INTERNATIONAL JOURNAL OF CURRENT ADVANCED RESEARCH
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 12; Issue 03 (A); March 2023; Page No. 1841-1845
DOI: http://dx.doi.org/10.24327/ijcar.2023.1845.0408

Research Article

PREOPERATIVE NEBULIZATION WITH MAGNESIUM SULFATE VERSUS KETAMINE FOR PREVENTION OF ENDOTRACHEAL TUBE INDUCED POSTOPERATIVE SORETHROAT-A PROSPECTIVE, RANDOMIZED, COMPARATIVE CLINICAL STUDY

Darshna D Patel, Priyankaben Patel, Vidhi Patel and Kavan Patel

202, Vaidehi Residency, 44/1, Arunoday, Society, Alkapuri, Vadodara – 390007, India

A R T I C L E I N F O

Article History:
Received 4th December, 2022
Received in revised form 25th January, 2023
Accepted 18th February, 2023
Published online 28th March, 2023

Key words:

Nebulization, Ketamine, Magnesium sulfate, Postoperative sorethroat

A B S T R A C T

Background: Sore throat is a common postoperative complaint in patients receiving general anaesthesia requiring endotracheal intubation. Incidence ofpost operative sorethroat (POST) is 21-65%. Though it is a minor complication but valid reason for dissatisfaction and morbidity among patients. **Objective:** Primary objective of the study is to compare incidence & severity of POST at 4th hour in patients nebulized with ketamine and magnesium sulfate. To compare the incidence & severityof hoarseness of voice & cough. **Materials and methods:** After Institutional Ethics Committee approval and written informed consent, 144 patients who fulfilled the inclusion and exclusion criteria were randomly divided into two groups by sealed envelope method to receive magnesium sulfate 500mg in 4ml saline in Group M andketamine 50 mg in4ml saline nebulization in Group K 10 minutes before the start of general anaesthesia for 10 minutes. All patients received standard anaesthesia protocol. After extubation, all patients were enquired about the incidence and severity of POST, Hoarseness of voice & Cough at 0th, 2nd, 4th, 6th, 12th& 24thhours. **Results:** Overall incidence of POST was 25.69% Out of these 21 patients in group K (29.16%) & 16 patients in group M (22.22%) experienced POST(p=0.03). Although, Magnesium sulfate nebulization was significantly reduced incidence of POST as compared to ketamine (p=0.03), but on the basis of severity both the drugs are equally effective. (p=>0.05) In case of hoarseness of voice & cough reduced incidence & severity observed in both the groups. (p=>0.05). **Conclusion:** Preoperative nebulization with ketamine or magnesium sulfate is equally effective in reducing postoperative sore throat, hoarseness of voice and cough if given through nebulization ;10 minutes before induction of anaesthesia for 10 minutes.

INTRODUCTION

Post operative sorethroat (POST) is a common occurrence following general anaesthesia with endotracheal intubation. The incidence varies between 21-65% in literature.[1] The high variability of incidence is due to multiple factors involved in occurrence of POST like female sex, airway instrumentation, airway surgery, type of cuff, duration of surgery, position of the patient and intracuff pressure etc.[2]

The pathophysiological mechanism for POST is underlying mucosal injury that occurs due to various manouvres involved during endotracheal anaesthesia like, laryngoscopy, suctioning, endotracheal intubation and oro or nasogastric tube placement or throat packing. It is associated with oedema, congestion, and pain. Although post gets subsided spontaneously without any treatment, prophylactic management for decreasing its frequency and severity is still recommended.

Numerous nonpharmacological and pharmacological measures have been used for attenuating POST with variable success. Amongst the pharmacological interventions include 10% lidocaine spray, inflation of endotracheal tube cuff with 2%lignocaine, applying lignocaine gel or beclomethasone gel over endotracheal tube, gargles with magnesium sulfate or ketamine, ketamine nebulization or magnesium sulfate nebulization.

