Original Article

Safety and satisfaction level of magnesium sulphate following two routes of administration for the prevention of postoperative sore throat

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Abstract

Background: Tracheal intubation for general anaesthesia can be associated with distressing postoperative sore throat (POST). Different pharmacological agents via different routes have been studied for its prevention, but few studies have focused on the acceptability and safety of agents employed. This study compared the safety profile with use of intravenous and nebulised magnesium sulphate ($MgSO_4$), as well as patients' satisfaction level.

Methods: Eighty-four patients were randomized into three groups. Group I patients were nebulised with 3mls of normal saline (NS) and received 30mg/kg of IV $MgSO_4$ in 50mls of NS. Group II patients were nebulised with 225mg (3mls) of isotonic $MgSO_4$ and infused with 50mls of NS. Patients in group III were nebulised with 3mls of NS and infused with 50mls of NS.. Incidence of POST was assessed using a four-point scale proposed by Stout et al. The safety of $MgSO_4$ was assessed by measuring serum magnesium levels, and Likert scale was used to assess satisfaction levels following use of study medication. Data were analysed using SPSSv22.

Results: There were 84 patients with mean age of 35.2 years. Overall incidence of POST was 30.1%. Although the serum magnesium level was statistically higher among group I patients ($p < 0.01$), all the patients in this study had serum magnesium level within the normal limit. No patient expressed dissatisfaction with the use of $MgSO_4$.

Conclusion: Magnesium sulphate, administered intravenously or by nebulisation, is effective in reducing postoperative sore throat. Patients expressed satisfaction and there was no significant rise in serum magnesium levels detected.

Keywords: Tracheal intubation, $MgSO_4$, sore throat

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INTRODUCTION

Tracheal intubation for general anaesthesia is a common procedure in Anaesthetic practice. It is often associated with distressing complications such as postoperative sore throat, hoarseness and cough. Different pharmacological agents via different routes have been studied for the prevention of POST. However, few studies have focused on the safety of the agents used for this purpose. In this study, the effectiveness of intravenous and nebulised magnesium sulphate was compared. The safety of administration via the two routes was also compared. Over the years, non-pharmacological and pharmacological means have been used in an attempt to reduce the burden of POST. The non-pharmacological methods are simple and include the use of smaller sized tracheal tubes, gentle oropharyngeal suctioning, careful airway instrumentation, minimising number of laryngoscopy and intubation attempts, intubation after a fully relaxed larynx, minimising the intracuff pressure to less than 25cmH_2O, etc.

Some of the pharmacological agents used include different forms and routes of lidocaine,[1] steroids such as dexamethasone,[2] non-steroidal anti-inflammatory drugs (NSAIDs) such as benzydamine hydrochloride,[3] and N-methyl-D-aspartate (NMDA) receptor antagonists such as ketamine and magnesium sulphate.[4]

Magnesium sulphate is a common medication in clinical practice. In obstetric practice, it is the drug of choice for the prevention of seizure in women with pre-eclapmsia and prevention of seizure recurrence among women with eclampsia.[5,6] It has also been used in respiratory medicine for the management of acute and chronic asthma.[7] Magnesium sulphate has some minor side effects such as feeling warmth, facial flushing, nausea, vomiting, muscle weakness, somnolence, and dizziness. In high serum concentrations, more serious side effects such as loss of patellar reflex and respiratory depression can occur.[8]

Patients' satisfaction following medical intervention has become increasingly popular and play a central role in deciding upon treatment strategies. Studies have shown that adverse drug reactions play a significant role in a patient's level of satisfaction.[9] Evans et al[10] observed that an active process of getting feedback from patients is important in improving the standard of care. Gandhi et al[11] who used the Likert scale to get feedback from patients reported that the overall level of satisfaction was significantly lower among patients who experienced an adverse drug reaction compared to those who did not. Magnesium sulphate has been in use for several decades and found to be well tolerated, with minimal adverse effects, when used at therapeutic doses.[12, 13]

Systemic and local administration of magnesium sulphate has been shown to effectively attenuate the occurrence of airway complications associated with tracheal intubation.[14,15] However, there is paucity of literature in our environment that compared the safety and satisfaction level of this medication when used for the prevention of POST. This study therefore compared the safety and level of satisfaction of intravenous and nebulised magnesium sulphate for prevention of POST and provides evidence-based recommendations on its prevention in our environment.

