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Ketamine versus Magnesium Sulphate Gargle in Prevention of Post Operative Sore Throat after Endotracheal Intubation, Randomised Comparative Trial

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Abstract

Background: Postoperative sore throat is one of the most common complications afterendotracheal intubation. Both Ketamine and magnesium can block N-methyl-D-aspartic acid receptors and provide central and local analgesia. *Objectives:* To compare the efficacy of magnesium sulfate and ketamine gargle in preventionof postoperative sore throat. *Methodology:* A total of 90 patients posted for general anaesthesia with endotrachealintubation were enrolled in the study. Patients in ketamine group received ketamine gargle (50 mg) and magnesium group received magnesium sulfate gargle (20 mg/kg up to 30 mL normal saline) 15 minutes before the operation. Patient's complaint of postoperative sore throat, and its severity were measured and recorded at baseline in recovery room, and then 0, 4, 8, 12 and 24 hours after operation. *Results:* To analyse the association of sore throat in two groups Chi square test wasused. $p < 0.05$ was considered statistically significant Number of patients with sore throat were significantly lower in magnesium group compared to ketamine group at 0hr ($p<0.001$), 4th hr ($p <0.001$), 8th hr ($p <0.001$), 12th hr ($p<0.001$) and 24th hr ($p =0.006$) after the operation. *Conclusions:* Magnesium sulphate decreases sore throat and pain severity more effectively compared toketamine gargle.

Keywords: Ketamine; Magnesium; Postoperative Sore Throat; Complications.

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Introduction

Management of airway is central to the practice of anaesthesia & it encompasses the whole range of airway manipulations required during the course of anaesthesia. Endotracheal intubation forms an integral part of airway management. Cuffed endotracheal tubes prevent aspiration and hence are commonly used. However, local irritation, inflammation of the airway is a common sequelae to cuffed endotracheal intubation, which leads to post extubation morbidities like sore throat, cough & hoarseness of voice which is extremely distressing to the patient.

A number of different measures both pharmacological & non pharmacological have been studied to reduce the incidence & the severity of post extubation sore throat. Smaller sized tubes [1], high volume low pressure endotracheal tubes [2], careful instrumentation of the airway, adequate intracuff pressure, lubricating with lignocaine jelly [3], betamethasone gel [3], IV dexamethasone [4],

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beclomethasone inhalation [5], magnesium lozenges [6], Aspirin gargle [7] are some of the strategies used to reduce postoperative sore throat. However, each intervention is associated with side-effects which may not be desirable. Hence there is a need for an intervention which would prevent rather than treat post-operative sore throat which is effective, patient friendly and reliable.

N-methyl D aspartate (NMDA) receptors are present not only in the central nervous system but also in the peripheral nervous system [8]. These receptors contribute in inflammatory pain. Ketamine and Magnesium sulphate are NMDA antagonist with anti-nociceptive and anti-inflammatory properties, which may be the possible mechanism in prevention of post-operative sore throat (POST) [7,8,9].

Though there are several measures available for reduction of post operative sore throat,the problem still remains unresolved. Hence, newer methods to address thiscomplication have to be developed and the effectiveness of ketamine and magnesium sulphate in prevention of POST needs to be studied. Therefore, we undertook a study on the effect of ketamine gargle and compared it with magnesium sulphate gargle in prevention of post-operative sore throat.

Materials and Methods

A prospective randomised, double blind clinical study was approved by our institutional ethical committee for a period of one year. Written informed consent was obtained from patients. 90 (45 in group A and other 45 in group B) patients of physical status American society of anaesthesiologist (ASA) grade 1and 2, aged between 18 to 60 years undergoing elective surgeries under general anaesthesia with endotracheal intubation, Mallampati grade I and II were included in the study. Patients with anticipated difficult intubation,Head and neck surgery, Duration of surgery > 3hrs were excluded from the study.