Amongst the various interventions, the use of ketamine gargles has the highest success rates.[3] But the gargles require large amount of volume and so the chances of aspiration are there. As compared to gargles, nebulization route has good acceptance from patients. Mucosal injury during airway instrumentation leads to activation of N-methyl D-aspartate (NMDA) receptors which are responsilbe for nociception and inflammation. So we intend to compare the efficacy of nebulized ketamine versus nebulized magnesium sulfate, both of which are NMDA receptor antagonists with the primary objective of comparing the incidence and severity of sorethroat at 4th postoperative hour. Ketamine and Magnesium sulfate are both NMDA receptor antagonists.

Corresponding author:* **Darshna D Patel
202, Vaidehi Residency, 44/1, Arunoday, Society, Alkapuri, Vadodara – 390007, India

Previous studies have compared these agents individually with placebo using varied doses and application patterns.[4,5,6,7,8]

Aim of the our study was to compare the efficacy of nebulized ketamine versus nebulized magnesium sulfate for attenuation of postoperative sorethroat in patients undergoing general anaesthesia with endotracheal intubation.

MATERIAL AND METHODS

After approval from the Institutional Ethical Committee for Human Research-PG Research (IECBHR/133/2021), S.S.G. Hospital, Vadodara and from clinical trial registry of India(CTRI/2022/02/040289) we carried out this prospective, randomised comparative clinical study on 144 patients.

Sample size was calculated based on a study done by Segaran *et al*.[9] which showed a difference of 25% reduction in the incidence of postoperative sorethroat in patients receiving nebulized ketamine. With alpha error of 0.05% and power 80% the estimated sample size came to be 65 patients per group. On assuming 10% loss to follow up, the sample size required was 72 patients per group.

We included Patients with age group of 18-60 years of either sex with ASA status I, II,III having Mallampatti airway assessment of Grade I and II and posted for elective surgery under General anaesthesia requiring intubation and expected to last for less than three hours. We excluded patients who refused to give consent, patients with anticipated difficult airway or Mallampatti Grade III & IV, Preoperative sore throat, Active upper respiratory tract infections, Procedures requiring perioperative nasogastric tube placement or throat packing, Patients with a high risk of aspiration, Surgery involving oral cavity, nasopharynx, larynx or neck region, History of allergies/ bronchial asthma/ Chronic obstructive pulmonary disease, Surgery in prone position and Pregnant women. Patients were explained in detail about the purpose and methodology of study and after written informed consent, randomization was done by sealed envelope method. Patients were grouped into two groups.

Group K: Patients nebulised with Ketamine 50 mg(1 ml) in 4ml of normal saline

Group M: Patients nebulised with Magnesium sulfate (50%w/v)500 mg(1ml) in 4 ml of normal saline

Nebulization was done using nebulization mask attached to compressor nebulizer device for 10 minutes. After preoxygenation with 100% oxygen, conventional general anaesthesia was given using Inj. propofol and suxamethonium chloride. High volume low pressure cuff was inserted with an experienced anaesthesiologist (Size-7-7.5 mm ID for female patients and 8-8.5 mm ID for male patients) under direct vision. Tracheal tube cuff was inflated with air and the cuff pressure was maintained between 20-25 cm of H_2O by cuff pressure manometer. All patients who required the second attempt at intubation or traumatic intubation were excluded from the study. Anaesthesia was maintained with controlled ventilation through close circuit with oxygen: nitrous oxide(40:60), sevoflurane and vecuronium. At the end of operation, gentle oropharyngeal suction with soft suction catheter was done. Patients were extubated once all the criteria for extubation were met.

Incidence and severity of sore throat, Hoarseness of voice and Cough were assessed at immediate recovery period (o hour), 2,4,6,12 and 24 hours postoperatively.

Any Patient Having Soreness or Pain In Throat Was Considered As Having Sorethroat.

