et al*. concluded that ETT cuff pressures measured by a manometer could also significantly reduce post-operative sore throat.[19] Lee *et al*. found that prophylactic IV Dexamethasone is also beneficial in reducing POST.[20]

Both the drugs used in our study have been used and proven beneficial in reducing post-operative sore throat. The previous literature prove that Ketamine is superior to Magnesium Sulfate or any other drug in reducing the severity of post-operative sore throat. Hence, if used preoperatively in nebulized form, Ketamine has fewer adverse effects and reduces the frequency of post-operative sore throat to a significant level. The limitation of this study was the small sample size, and a cost-benefit analysis was not done.

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CONCLUSION

Ketamine nebulization is superior to Magnesium Sulfate, which has improved outcomes and quality of life with relatively few to no side effects. It is, therefore, a viable technique compared to other techniques to reduce the complication of POST.

Conflict of Intrest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

CRR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

MS & SQAS: Study design, data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

MRI: Drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

KB & AT: Critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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