A Comparative Study of Preoperative Ketamine and MgSO4 Nebulisation for Incidence of Post Operative Sore Throat after Endotracheal Intubation

Shalini Jain[1], Swapnil Kumar Barasker[2]

ABSTRACT

Introduction: Postoperative period consists of many complications of which sore throat (ST) has an incidence of 21-65%, which is a minor but valid reason for dissatisfaction and morbidity among patient.

Aims and Objective - To compare incidence of sore throat after nebulising preoperatively with MgSO4 and ketamine, in post operative period upto 24hours.

Material and Methods: One hundred fifty patients preoperatively assessed with ASA grade I-II, age (20-50years), females, undergoing laparoscopic cholecystectomy under general anaesthesia were enrolled. Patients were randomised into 3 groups; group MgSO4 (GM) nebulised with 3ml of 225mg isotonic MgSO4, group ketamine (GK) nebulised with 3ml containing 50mg ketamine and group saline (GS) nebulised with 3ml normal saline, for 10 minutes. General anaesthesia was induced 5minutes after nebulisation. Haemodynamic monitoring was done during nebulisation and induction. ST monitoring was done in recovery room at 2,4,8,12 and 24hours post extubation. It was graded 0-III based on the severity.

Results- The incidence of ST was 37.3% (56/150); 60% in GS (30/50), 30% in GM (15/50), 22% in GK (11/50) ($p<0.05$ for both GK and GM on comparing with GS), least with GK but insignificant on comparison with GM ($p=0.37$). Haemodynamic response to laryngoscopy was significantly ($p<0.05$) attenuated in GK.

Discussion: GK and GM had significantly reduced incidence of ST after nebulisation on comparison with control group. Among GK and GM incidence was least with GK, but was statistically insignificant. Haemodynamic attenuation in response to intubation was observed in GK.

Conclusion: Incidence of ST was significantly less with ketamine and MgSO4 nebulisation.

Keywords: Ketamine, MgSO4, Nebulisation, Sore Throat, Endotracheal Intubation

INTRODUCTION

Sore throat (ST), a common complaint of postoperative period after tracheal intubation is being considered as a minor complication, but is a valid reason of dissatisfaction and morbidity among patient.[1] The incidence of ST is 21–65% in patients receiving general anaesthesia (GA) with tracheal intubation.[2,3] Various non pharmacological and pharmacological trials have been used for attenuating ST with no proven single modality. The pharmacological methods used to reduce ST include use of beclomethasone gel, gargling with azulene sulphonate, ketamine, licorice, magnesium sulphate, etc.[4-6] N-methyl-D-aspartate (NMDA) have a proven role in nociception and inflammation.[7,8] NMDA receptors are found in peripheral nerves and in the central nervous system.[9,10] Ketamine and MgSO4 both are N-methyl-D-aspartate (NMDA) receptor antagonist. Ketamine has been used as a gargle for reducing the incidence and severity of ST due to its anti-nociceptive and anti-inflammatory effects.[6,8] It has also been used in form of nebulisation to prevent ST.[11-13]

Magnesium is an antagonist of the NMDA receptor ion channel[14] and it is available as powder, paste, or solution. It has also been used in form of nebulisation to prevent ST.[15,16]

Nebulisation can be considered better than gargle as: it is an easy way to administer the drug, smaller volume of drug is required, better patient cooperation is likely and no risk of aspiration. In the present study, effect of nebulised magnesium sulphate and nebulised ketamine for attenuating the incidence of ST was evaluated.

MATERIAL AND METHODS

The present study was carried out in the Department of Anaesthesiology, M.G.M. Medical College and M.Y. Hospital, Indore, M.P., following approval by the Institutional Ethics Committee. The study comprises of female patients posted in the routine theatre list for laparoscopic cholecystectomy.

Eligibility criteria was used to enroll patients for study. Written informed consent from the eligible patients were taken, after explaining them the study. Inclusion criteria for patients were: ASA physical status I–II, age group of 20 to 50 years, surgery in supine position under GA, duration of anaesthesia <2Hrs,upper lip bite test - I/II, thyromental distance >6.5cm, and adequate range of neck motion.

Exclusion criteria for patients were history of - preoperative sore throat or recent upper airway infection, oral surgeries, asthma, chronic obstructive pulmonary disease, head and neck surgeries, pregnant women, Mallampati grade >II, known allergies to study drug, patient on chronic medication (NSAID, Steroids), those who required more than one attempt at intubation., known smoker, subjects who cough or bucked before extubation, time of intubation >15 seconds.