Severity of sorethroat was graded as follows [3]

0- No sore throat at any time since the operation
1- Minimal - Patient answered in the affirmative when asked about sore throat
2- Moderate - Patient complained of sore throat on his/her own
3- Severe - Patient is in obvious distress

Hoarseness of voice was graded as follows. [10]

0- No complaint of hoarseness at any time since the operation
1- Minimal - Minimal change in quality of speech. Patient answers in the affirmative only when enquired about
2- Moderate - Moderate change in quality of speech of which the patient complains on his/her own
3- Severe - Gross change in the quality of voice perceived by the observer

Cough was graded as follows. [10]

0- No cough at any time since the operation

1-Minimal
2- Moderate
3- Severe

Side effects, if any like nausea, vomitting or dry mouth were noted. Data were collected for clinical case study subjectively. Statistical analysis of the data were done using Student 'T' test or Paired 'T' test for all continuous variables and chi-square test for categorical data using MedCalc software.

RESULTS

Demographic data and duration of surgery were comparable in both the groups. Out of 144 patients, 37 patients at some point of time had complaint of sore throat. So overall incidence of postoperative sore throat in our study was **25.69 %**. Sixteen (16) patients in group M **(22.22%)** and 21 patients in group K (**29.16%**) had POST at some point of the study which was clinically significant (**p=0.03**). POST at 0 hour occurred in 13 patients in group K versus 3 patients in group M (**p=0.031**), which was significant. Five patients in group K versus 8 patients in group M **(p=0)** experienced POST at 2nd hour post operatively.

Graph-1 Incidence of POST

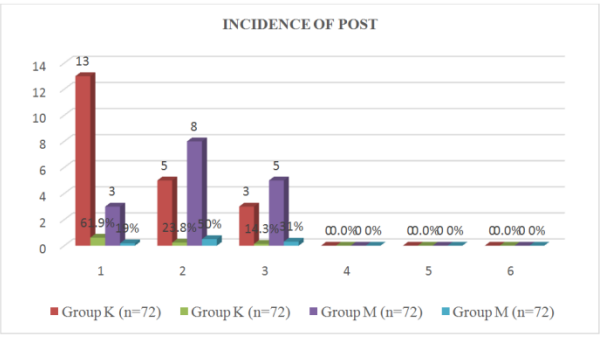

Table-1 Severity of POST

Time Post-extubation (hrs)	Severity Score(POST)	Group K (N=72)		Group M (N=72)		P value
		No.	%	No.	%	
0	0	59	81.94%	69	95.83%	X2=7.236 df=3 **p=0.0648**
	1	9	12.50%	2	2.77%	
	2	3	4.16%	1	1.38%	
	3	1	1.38%	0	0.0%	
2	0	59	81.94%	62	86.11%	X2=2.800 df=2 **p=0.2466**
	1	8	11.11%	9	12.50%	
	2	5	6.94%	1	1.38%	
	3	0	0.0%	0	0.0%	
4	0	62	86.11%	65	90.27%	X2=2.994 df=2 **p=0.2238**
	1	9	12.50%	4	5.55%	
	2	1	1.38%	3	4.16%	
	3	0	0.0%	0	0.0%	
6	0	71	98.61%	70	97.22%	**p=1**
	1	1	1.38%	2	2.77%	
	2	0	0.0%	0	0.0%	
	3	0	0.0%	0	0.0%	
12	0	72	100.0%	71	98.61%	P=1
	1	0	0.0%	1	1.38%	
	2	0	0.0%	0	0.0%	
	3	0	0.0%	0	0.0%	
24	0	72	100.0%	72	100.0%	X2=0.00694 df=1 **p=0.9336**
	1	0	0.0%	0	0.0%	
	2	0	0.0%	0	0.0%	
	3	0	0.0%	0	0.0%	
TOTAL		**21**	**100.0%**	**16**	**100.0%**	

Table-2 Incidence of hoarseness of voice

Time of incidence of hoarseness of voice (Post-op) (in hours)	Group K (n=72)		Group M (n=72)		P Value
	No.	%	No.	%	
0	5	83.3%	2	66.7%	
2	1	16.7%	1	33.3%	
4	0	0.0%	0	0.0%	1
6	0	0.0%	0	0.0%	
12	0	0.0%	0	0.0%	
24	0	0.0%	0	0.0%	
Total	**6**	**100.0%**	**3**	**100.0%**	

