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Original Research Article

Magnesium Sulphate versus Ketamine Nebulisation on the Incidence of Post-Operative Sore Throat: A Randomised Control Study

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Abstract

Background: In this study, we wanted to evaluate the efficacy of Magnesium Sulphate and Ketamine nebulisation in prevention of Post-Operative Sore Throat (POST).

Methods: The present hospital based randomized comparative clinical study was conducted on 140 patients, who underwent surgeries with endotracheal intubation, after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Results: At 0, 6 and 12 hours post extubation, there was significant difference in Post-Operative Sore Throat grades between Magnesium Sulphate and Ketamine groups ($p < 0.0001$, $p = 0.04$ and $p = 0.014$ respectively).

Conclusion: Both Magnesium Sulphate and Ketamine nebulisation reduced the frequency and severity of Post-Operative Sore Throat, but Magnesium Sulphate nebulisation has been shown to be significantly better than Ketamine nebulisation in this regard, contributing to a smoother recovery and greater patient satisfaction.

Keywords: Ketamine, Magnesium Sulphate, Post-Operative Sore Throat.

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 are 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 & nonpharmacological have been studied to reduce the incidence & severity of post extubation sore throat. Among the non-pharmacological methods, smaller sized tubes,[1,2] high volume low pressure endotracheal tubes,[3] careful instrumentation of the airway, minimizing

the number of laryngoscopy attempts, gentle oropharyngeal suctioning, filling the cuff with an anaesthetic gas mixture,[4] minimizing intra-cuff pressure < 20 mm hg, fully deflating the cuff before extubation, have been reported to decrease the incidence of sore throat. Pharmacological measures for attenuating sore throat are lubricating with Lignocaine jelly,[5] Betamethasone gel, IV Dexamethasone,[6] beclomethasone inhalation,[7] Fluticasone inhalation, Magnesium lozenges,[8] gargling with Aspirin,[9] azulene sulphonate, Ketamine, Benzydamine Hydrochloride[10] and intra-cuff administration of alkalised Lignocaine[11] are some of the strategies used to reduce Post-Operative Sore Throat.

However, each intervention is associated with side-effects which may not be desirable. Hence, there was a need for an intervention which would prevent rather than treat Post-Operative Sore Throat which would be 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. 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).[12] Though there are several measures available for reduction of post-operative sore throat, the problem still remains unresolved.

Hence, newer methods to address this complication had to be developed and the effectiveness of Ketamine nebulisation and Magnesium Sulphate nebulisation in prevention of POST needed to be studied. We undertook a study on the effect of Ketamine nebulisation and compared it with Magnesium Sulphate nebulisation in prevention of Post-Operative Sore Throat. The main advantage of nebulised drugs is that they are deposited directly into the respiratory tract and thus higher drug concentrations can be achieved in the bronchial tree and pulmonary bed with fewer adverse effects than when systemic route is used.

Aims and Objectives

- To compare the efficacy of Magnesium Sulphate nebulisation and Ketamine nebulisation in prevention of Post-Operative Sore Throat in patients undergoing endotracheal intubation for surgeries under general anaesthesia.
- To assess hemodynamic responses after nebulisation and during induction of general anaesthesia.
- To know the safety profile of the drugs.

Methods

A total of 140 patients posted for surgeries under general anesthesia with endotracheal intubation were enrolled in the study. Patients in Ketamine group (Group K) received Ketamine nebulisation (50 mg, 1 ml with 2 ml of normal saline) and Magnesium Sulphate group (Group M) received Magnesium Sulphate nebulisation (225 mg, 3 ml) 10 minutes before induction. Patient complaints of Post Operative Sore Throat and its severity was measured and recorded at baseline in the recovery room and then at 0, 6, 12th hour after surgery.

POST was graded on a four point scale(0-3) [16]:

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)

Inclusion Criteria

- ASA physical status I and II.

- Age between 20 to 60 years of either sex.
- Patients who have given written informed consent.
- Patients undergoing elective surgeries in supine position under general anaesthesia.
- Surgeries lasting for approximately two hours.

Exclusion Criteria

- Patients refusing to participate in the study.
- Patients with anticipated difficult intubation.
- Patients with neuromuscular disease, allergy or hypersensitivity to the drugs.
- Patients with history of pre-operative sore throat, history of oral surgeries, head and neck surgeries, on non-steroidal anti-inflammatory drug medication, history of smoking, chronic obstructive pulmonary disease.
- Patients who required more than one attempt at intubation.

Sample Size

Calculation of sample size was based on the assumption that the incidence of POST is 65 % and to show a 20 % difference in the incidence at $\alpha = 0.05$, confidence interval of 95 % and a power 80 %, we required a sample size of 70 patients per group (on adding 10 % of patients for possible loss to follow up).