A total sample size of 90, sample size calculation done by using open episoftware version 2.3.1. at 95% confidence limit and 80% power of the study. According to study conducted by Rudra A [10] 45 patients having sore throat in ketamine group mean is 40% and study conducted by Borazan H [6], on 45 patients having sore throat in magnesium group mean is 14%. So sample size calculated is 45 in each group, hence the total sample size is 90.

Methodology

A total of 90 patients undergoing elective surgeries of a maximum duration of 3 hours under general anaesthesia were included in the study. Patients randomly divided into two groups by using computer generated table.

- Group A received preservative free ketamine 1 ml (50mg) in 29ml Normal saline (NS)
- Group B received 20mg/kg of magnesium sulphate diluted in normal saline making total volume of 30 ml.

Patients were asked to gargle for 30 seconds 5 minutes prior to induction. Standard non-invasive monitoring was done throughout the procedure. Following pre-oxygenation, patient were pre-medicated with Inj.glycopyrrolate 0.005mg/kg iv, Inj.midazolam 0.05mg/kg iv and Inj.fentanyl 2mcg/kg iv.

Induction of anaesthesia was done with 2mg/kg of Inj.propofol iv sufficient to obtund the eye-lash reflex, followed by Inj.vecuronium 0.1 mg/kg iv with an appropriate sized endotracheal tube. Tracheal intubation was performed by an experienced anaesthesiologist having experience of >3 years. The endotracheal tube was lubricated with 2% lignocaine jelly at room temperature. Immediately after intubation, cuff of the endotracheal tube was filled with a volume of room air required to prevent a palpable air leak.

Anaesthesia was maintained with isoflurane, fentanyl, vecuronium and supplemented with oxygen 33% in nitrous oxide. Intracuff pressure was maintained throughout the procedure between 18-22 cm H_2O using handheld pressure gauge. Supplemental analgesia during surgery was maintained with small doses of iv Fentanyl.

Residual neuromuscular relaxation with vecuronium was antagonized with Inj. Neostigmine iv (0.05mg/kg body weight) and Inj. Glycopyrrolate iv (0.01mg/kg body weight) on completion of surgery. Oropharyngeal suction before extubation was done under direct vision to avoid trauma to the tissues, confirming that secretion clearance was complete.

The patients were interviewed regarding post operative complaints. If they did not complain about sore throat then a leading question was asked regarding the same at 0, 4, 8, 12 and 24 hours after the procedure.

POST was graded on a four-point scale (0-3):

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). Other side-effects, if any, were also noted.

Statistical Analysis

Data were entered in MS-Excel analysed by using SPSS V22. Descriptive statistics like Mean and Standard Deviation were applied for quantitative data. t-test was applied for finding significance in quantitative data. Qualitative data were represented in the form of percentages. Chi-square test was done for finding significance in qualitative data. $p<0.05$ was considered as statistically significant.

Results

The present study was conducted to compare the efficacy of ketamine gargle and magnesium sulphate gargle in prevention of postoperative sore throat following endotracheal intubation in patients receiving general anaesthesia.

90 ASA grade I-II patients between 18-60 years of age, of both the sex were included in the study. 45 patients in Group A (Ketamine gargle) and 45 patients in Group B (Magnesium sulphate gargle).

Demographic data concerning patients age (p-0.61), Weight (p-0.49), Sex (p-0.29) and duration of surgery (p-0.46) were comparable in both the groups Table 1.

Incidence of sore throat was lower in Group B than in Group A at intervals 0 hr, 4th hrs, 8th hrs, 12th hrs, 24th hrs. Statistically significant at all instances with p value of <0.05 Table 4, 5, 6.