Table-3: Incidence of cough

Time of incidence of cough (Post-op) (in hours)	Group K (n=72)		Group M (n=72)		P Value
	No.	%	No.	%	
0	5	83.3%	5	100.0%	
2	1	16.7%	0	0.0%	P=1.0 (fischer exact test)
4	0	0.0%	0	0.0%	
6	0	0.0%	0	0.0%	
12	0	0.0%	0	0.0%	
24	0	0.0%	0	0.0%	
Total	**6**	**100.0%**	**5**	**100.0%**	

POST at 4th hour occurred in 3 patients in group K versus 5 patients in group M (**p= 0**), which was significant. Patients who experienced and complained of POST were compared for severity of POST. While comparing the severity of POST, a higher incidence of Grade 2 **(moderate**) sore throat was observed in Ketamine group as compared to Magnesium sulfate group at 2nd and 4th hour post-operatively. **No incidence of severe [Grade 3] sore throat was observed in Magnesium sulfate Group** at any point of time during study.

Incidence of Hoarseness of voice was lower in Group M compared to group K. At 0 hr i.e. immediate post operative period, 5 patients experienced hoarseness of voice in group K compared to 2 patients in group M. At 2nd post operative hour, 1 patient from each group experienced hoarseness of voice. At 4^{th}, 6th, 12^{th} & 24^{th} post operative hours, not a single patients from each group experienced hoarseness of voice. So, there was no statistically significant difference in the incidence of Hoarseness of voice**(p=1)**.

At 0 hr in each group 5 patients experienced cough. At 2nd post operative hour, only 1 patient had cough in group K while none in group M. So, there was no statistically significant difference in case of incidence of cough in between both the groups**.**

DISCUSSION

Post-operative sore throat (POST) is a common complain after general anaesthesia using endotracheal intubation. Amongst the various adverse events of post endo tracheal intubation, it is considered as the second leading minor adverse event after post-operative nausea and vomiting.[11] Though it is minor and self limiting, it is causing discomfort to the patients and even may increase the duration of stay in the hospital. So Prophylactic management for decreasing its frequency and severity is still recommended to improve the quality of post anaesthesia care. POST is a description representing a broad constellation of signs and symptoms of laryngitis, tracheitis, hoarseness, cough or dysphagia with incidence varying from 21% to 65% after endotracheal intubation.[12] Research indicates that POST can be attenuated using a multi modal approach consisting of non-pharmacological and pharmacological interventions.

Ketamine is shown to be a promising agent to reduce POST. It is a phencyclidine derivative. It is a noncompetitive antagonist of N-methyl-D-aspartic acid (NMDA) receptor. The primary site of action is in the central nervous system (CNS) and parts of the limbic system. It is known that NMDA receptors have a role in inflammation and nociception. NMDA receptors are found not only in CNS but also in the peripheral nerves. Experimental studies show that peripherally administered NMDA receptor antagonists are involved with antinociception and anti-inflammatory cascade, thus preventing POST.[13]