The study was a prospective, randomised, double blind, comparative study done over a definite period of time. The required number of patients for study were calculated assuming

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the incidence of ST to be 65%. With expectation of incidence of ST decrease by 50% after using Ketamine or $MgSO_4$ nebulisation. For a 90% power, $\alpha = 0.05$ and $\beta = 0.01$, 144 patients (48 in each group) were required. To compensate for possible dropouts, we enrolled 150 patients (50 for each group) Patients were randomised into 3 groups with help of computer generated random number tables, with sealed opaque envelopes prepared by anaesthesiologist not part of this study. A total of one hundred fifty (fifty patients in each group) patients were enrolled in the current study. Group $MgSO_4$ (GM) nebulised with 3ml of 225 mg isotonic $MgSO_4$, Group ketamine (GK) nebulised with 1ml containing 50 mg ketamine diluted upto 3ml by NS, Group saline (GS) nebulised with 3ml normal saline. All groups were nebulised for 10 minutes.

Nebulisation was done using Omron NEC-28 nebuliser machine. GA was induced 5minutes after nebulisation in all the 3 groups. Haemodynamic monitoring was done during nebulisation and induction.

ST monitoring was done in recovery room at 0, 2, 4, 8, 12 and 24 hours post extubation. ST was graded 0-III based on severity. The study drugs were administered in a double blind fashion. Nebulisation was prepared and administered by an anaesthesiologist not part of study. Anaethesiologist intubating and collecting observation was blinded for nebulisation drugs. Patients of both the groups received same and standardised medication for induction and analgesia peri operatively. Patients of both groups received following drugs as premedication, 30mins prior to induction of anaesthesia; Inj.Glycopyrrolate (0.2mg), Inj.midazolam (0.02mg/kg).

The intra operative monitoring included continuous electrocardiography,non invasive blood pressure, pulse oximetry (SpO_2), End tidal CO_2 ($EtCO_2$) and cuff pressure monitoring. The induction regimen was standardized for all groups as followed: after 3 min of administration of oxygen, fentanyl 2.0µg/kg was injected; followed by propofol 2.0mg/kg. Immediately afterwards, Rocuronium (0.9mg/kg) was injected over a period of 5sec, followed by intubation at 60 seconds. Laryngoscopy was done using Macintosh laryngoscope blade size 3 or 4 (as per patient). The trachea was intubated with tracheal tube of internal diameter of 7–7.5 mm. The same anaesthesiologist performed the intubation in all patients. The tracheal tube cuff was inflated until no air leakage could be heard with a stethoscope at peak airway pressure of 20 cm of H_2O, which was checked intraoperatively at an interval of every 15 minutes.

Heart rate (HR) and Blood pressure mean (MAP) were recorded during nebulisation, before and just after induction and 5 minutes after induction. GA was maintained with oxygen 50% in nitrous oxide and isoflurane 1.2 MAC and atracurium maintenance 0.1mg/kg, IV ondansetron 4 mg was administered 15 min prior to end of surgery and then 8 hours in the postoperative period. IV dexamethasone 8 mg as a single dose was given as rescue antiemetic. At the completion of surgery, with the patient adequately anaesthetised, special care was taken when suctioning posterior pharynx using only blunt suction catheter. Inspiratory oxygen concentration was increased to 100%.

The neuromuscular block was reversed with IV neostigmine (50 µg/kg) and glycopyrrolate (10 µg/kg) while awaiting the return of spontaneous ventilation.

Extubation was done on return of spontaneous ventilation and patient following commands. For post operative analgesia IV paracetamol 1gm 8hourly was given.

Inj tramadol 100 mg iv infusion over half hour was given if patient complained of pain at operative site.

Patients were assessed postoperatively for 24hours, by asking questionnaire for Sore throat (ST),

Sore throat (ST)- defined as continuous throat pain

Do you have sore throat?

If the answer was no, ST was graded 0 = no sore throat;

If the answer was yes, ST was graded as follows:

I = mild (pain with deglutition)

II = moderate (pain present constantly and increasing with deglutition),

III = severe (pain interfering with eating and requiring analgesic medication)

STATISTICAL ANALYSIS

Appropriate statistical tools were used for analysis of results. Result were considered statistically significant when $p < 0.05$. Data are expressed as mean (standard deviation). To see the normality of age, weight and haemodynamics before nebulisation Shapiro Wilks test was used. To see difference in age, weight, time of intubation and duration of anaesthesia between the groups, mean and standard deviation was calculated and ANOVA was applied. Haemodynamic variables between the groups were compared with ANOVA and with in group were compared using paired t test. Difference in the incidence of ST were compared with Fischer's exact test or chi square test.