Table 1: Demographic Data

Variables	Group A (N=45)	Group B (N=45)
Age (years)	32.11 ± 10.27	33.24 ± 10.42
Weight (Kg.)	61.42 ± 8.73	60.22 ± 7.82
Gender (Male/Female)	23/22	18/27
Duration of surgery (mins)	122.44 ± 18.08	119.67 ± 17.10

Table 2: Shows incidence of sore throat at 0 Hr

Group	Sore Throat at 0th Hr				Chi-Square Value	P-value
	Grade-0	Grade-1	Grade-3	Grade-4		
Group-A	0	7	24	14	26.87	<0.001
	0.0%	15.6%	53.3%	31.1%		
Group-B	2	28	13	2		
	4.4%	62.2%	28.9%	4.4%		

Table 3: Shows incidence of sore throat at 4th Hr

Group	Sore Throat at 4th Hr			Chi-Square Value	P-value
	Grade-0	Grade-1	Grade-2		
Group-A	3	17	25	22.86	<0.001
	6.7%	37.8%	55.6%		
Group-B	15	25	5		
	33.3%	55.6%	11.1%		

Table 4: Shows incidence of sore throat at 8th Hr

Group	Sore Throat at 8th Hr			Chi-Square Value	P-value
	Grade-0	Grade-1	Grade-2		
Group-A	9	27	9	32.17	<0.001
	20.0%	60.0%	20.0%		
Group-B	35	10	0		
	77.8%	22.2%	0.0%		

Table 5: Shows incidence of sore throat at 12th Hr

Group	Sore Throat at 12th Hr		Chi-Square Value	P-value
	Grade-0	Grade-1		
Group-A	24	21		
	53.3%	46.7%		
Group-B	43	2	21.08	<0.001
	95.6%	4.4%		

Table 6: Shows incidence of sore throat at 24th Hr

Group	Sore Throat at 24th Hr		Chi-Square value	P-value
	Grade-0	Grade-1		
Group-A	38	7		
	84.4%	15.6%		
			7.59	0.006
Group-B	45	0		
	100.0%	0.0%		

Discussion

In modern anaesthetic practice, many of the general anaesthetic procedures are carried out with endotracheal intubation. Postoperative sore throat (POST) is a well-recognized side effect after endotracheal intubation [11]. But the discomfort produced by sore throat makes it one of the most undesirable side effect in the postoperative period [12].

POST(Post-operative sore throat) represents a broad constellation of signs and symptoms of laryngitis, tracheitis, hoarseness, cough or dysphagia with incidence varying from (21-65%) [10] after endotracheal intubation.

Identification of the factors associated with an increased risk of POST will allow anaesthesia providers to avoid combination of controllable factors, decrease the incidence of POST and improve post anaesthetic outcomes. Multi modal approach can be used for attenuation of POST. These consist of non-pharmacological and pharmacological interventions. Smaller sized endotracheal tubes [1], lubricating the endotracheal tube with water soluble jelly [3], careful airway instrumentation, intubation after full relaxation, gentle oropharyngeal suctioning, and minimizing intra-cuff pressure [11] are some of the non-pharmacological measures to reduce the incidence of POST.

Pharmacological interventions include beclomethasone inhalation [5], IV steroids [4], IV preservative free lignocaine, gargling with azulene sulfonate[13] etc. But all such manoeuvres have their own limitations and have not been able to successfully deal with this distressing side-effect.

Ketamine and magnesium both can block N-methyl- D-aspartic acid (NMDA) receptor. Ketamine relaxes the tracheal muscle contraction through a mechanism independent of NMDA receptors [8]. In addition, the decreased bronchomotor tone induced by ketamine is probably due to its interference with Ca2+ (a required step necessary to maintain the contraction). In this sense, magnesium could probably block the Ca entrance into tracheal muscle in a more effective manner. Recent reports of the incidence of postoperative sore throat following anaesthesia have claimed that the incidence of postoperative sore throat does not necessarily reflect damage caused by the tracheal tube cuff but more of increased muscle contracture. By preventing central sensitization, preemptive analgesia along with intensive multimodal analgesic interventions could theoretically reduce postoperative sore throat incidence and severity. Hence, in our study we compared pre-emptive ketamine gargle with mgso4 gargle as a means to prevent post-operative sore throat.

In our study the number of male patients was 23 in ketamine group & 18 in $MgSO_4$ group. The number of female patients was 22 in ketamine group and 27 in $MgSO_4$ group. When compared the difference was not found to be statistically significant (p=0.29).