Ketamine has been used as a gargle for reducing the incidence and severity of POST. It also has been used in the form of nebulization . Nebulization is considered better than gargle as it is easy way to administer the drug, smaller volume of drug is required and better patient cooperation is likely. Also there is no risk of aspiration and the drug is reaching to lower airways too. [12,5] Nebulisation also have an advantage of evenly distributing the drug over all areas exposed to instrumentation and mucosal damage while the gargle and lozenge forms are restricted to the supraglottic region with considerable inter-patient variability during administration. Magnesium is also being used to prevent POST through either gargles or nebulisation.In our study,out of 144 patients, 37 patients at some point of time had complaint of sore throat. So overall incidence of postoperative sore throat was **25.69 %**. Sixteen(16) patients in group M**(22.22%**) and 21 patients in group K (**29.16%**) had POST at some point of the study which was clinically significant (**p=0.03**). The proposed mechanism for the anti-inflammatory and antinociceptive effect of magnesium sulfate is thought to be by reducing the release of inflammatory mediators such as histamine, leukotrienes, and thromboxanes.[14] Magnesium also antagonizes NMDA receptors. It is also noted that the effect of magnesium was due to the direct contact of magnesium ions with the pharyngeal wall. **Jain S. *et al***.[5] conducted similar study in which they observed incidence of sore throat was significantly reduced in ketamine compared to control group**(p=0.002).** magnesium also decreases incidence of sore throat which was statistically significant compared to control group (p=0.004). There was no any significant difference between ketamine and magnesium (p=0.37). Total incidence of sore throat with ketamine was 22% and with magnesium was 30%. Rajan *et al*.[15] compared three study groups ketamine (50mg), magnesium (500mg), and magnesium (250mg) with control group (normal saline). They noted in their study that both ketamine and magnesium sulfate (500mg) decrease incidence of sore throat at 0, 2, 4 hr which was statistically significant compared to control group (NS). All the groups decrease incidence of sore throat at 12th and 24th hr compared to control group but it was statistically non significant. The decrease in incidence of sore throat was highest in ketamine group followed by magnesium group (500mg) followed by magnesium (250mg). M o orji *et al*[16], compared the incidence and severity of post-operative sore throat at 2, 4, 8, 12 and 24 hours after extubation. Following pre-induction administration of nebulized Magnesium and Ketamine, they observed that the incidence of sore throat at 4, 8, 12 and 24 hours post tracheal extubation were significantly lower in the Magnesium (p = 0.009, 0.006,≤0.0001, 0.003) and Ketamine group (p = 0.041, 0.006, 0.001, 0.003) compared with the saline group . Patients also had significantly less severe sore throat at 4th and 8th hours post extubation in both Magnesium and Ketamine groups (p = 0.0 11, 0.041).so, they concluded that Pre-induction nebulization of Ketamine or Magnesium can decrease the incidence and severity of sore throat in the first 24 hours after anaesthesia. **Segaran, *et al*** [9] noted in their study that 50% patients in magnesium group and 25% patients in ketamine group developed sore throat. There was no sore throat in any patients at 0hr after extubation. There was decreased incidence of sore throat at 2nd hr in ketamine group compared to magnesium group but it was statistically non-significant, (p=0.154). Incidence of sore throat at 4th hr (p=0.013) and 6th hr (p=0.019) was statistically significantly lower in ketamine group compared to magnesium group. No one developed sore throat in any group at 24th hr.

In our study, at 0 hr, 5 patients had complaint of hoarseness of voice in Group K while in Group M only 2 patients had complaint of hoarseness of voice. In group K from 5 patients 4 had mild symptoms while 1 had moderate .On the contrary in group M, one had mild while another had moderate symptoms.(p=1) At 2nd hr only 1 patient had complaint of moderate hoarseness of voice in group K while in group M one patient had mild hoarseness of voice. At 4^{th} hr,6^{th} hr,12^{th} hr,24^{th} hr there were no reported incidence of hoarseness of voice .

Similarly, **Rajan *et al***.[15] noted in their study that attenuation in incidence of hoarseness of voice seen with ketamine, magnesium (250mg) and magnesium (500) mg at 0hr, 2nd hr, 4th hr and 12th hr. Maximum decrease in hoarseness was seen in ketamine continuously which was followed by magnesium group (500) and magnesium (250). Statistically significant decrease in incidence of hoarseness of voice was seen at 0hr in ketamine (p=0.002) and magnesium (500) (p=0.014) compared to control group. No one developed hoarseness of voice at 24th hr in any group. **Patel N *et al*** [17], also studied incidence of hoarseness of voice and showed that there was statistically significant reduction in hoarseness of voice in group K compared to group M at 2nd hr(p=<0.01),4^{th} hr (p=<0.01) and 12^{th} hr (p=<0.01) .

Limitations of This Study

There are a few limitations of our study. **No formal sedation scale** was used and we were also **not able to measure plasma levels of both drugs** during the study period. We cannot rule out the contribution of the systemic effect of the drugs in our results. The safety and dosage of the drugs used for inhalation need further investigation even though we did not find any adverse effects after their use as doses which were used in the study were quite less compared to those causing adverse effects.