METHODOLOGY

Following the institutional Research and Ethical Committee approval with no. UPTH/ADM/90/S.II/VOL.XI/919, a prospective, randomized, double-blind, placebo-controlled study was conducted in which 84 ASA I & II patients who had abdominal surgery under combined epidural and general anaesthesia with tracheal intubation were recruited. An informed written consent was obtained from the participants of this study. All patients with anticipated difficult airway, anticipated prolonged surgery lasting more than three hours, history of smoking, airway complaints, ASA III and higher, and emergency cases were excluded from the study. Sample collection commenced in mid-December 2021 and continued till the last sample was collected on March 24th 2022.

Eighty-four patients (32 males and 52 females) aged18 – 65 years who met the inclusion criteria were randomly allocated into three groups using a simple randomisation technique.

Group I (n = 28) patients were nebulised with 3ml of normal saline (placebo), and received 30mg/Kg of IV $MgSO_4$ in 50ml of normal saline.

Group II (n = 28) patients were nebulised with 225mg (3ml) of isotonic $MgSO_4$ and infused with 50ml of normal saline (placebo).

Group III (n = 28) patients were nebulised with three ml of normal saline (placebo) and infused with 50ml of normal saline (placebo).

Intravenous medication was administered after induction and tracheal intubation to minimise the clinical surrogates of magnesium toxicity. Electrocardiography, non-invasive blood pressure, and pulse oximetry were recorded and continuously monitored in all patients throughout anaesthesia and surgery. Anaesthesia was induced with 2mg/kg of intravenous propofol plus 2µg/kg of fentanyl, and tracheal intubation was facilitated with intravenous suxamethonium, 2mg/kg. Females were intubated using size 7mm internal diameter endotracheal tube, while males were intubated using a size 8mm tube. All the endotracheal tubes were lubricated with chlorhexidine gel.[17] Direct laryngoscopy and intubation were performed by the same researcher Thereafter, the endotracheal tube cuff was inflated and maintained at 25cmH_2O using a hand-held cuff manometer (AMBU VBM CE0123 model). The cuff pressure was checked every 30 minutes to ensure a constant intra-cuff pressure.

Anaesthesia was maintained with infusion of 0.025 – 0.2mg/kg/min of propofol and muscle relaxation with 0.1mg/kg of intravenous pancuronium. Intraoperative analgesia was achieved with 0.5 - 1mg/kg of 0.5% plain bupivacaine via epidural catheter which was activated immediately after intubation.

At the end of surgery, the oropharynx was suctioned under direct vision, and anaesthetic agents were discontinued. Reversal of residual neuromuscular blockade was achieved using 10µg/kg of intravenous glycopyrrolate followed by 50µg/kg of intravenous neostigmine. With clinical evidence of adequate reversal and stable vital signs, endotracheal tube was fully deflated and patient was extubated and subsequently transferred to the post anaesthesia care unit (PACU) where essential monitors were then attached for monitoring of non-invasive blood pressure, pulse rate, oxygen saturation and any complications arising from surgery or administration of study medication.

The time of arrival in PACU (estimated at about 10minutes post-extubation) was recorded as 0hour and patients were interviewed using a scale of 0 to 3 to determine incidence and severity of POST as follows:

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 in voice or hoarseness, associated with throat pain). [18]

Postoperatively, blood sample was collected from the patients for serum magnesium estimation at the time of arrival in PACU, which is used to determine the safety of magnesium sulphate, while the Likert scale[16] was used to assess patients' level of satisfaction following administration of study medication, where score 1= very unsatisfied and 5= very satisfied. The occurrence of POST was assessed using a four-point scale proposed by Stout et al.[18] One patient was excluded because the surgery lasted beyond one hundred and eighty minutes unexpectedly. The proforma for data collection was used to collect all data.