The incidence of sore throat increases with the duration of procedure. Hence in our study the duration of procedure was defined. Duration was standardized in both the groups. Any patient whose surgery lasted for more than 3 hrs was excluded from our study. The duration of the procedure in ketamine group was 122.44±18.08 minutes while in mgso4

group it was 119.67±17.10 minutes. When compared the difference was not found to be statistically significant (p=0.75).

The use of cuffed tubes, Stout D M. et al. (1987) [1] showed a higher incidence of sore throat by larger size tube compared with smaller size, hence in our study we used 7.5 mm tube for female patients and 8.5mm tube for male patients in both the groups.

Incidence of post operative sore throat has been found to be higher when tubes with high pressure low volume cuffs are used in comparison with tubes with high volume low pressure cuffs. Hence in our study we used portex tubes that have a high volume low pressure cuff in all patients [11]

Previous studies have reported that POST is associated with increase in cuff pressure. Excessive inflation of endotracheal tube cuff produces high pressure on the tracheal wall thereby affecting perfusion of the tracheal mucosa resulting in its ischaemic necrosis. When pressure in the endotracheal tube cuff exceeds 22 mm hg, blood flow in the tracheal mucosa begins decreasing and reduces markedly when the pressure reaches 30 mm hg hence in our study we maintained the intra-cuff pressure between 18-22 mm hg in both the groups.

Trauma during insertion of the endotracheal tube is associated with higher incidence of post operative sorethroat [11], hence in our study all the intubations were done by an anaesthesiologist with a minimum experience of 3 years to avoid unnecessary trauma.

Blind suctioning causes trauma to the pharyngolaryngeal structures that increases the chances of post-operative sore throat. Suctioning was strictly done under vision in our study. High anaesthetic air flow rates cause drying of the mucosa that inturn leads to increased incidence of post-operative sore throat, our study used O_2:N_2O in a ratio of 1:1 with fresh gas flow of 4 liters [14].

The incidence of postoperative sore throat varied with the type of questioning employed. Various investigators have used various techniques to elicit sore throat in postoperative period. Harding C J. et al. [15] conducted a study in 1987 that showed higher incidence of sore throat by direct questioning. Hence in our study we have used a scale in which patient is asked about his complaints in the postoperative period. If the patient does notcomplain of sore throat then a direct question pertaining to sore throat, cough, hoarseness was asked.

Placement of throat pack around the endotracheal tube increases the incidence of POST [16]. However, in our study, throat pack was not inserted in any of the patients.

Our study found that Gargling with 50mg of Ketamine diluted with 29ml of NS 5 minutes before induction successfully reduced the incidence & severity of post-operative sore throat. Immediately after extubation 14/45 patients in ketamine group complained of severe POST as compared to only 2/45 patients in mgso4 group.

At four hours post extubation 25/45 patients in ketamine group complained of moderate sore throat while only 5/45 in $MgSO_4$ group experienced sorethroat. When compared statistically the difference in incidence of POST at 0 and 4 hours post extubation was found to be statistically significant ($p<0.001$).

At 8 hours post extubation 9/45 patients in ketamine group complained of moderate sore throat while no patients experienced sorethroat in mgso4 group. When compared statistically the difference in incidence of POST at 0 , 4 and 8 hours post extubation was found to be statistically significant ($p<0.001$).

At 12 hours post extubation only 2/45 patients in $MgSO_4$ group complained of mild sore throat while none had moderate or severe symptoms. However in ketamine group, although no patients had moderate or severe symptoms, 21/45 patients still experienced mild sore throat. 7/45 patients had mild sore throat even at 24 hours following extubation in saline group while none of the patients in $MgSO_4$ group complained of any sore throat. When compared statistically the difference in incidence of POST at 12 and 24 hours post extubation was found to be statistically significant ($p<0.001$).