RESULTS

One hundred and fifty female patients were enrolled in the present study. Patients were randomised into three groups of 50 patients. All patients completed the study, and neither patient was lost in follow up nor excluded from analysis. There was no significant difference present between groups regarding age, weight, time of intubation and duration of anaesthesia. ($p>0.05$) The mean HR and MAP before and after nebulisation was comparable in between the groups ($p>0.05$). The change in HR and MAP within the groups was not significant during nebulisation. ($p>0.05$) (Table-1).

The HR and MAP before and after induction was comparable in between the groups ($p>0.05$). The change in MAP within the groups was not significant during induction ($p>0.05$). The change in HR within the groups was not significant between before and just after induction in GK ($p=0.717$), but was significant in GM ($p=0.002$) and GS ($p=0.004$) (Table 1 and Figure 1).

The overall incidence of ST in the present study was 37.3% (56/150). In GS, the incidence of ST was observed to be 60% (30/50). In GM, the incidence was 30% (15/50), and 22% in GK (11/50). On comparing the incidence of ST between GK with GS significant difference was present ($p=0.002$). On comparing the incidence of ST between GM with GS significant difference was present ($p=0.004$). But no significant was present on comparison between GK and GM ($p=0.37$) (Table 2 and Figure 2).

DISCUSSION

The overall incidence of ST in the current study was 37.3%, with

Group	Parameter	G.K (n=50)	GM (n=50)	GS (n=50)	p - value
Before nebulisation (0 min)	Heart Rate (/min)	86.8 (10.16)	85.2 (15.66)	87 (13.95)	0.970
	Blood Pressure (Mean)	90.6 (5.73)	92.2 (6.38)	91.4 (6.12)	0.918
During nebulisation (5 mins)	Heart Rate (/min)	89.8 (9.34)	89.2 (16.18)	86.2 (14.48)	0.906
	Blood Pressure (Mean)	91 (5.43)	92.2 (7.69)	93.4 (10.71)	0.900
After nebulisation (10mins)	Heart Rate (/min)	88.6 (9.58)	88.2 (14.13)	89.2 (13.37)	0.992
	Blood Pressure (Mean)	94.6 (5.77)	90.6 (12.76)	91.8 (12.21)	0.835
Before laryngoscopy	Heart Rate (/min)	91.4 (14.89)	87.8 (11.97)	90 (15.76)	0.923
	Blood Pressure (Mean)	95.6 (5.41)	90.2 (13.38)	92 (11.66)	0.726
Just after laryngoscopy	Heart Rate (/min)	91.8 (14.65)	99 (12.17)	102.8 (14.09)	0.457
	Blood Pressure (Mean)	89.8 (7.19)	91.8 (7.01)	93.4 (9.32)	0.775
After 5mins of laryngoscopy	Heart Rate (/min)	91 (14.26)	89.8 (11.97)	91.2 (14.55)	0.985
	Blood Pressure (Mean)	87 (8.12)	86.6 (10.16)	86.8 (12.65)	0.998

Table-1: Haemodynamic parameters (HR and MAP) during nebulisation and laryngoscopy

ST at	Grade	GK (n=50)	GM (n=50)	GS (n=50)	p-value
0 hr	I	2	3	6	0.279
	II	0	0	0	
2 hrs	I	1	1	5*	0.027*
	II	2	3	6	
4 hrs	I	2	3	11*	0.000*
	II	4	6	12*	
8 hrs	I	5	5	8	0.062
	II	3	4	9	
12 hrs	I	4	4	8	0.076
	II	2	3	6	
24 hrs	I	2	2	4	0.086
	II	0	0	3	