Data were analysed using Statistical Product and Service Solutions (SPSS) version 22 software manufactured by IBM Corp in

Armonk, New York, USA. Tables and charts were used to present data as appropriate. Quantitative data such as incidence of postoperative sore throat was presented as frequencies and proportions. The Chi-Square test or Fisher's Exact test was used to test for difference in proportions, while the independent t-test was used to test for difference in mean between any two groups. The differences in mean across the three groups was assessed using one-way analysis of variance (ANOVA) test and the Duncan multiple range test (DMRT). A p-value of less than or equal to 0.05 was considered statistically significant.

RESULTS

Of the 84 patients recruited, 83 completed the study as one patient was excluded because the surgery lasted beyond one hundred and eighty minutes unexpectedly. The three groups were statistically similar in terms of age, weight, height, BMI, and American Society of Anesthesiologists' (ASA) physical status classification, duration of laryngoscopy, intubation attempts, and duration of surgery (Table 1 and 2). The incidence of POST was found to be 30.1% (25)(Figure 1).

Table 3 showed the mean and range of the serum magnesium level across all three groups. The range for Groups I, II, and III were 1.8 - 2.2mg/dl, 1.6 – 2.1mg/dl, and 1.6 – 2.1mg/dl respectively. The mean values were 1.98±0.12, 1.86±0.17 and 1.82±0.82 for groups I, II, and III respectively. Although there was a significant statistical difference among these groups ($p < 0.01$), the ranges were all within the normal serum level, without any incidence of hypermagnesaemia. A statistically significant difference in serum magnesium was also seen between groups I and II (Table 4).

The level of satisfaction across all three groups following administration of study medications is illustrated in table 5. Both routes of drug administration were well tolerated by all patients and no patient expressed dissatisfaction with either the nebulised or intravenous drug administration, and there was no statistically significant difference among the three groups ($p = 0.34$ for the nebulisation and $p = 0.44$ for the intravenous administration).

Table 1: Patients demographic characteristics across study groups

Variables	Group 1 (Intravenous) n=27	Group 2 (Nebulised) n=28	Group 3 (Control) n=28	χ^2/ANOVA	p-value
Age(years) n(%)					
10-19	1 (3.70)	1 (3.57)	1 (3.57)		
20-29	8 (29.63)	7 (25.0)	12 (42.86)		
30-39	8 (29.63)	9 (32.14)	9 (32.14)	3.70	0.883
40-49	5 (18.52)	7 (25.0)	4 (14.29)		
≥50	5 (18.52)	4 (14.29)	2 (7.14)		
Mean (SD)	36.25±11.17	37.79±12.03	32.71±9.05	1.62^{β}	0.205
[Range]	[12-54]	[19-67]	[12-52]		
Weight (kg)					
Mean (SD)	78.49±11.57	76.89±10.41	81.13±11.39	1.04^{β}	0.360
[Range]	[59-105]	[58-95]	[61-107]		
Height (m)					
Mean (SD)	1.70±0.0412	1.70±0.036	1.69±0.048	0.83^{β}	0.439
[Range]	[1.62-1.79]	[1.62-1.76]	[1.54-1.75]		
BMI					
Mean (SD)	26.99±3.642	26.23±2.93	28.37±4.298	2.47^{β}	0.091
[Range]	[21.94-37.20]	[21.02-31.89]	[23.03-41.74]		
ASA class (n (%))					
1	18 (66.67)	16 (57.14)	13 (46.43)	2.63	0.269
11	9 (33.33)	12 (42.86)	15 (53.57)		

n = number

Table 2: Intraoperative clinical characteristics such as duration of laryngoscopy, intubation attempts, duration of surgery and surgery complications in intravenous $MgSO_4$, nebulised $MgSO_4$ and placebo groups