This shows that mgso4 gargle just prior to induction of general anaesthesia significantly reduces the incidence and severity of POST compared to ketamine gargle. However it was not found to be effective in prevention of POST as 28/45 patients in $MgSO_4$ group complained of mild sore throat at 0 hours ie., immediate post extubation.

The findings of our study correlate with a study done by Canbay et al. [12] in 2008. In this study the author studied the effects of a ketamine gargle on POST. Forty-six patients undergoing septorhinoplasty were included in the study and divided into two groups, one received ketamine gargle 40mg and other normal saline for thirty seconds prior to induction of general anaesthesia. They found that both the incidence and severity of POST was reduced in the ketamine group. None of the

ketamine patients reported severe POST symptoms at any interval while fifteen of the saline gargle patients reported severe symptoms. Two patients of ketamine group reported moderate symptoms in the immediate postoperative period while thirteen patients in the saline group reported moderate symptoms thus showing that ketamine gargle significantly reduces the incidence and severity of POST.

The findings of our study also correlated with the following studies. In 2009, Rudra et al. [10], conducted a prospective, randomized, placebo-controlled, and single–blinded studyassigning 40 ASA grade I patients undergoing abdominal and pelvic surgery under general anaesthesia to 2 groups, one group received drinking water 30 ml and another received preservative free ketamine 1ml (50mg) in 29ml of drinking water to gargle for 40 seconds. The researchers reported that the number of patients in Control group had significantly more incidence of POST at 4, 8 and 24hours (85%, 75%, and 60%) than in patients having ketamine gargle (40%, 35%and 25%) concluding that gargling with ketamine effectively attenuated POST, with no adverse reactions.

The findings of our study also correlated with the following studies. In 2012, Borazan H [6], conducted a prospective, randomized, placebo-contolled, and single blinded studyassigning 70 ASA grade I and II patients undergoing orthopaedic surgery, randomly allocated into 2 groups to either receive placebo or magnesium lozenzes to be dissolved by sucking 30 mins preoperatively. Patients were assessed for incidence and severity of POST at 0, 2, 4, and 24 h post-operatively. The incidence of POST at 4th hr was higher in control group than in magnesium group. Thus they concluded that administration of magnesium lozenge 30mins preoperatively is effective to reduce both incidence and severity of POST in the immediate postoperative period.

The findings our study correlate also correlated with the following studies. In 2015 Teymourian H et al. [8], conducted a study on 100 patients with American Society ofAnesthesiologist (ASA) class 1, 2 candidate for emergency acute appendicitis surgery and age ranges 25-75 years were enrolled in the study and randomly allocated to ketamine or magnesium groups. Patients in ketamine group received ketamine gargle (0.5mg/kg) and magnesium group received magnesium sulfate gargle (20mg/kg upto 30ml dextrose water 20%) 15 mins before the operation. Patient complaint of POST and its severity measured by VAS were recorded at baseline in recovery room, and then 2, 4, and 24hrs after operation. They concluded that magnesium at low dose decreases sore throat and pain severity more effectively compared to ketamine gargle.

In 2017 Chattopadhyay S et al. [7], conducted a study , comparison between preoperative aspirin and magnesium sulfate gargle- A prospective, randomized, double- blind study. 56 patients ASA grade I and II, aged 25-50 yrs, scheduled for day care surgery, were randomly allocated to group A receiving aspirin gargle (325mg tablet) and group M receiving magnesium sulfate (20mg/kg gargle). Patients were asked to gargle with this mixture for 30s, 15min before induction of anaesthesia. Episodes of POST were measured at 0, 2, 4, 6, 9, 12, and 16h postoperatively with a four- point scale. They concluded that preoperative magnesium sulphate gargle significantly attenuated the incidence and severity of POST, especially in the early postoperative period, with no adverse effects in patients undergoing day care surgery under general anaesthesia.

Conclusion

Mgso4 gargle significantly reduces the incidence and severity of postoperative sore throat compared to ketamine gargle, hence contributing to smoother recovery and greater patient satisfaction.

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