Table-2: Incidence of ST

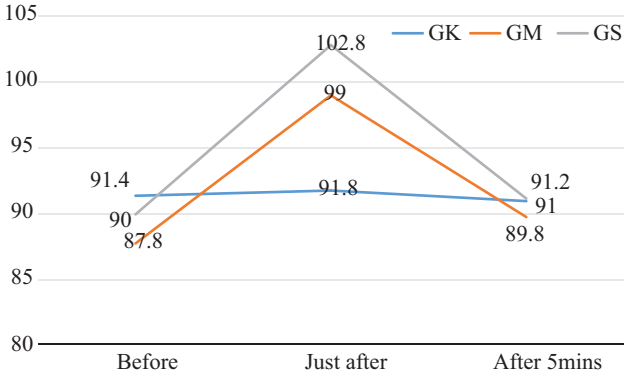

Figure-1: Change in HR during laryngoscopy

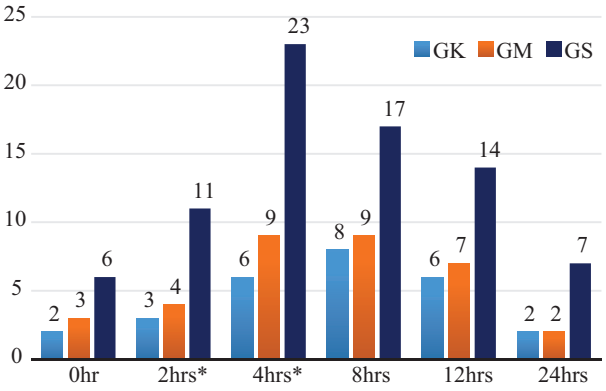

Figure-2: Incidence of ST

60% in control group, 30% and 22% in groups nebulised with $MgSO_4$ and ketamine respectively. In previous studies incidence of ST was 21–65% in patients receiving GA with tracheal intubation.[2,3] In the present study, it was observed that there was a significant reduction in ST overall incidence and attenuation at 2 hrs and 4 hrs in post operative period on nebulisation with ketamine and $MgSO_4$ in comparison to Normal saline.

Ahuja et al[11] in their study reported the incidence of ST at 2 and 4 hr was significantly reduced with ketamine nebulisation. In a similar study, by S Jain et al[12] ketamine nebulisation was compared with ketamine clonidine mixture nebulisation, with attenuation was found to be greater with later. But significant difference between the two was not reported. A Bhagyashree et al[13] compared Ketamine nebulisation is an effective alternative to ketamine gargle in attenuating ST, with no statistical difference between the two. Both the groups showed more than 50% reduction from the reported incidence.

Gupta et al.[15] also assessed the efficiency of preoperative nebulization of magnesium sulfate and found that the incidence and severity of POST were reduced at rest and on swallowing at all-time points ($P < 0.05$).Yadav et al[16] observed magnesium sulfate lessened the pain during swallowing at 4 h postsurgery compared to normal saline.

The proposed mechanism of effect of ketamine and $MgSO_4$ was possibly due to topical effect that attenuated the local inflammation and also due to peripheral analgesic effect.

Borazan et al[17] used magnesium lozenge ($MgCl_2$, 610mg) which significantly decreased the incidence of POST at 2hrs and 4hrs, but not at 24 hrs postoperatively.

In 1999, McHardy FE and Chung F[18] concluded that non pharmacological factors increases the incidence of POST, of which direct trauma to larynx and pharynx where the main cause. The highest incidence of sore throat and other airway related symptoms tends to occur in patients who have undergone tracheal intubation.

Several pharmacological agents have been found to prevent POST. Of which first came local anaesthetic agents.[19] Lidocaine is the most popular agent in this category[19,20] but some authors found them not to be beneficial.[18] In 2014, David m kalil et al[21] in their meta analysis review of 11 RCTs examined evidence of nonsteroidal and nonlocal anesthetic topical pharmacological interventions to prevent POST. Of which ketamine[6,22-24] and aspirin gargle[25] were most promising.

It is known that NMDA has role in inflammation and nociception. NMDA receptors are present in peripheral nerves and CNS. So,

NMDA receptor antagonist like ketamine and $MgSO_4$ attenuate ST by acting on peripheral nerves of pharyngeal mucosa. Both ketamine and $MgSO_4$ have been used for analgesia by their systemic action. The dose and route used in current study is less likely to have systemic effects. In previous studies haemodynamic effect of nebulisation with ketamine and $MgSO_4$ was not evaluated. In current study it was observed that the change in HR was significantly less on laryngosopy in ketamine group. This could be due to local analgesic effect of ketamine or due to systemic action. As 30% of drug deposits in alveoli when nebuliser produces particles of size 5-8micron.

Limitation

Serum levels of MgSO4 and ketamine were not measured. Since the nebuliser used in the study produced droplets of size 5-8 microns, only 37-60% of the drug was deposited in oropharynx.

CONCLUSION

Pre operative nebulisation with ketamine and MgSO4 is simple and easy answer to reduce the incidence of ST in patients undergoing tracheal intubation under GA.

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