Variables	Group I (Intravenous) n=27	Group II (Nebulised) n=28	Group III (Control) n=28	χ^2/ANOVA	p-value
Duration of Laryngoscopy (secs)					
Mean (SD) *[Range]*	17.04±4.96 [11-30]	15.07±3.43 [10-24]	16.18±5.767 [9-35]	1.17^{β}	0.32
Intubation Attempts n (%)					
1	24 (88.9)	26 (92.9)	25 (89.3)		
2	2 (7.4)	2 (7.1)	3 (10.7)	2.33	0.68
3	1 (3.7)	0 (0.0)	0 (0.0)		
Mean (SD) [Range]	1.18±0.47 [1-3]	1.07±0.26 [1-2]	1.10±0.32 [1-2]	0.63^{β}	0.53
Duration of Surgery (min)					
Mean (SD) [Range]	114.71±31.22 [70-131]	124.57±22.23 [76-162]	117.79±21.16 [75-132]	1.11^{β}	0.33
Complications n (%)					
Yes	0 (0)	0 (0)	0 (0)		
No	27 (100)	28 (100)	28 (100)		

Statistically significant (p≤0.05),* *c^2 =*** *Chi-Square, Analysis of Variance = ANOVA Test* $^{\beta}$
n = number

Table 3: Comparison of serum magnesium across Group I (Intravenous $MgSO_4$), Group II (nebulised $MgSO_4$), and Group III (Placebo)

Variables	Group I (Intravenous) n=27	Group II (Nebulised) n=28	Group III (Control) n=28	ANOVA	p-value
Serum Magnesium					
Mean (SD) *[Range]*	1.98±0.12 [1.8-2.2]	1.86±0.17 [1.6-2.1]	1.82±0.18 [1.6-2.1]	7.62^{β}	**<0.01***

**Statistically significant (p≤0.05), Analysis of Variance = ANOVA Test* $^{\beta}$

Table 4: Serum magnesium across groups 1 (intravenous) and 2 (nebulised) in the study

Variables	Group1 (Intravenous) n=27	Group 2 (Nebulised) n=28	t-test	p-value
Serum Magnesium				
Mean (SD) *[Range]*	1.98±0.12 [1.8-2.2]	1.86±0.17 [1.6-2.1]	3.02^{μ}	**<0.01***

Statistically significant (p≤0.05),* ***t-test**=Student t-test* $^{\mu}$

Table 5: Likert scale to assess level of satisfaction with nebulised and Intravenous medications across intravenous $MgSO_4$, nebulised $MgSO_4$ and placebo groups

Variable	Group I (Intravenous) n=27	Group II (Nebulised) n=28	Group III (Placebo) n=28	
	n (%)	n (%)	n (%)	
(Nebulised medication)				
Very Unsatisfied (1)	0 (0.0)	0 (0.0)	0 (0.0)	
Unsatisfied (2)	0 (0.0)	0 (0.0)	0 (0.0)	
Neutral (3)	3 (11.1)	2 (7.1)	2 (7.1)	0.34
Satisfied (4)	11 (40.7)	17 (60.7)	10 (35.7)	
Very satisfied (5)	13 (48.2)	9 (32.2)	16 (57.2)	
(Intravenous medication)				
Very Unsatisfied (1)	0 (0.0)	0 (0.0)	0 (0.0)	
Unsatisfied (2)	0 (0.0)	0 (0.0)	0 (0.0)	
Neutral (3)	3 (11.1)	2 (7.1)	4 (14.3)	0.44
Satisfied (4)	11 (40.7)	15 (53.6)	8 (28.6)	
Very satisfied (5)	13 (48.2)	11 (39.3)	16 (57.1)	