References

1. Higgins PP, Chung F, Mezei G. Postoperative sore throat after ambulatory surgery. Br J Anaesth 2002; 88:582‑4.)
2. K El-Boghdadly, C R Bailey, M D Wiles. Post-operative sore throat: a systematic review, Anaesthesia 2016,71,706-717
3. Canbay O, Celebi N, Sahin A, Celiker V, Ozgen S, Aypar U. Ketamine gargle for attenuating postoperative sore throat. Br J Anaesth 2008;100:490-3.
4. Ahuja V, Mitra S, Sarna R. Nebulized ketamine decreases incidence and severity of post-operative sore throat. Indian J Anaesth. 2015;59:37-42.
5. Jain, S., Bendwal, H., Gohiya, S., Alwani, N., Pancholi, S., and Romday, R. Comparison of nebulized ketamine and ketamine with clonidine in postoperative sore throat.International Surgery Journal. 2017;4:1579-1583.
6. Amingad, Bhagyashree, and Shruthi Jayaram. Comparison of ketamine nebulisation with ketamine gargle in attenuating post operative sore throat. Indian Journal of Clinical Anaesthesia. 2016;3.3: 347-351.
7. Gupta SK, Tharwani S, Singh DK, Yadav G. Nebulised magnesium for prevention of postoperative sore throat. Br J Anaesth. 2012;108:168–9.
8. Yadav Monu, Chalumuru Nitish, Gopinath Ramachandran. Effect of magnesium sulfate nebulization on the incidence of postoperative sore throat. *Journal of Anaesthesia and clinical pharmacology*. 2016:32:2:168-171.
9. Sivakumar Segaran, Arish T. Bacthavasalame, Ranjan R. Venkatesh, Mamie Zachariah, Sagiev Koshy George, and Ravichandran Kandasamy: Comparison of Nebulized Ketamine with Nebulized Magnesium Sulfate on the Incidence of Postoperative Sore Throat: Anesth Essays Res. 2018 Oct-Dec; 12(4): 885–890
10. Harding CJ, McVey FK. Interview method affects incidence of postoperative sore throat. Anaesthesia 1987; 42: 1104–7
11. Lehmann M, Monte K, Barach P, Kindler CH. Postoperative patient complaints: a prospective interview study of 12,276 patients. J Clin Anesth. 2010;22:13–21.
12. Thomas D, Bejoy R, Zabrin N, Beevi S. Preoperative ketamine nebulization attenuates the incidence and severity of postoperative sore throat: A randomized controlled clinical trial. Saudi J Anaesth2018;12:440-5
13. De Kock M, Loix S, Lavand'homme P. Ketamine and peripheral inflammation. CNS Neuroscience and therapeutics 2013;19:403-10. Borazan H, Kececioglu A, Okesli S, Otelcioglu S. Oral magnesium lozenge reduces postoperative sore throat: A randomized, prospective, placebo-controlled study. Anesthesiology 2012;117:512-8.
14. Rajan S, Malayil GJ, Varghese R, Kumar L. Comparison of usefulness of ketamine and magnesium sulfate nebulizations for attenuating postoperative sore throat, hoarseness of voice, and cough.Anesth Essays Res 2017;11:287-93.
15. M.O. Orji1, B.B. Osinaike1, S.D. Amanor-Boadu1, and A. Ugheoke2 Nebulized magnesium versus ketamine for prevention of post operative sore throat in patients for general anaesthesia Ann Ibd. Pg. Med 2020. Vol.18, No.1 3 -8
16. Patel N, Dhuliya S, Shah D. Comparative evaluation of incidence of post operative sore throat after nebulization with ketamine and magnesium sulfate in patients undergoing general anaesthesia requiring endotracheal intubation. Indian J Clin Anaesth 2022;9(2):227-232

How to cite this article:

Darshna D Patel *et al (*2023) 'Preoperative Nebulization With Magnesium Sulfate Versus Ketamine For Prevention of Endotracheal Tube Induced Postoperative Sorethroat-A Prospective, Randomized, Comparative Clinical Study', *International Journal of Current Advanced Research*, 12(01), pp. 1841-1845. DOI: http://dx.doi.org/10.24327/ijcar.2023.1845.0408

****