The sample size was calculated using the formula,

$$p = \frac{p1 + rp2}{1+r}$$

$$n \geq \frac{[Z_{1-\alpha/2} \sqrt{(r+1)\, p\,(1-p)} + Z_{1-\beta} \sqrt{rp_1(1-p_1) + p_2(1-p_2)}]^2}{r\,(p_2-p_1)^2}$$

Where,

r = ratio between number of patients in each group.

p_1 and p_2 = percentage of complete responders in each group.

Method of collection of data

Seventy patients aged between 18 years and 60 years of physical status ASA grade 1 and ASA grade 2 undergoing elective surgeries were included in the study after ethical clearance from the college ethical committee.

Each patient was visited pre-operatively and the procedure explained and written informed consent was obtained. Complete blood count (CBC), blood grouping, blood sugar, bleeding time, clotting time, blood urea, serum creatinine, serum electrolytes (sodium, potassium, chloride), chest x-ray, ECG were done as institutional protocol. All patients were pre-medicated with tablet alprazolam 0.5 mg previous night of surgery.

Statistical Methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented in Mean ± SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5 % level of significance.

The following assumptions on data are made.

- Dependent variables should be normally distributed.
- Samples drawn from the population should be random. Cases of the samples should be independent.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

Chi-square/ Fisher's exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Non-parametric setting was used for qualitative data analysis.

Statistical Software

The statistical software namely Statistical Package for Social Sciences (SPSS 21.0) was used for the analysis of the data.

Results

Table 1

Incidence of Sore Throat at 0 Hour							
			POST 0 hours			**Chi-square**	**P**
		Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	21.5	< 0.0001
Group K	N	0	0	42	28		
	%	0	0.00 %	60.00 %	40.00 %		
Group M	N	0	16	41	13		
	%	0	22.90 %	58.60 %	18.60 %		
Incidence of Sore Throat at 6th Hour							
		POST 6 Hours				**Chi-square**	**P**
		Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	6.4	0.04
Group K	N	26	38	6	0		
	%	37.10 %	54.30 %	8.60 %	0		
Group M	N	26	44	0	0		
	%	37.10 %	62.90 %	0.00 %	0		
Incidence of Sore Throat at 12th Hour							
		POST 12 Hours				**Chi-square**	**P**
		Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	5.99	0.014
Group K	N	37	33	0	0		
	%	52.90 %	47.10 %	0	0		
Group M	N	51	19	0	0		
	%	72.90 %	27.10 %	0	0		

At 0 hours post extubation, in Ketamine group, 60 % had Grade 2 sore throat, 40 % had Grade 3 sore throat. In Magnesium Sulphate group, 22.9 % had Grade 1 sore throat, 58.6 % had grade 2 sore throat and 18.6 % had Grade 3 sore throat. There was significant difference in post-operative sore throat grade between two groups ($p < 0.0001$).

At 6 hours post extubation, in Ketamine group, 37.1 % had Grade 0 sore throat, 54.3 % had Grade 1 sore throat and 8.6 % had Grade 2 sore throat. In Magnesium Sulphate group, 37.1 % had Grade 0 sore throat, 62.9 % had Grade 1 sore throat. There was significant difference in post-operative sore throat grade between the two groups ($p = 0.04$).

At 12 hours post extubation, in Ketamine group, 52.9 % had Grade 0 sore throat, 47.1 % had Grade 1 sore throat and in Magnesium Sulphate group, 72.9 % had Grade 0 sore throat and 27.1 % had Grade 1 sore throat. There was significant difference in POST grade between two groups ($p = 0.014$).

Discussion

Ketamine and Magnesium Sulphate both can block N-methyl- D-aspartic acid (NMDA) receptor. Ketamine relaxes the tracheal muscle contraction through a mechanism independent of NMDA receptors. [13] 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 Sulphate could probably block the Ca2+ entrance to tracheal muscle in a more effective manner. Recent reports of

the incidence of Post-Operative Sore Throat following anaesthesia have claimed that the incidence of Post-Operative Sore Throat does not necessarily reflect damage caused by the tracheal tube cuff but more of increased muscle contracture. By preventing central sensitization, pre-emptive analgesia along with intensive multimodal analgesic interventions could theoretically reduce Post-Operative Sore Throat incidence and severity. Hence, in our study, we compared pre-emptive Ketamine nebulisation with Magnesium Sulphate nebulisation as a means to prevent Post-Operative Sore Throat.

Increased incidence of sore throat has been reported in patients when succinylcholine is used to facilitate endotracheal intubation (14 % in the group that received succinylcholine as compared to 17 % in the group that did not). [14] Hence, in our study, we did not use succinylcholine for endotracheal intubation. All intubations were facilitated using Inj. Vecuronium 0.1mg/kg iv. 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 use 7.5 mm tube for female patients and 8.5 mm 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. [3]

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 to decrease and reduces markedly when the pressure reaches 30 mmHg. In our study, we did not monitor intra-cuff pressure, but we kept peak airway pressure at 20 cm of water where no air leak was heard.

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 in turn leads to increased incidence of post-operative sore throat, our study used O2 : N2O in a ratio of 1 : 1 with fresh gas flow of 4 litres.

The incidence of Post-Operative Sore Throat varied with the type of questioning employed. In our study, we have used a scale in which patient is asked about his/her complaints in the post-operative period. If the patient does not complain of sore throat, then a direct question pertaining to sore throat, cough, and hoarseness was asked.

Placement of throat pack around the endotracheal tube increases the incidence of POST. [15] However, in our study, throat pack was not inserted in any of the patients.

Teymourian H et al. [13] conducted a study on 100 patients with ASA grade I and II randomly allocated to Ketamine or Magnesium Sulphate groups. Patients in Ketamine group received Ketamine gargle (0.5 mg/kg) and Magnesium Sulphate group received Magnesium Sulphate gargle (20 mg/kg up to 30 ml dextrose water 20 %) 15 minutes before the surgery. Patient complains of POST and its severity which was measured by VAS was recorded at baseline in recovery room, and then 2, 4, and 24 hours after operation. Number of patients with sore throat were significantly lower in Magnesium Sulphate group compared to Ketamine group at 2 hours ($p = 0.032$), 4 hours ($p - 0.02$) and 24 hours ($p = 0.01$). They concluded that Magnesium at low dose decreases sore

throat and pain severity more effectively compared to Ketamine gargle.

We chose nebulisation of the drugs over gargling as gargling required large volume which came with an additional risk of aspiration and the drugs were not palatable. Also, the main advantage of nebulised drugs is that they are deposited directly into the respiratory tract and thus higher drug concentrations can be achieved in the bronchial tree and pulmonary bed with fewer adverse effects than when systemic route is used. [16]

In our study, the number of male patients were 36 in ketamine group and 29 in magnesium sulphate group. The number of female patients were 34 in ketamine group and 41 in magnesium sulphate group. When compared, the difference was not found to be statistically significant ($p = 0.23$). [17]

At 0 hours post extubation, in Ketamine group, 60 % had Grade 2 sore throat, 40 % had Grade 3 sore throat. In Magnesium Sulphate group, 22.9 % had Grade 1 sore throat, 58.6 % had Grade 2 sore throat and 18.6 % had Grade 3 sore throat. There was significant difference in Post-Operative Sore Throat grade between two groups ($p < 0.0001$).

At 6 hours post extubation, in ketamine group, 37.1 % had Grade 0 sore throat, 54.3 % had Grade 1 sore throat and 8.6 % had Grade 2 sore throat. In MgSo4 group, 37.1 % had Grade 0 sore throat, 62.9 % had Grade 1 sore throat. There was significant difference in post-operative sore throat grade between the two groups ($p = 0.04$).

At 12 hours post extubation, in Ketamine group, 52.9 % had Grade 0 sore throat, 47.1 % had Grade 1 sore throat and in Magnesium Sulpahte group, 72.9 % had Grade 0 sore throat and 27.1 % had Grade 1 sore throat. There was significant difference in POST grade between two groups ($p = 0.014$). At 24 hours post extubation in Ketamine Group, 71.4 % had Grade 0 sore throat, 28.6 % had Grade 1 sore throat and in MgSO4 group, 82.9 % had Grade 0 sore throat and 17.1 % had Grade 1 sore throat. There was no significant difference in POST grade between two groups ($p = 0.1$). In the study conducted by Teymourian H et al. [13] in 2015, number of patients with sore throat were significantly lower in magnesium group compared to ketamine group ($p = 0.01$). This was clinically relevant to our study.

In our study, both Ketamine and Magnesium Sulphate nebulisation have reduced the incidence and severity of POST but Magnesium Sulphate nebulisation when compared to Ketamine nebulisation has proven to be better in reducing the incidence and severity of POST. Our results are comparable with the study conducted by Teymourian H et al. [13]

Conclusion

In conclusion of our study, both Magnesium Sulphate and Ketamine nebulisation have reduced the incidence and severity of Post-Operative Sore Throat but Magnesium Sulphate nebulisation has significantly proven to be better than Ketamine nebulisation in reducing the incidence and severity of Post-Operative Sore Throat, hence contributing to smoother recovery and greater patient satisfaction.

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