**Statistically significant ($p \leq 0.05$)*
n=number

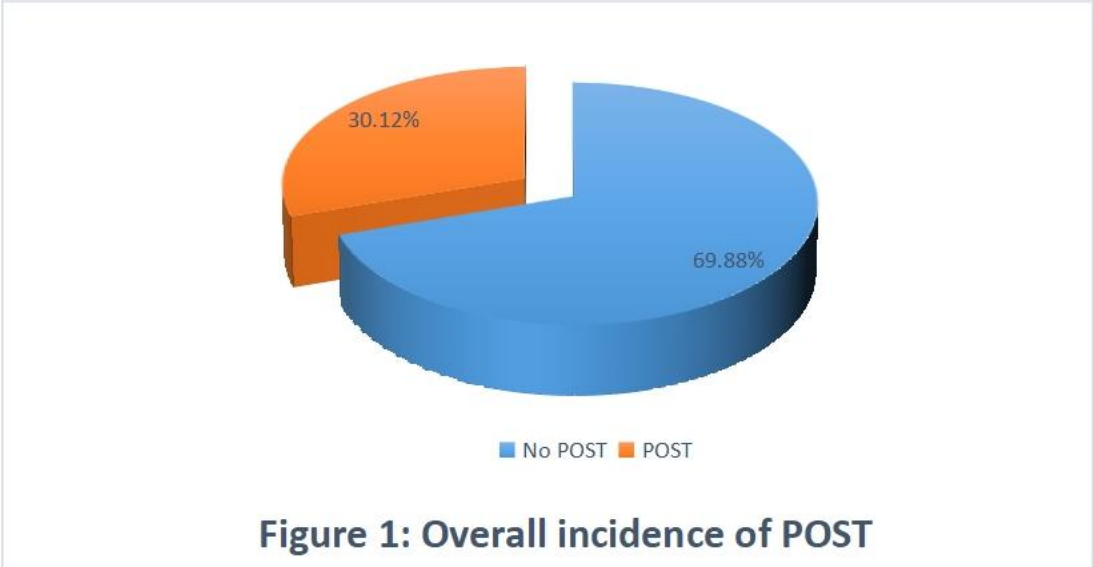

Figure 1: Overall incidence of POST

DISCUSSION

This study showed that magnesium sulphate was effective in reducing the incidence and severity of POST when administered intravenously or via the nebulised route. Postoperative sore throat is a relatively minor but distressing postoperative airway complication. In similar studies, Orji et al[19] reported an incidence of 30.3%, while Jain et al[20] reported an incidence of 37.3%. These were similar to the finding in this study.

It has also been shown by this study that it is safe to use $MgSO_4$, at a dose of 30mg/kg intravenously and 225mg by nebulisation, for the prevention of POST. All the patients in the three groups had serum magnesium level within the normal limits The normal laboratory serum magnesium level is about 1.6mg/dl – 2.5mg/dl (1.32mEq/L – 2.06mEq/L). The minor side effects of magnesium can be seen at serum concentrations of 4 – 7mg/dl (3.29 – 5.76mEq/L), while absent patellar reflex is seen at 7 - 12mg/dl (5.76 – 9.87mEq/L) and respiratory depression occurs at >12mg/dl (9.87mEq/L). Cardiac dysfunction can be observed at > 30mg/dl (>24.69mEq/L). [21]

The administration of magnesium sulphate as an aerosol does not significantly increase the serum magnesium level. This lack of evidence of systemic absorption following nebulisation with magnesium sulphate was reported by Rajan et al[22] and was demonstrated in this study as no statistically significant difference was seen between nebulised and control groups. This finding was corroborated by Bessmertny et al[23] whose study on the safety of safety of magnesium sulphate and reported that there was no statistically significant difference in the serum magnesium level, heart rate and blood pressure between patients who were nebulised with magnesium sulphate and those who were not.

The use of intravenous magnesium sulphate at a dose of 30mg/kg could lead to a rise in serum magnesium level, but not enough to cause hypermagnesaemia. This was seen in this study and supported by the research reported by Kara and colleagues [24] who analysed the serum magnesium level of twenty-four patients who received intravenous magnesium sulphate 30mg/kg bolus, followed by 500mg/h as continuous infusion for twenty hours. Blood samples for determination of serum magnesium concentration were obtained before the start of the intravenous study-drug administration and immediately after the end of the infusion. Similar to the outcome in this study, their postoperative serum magnesium level was found to be within normal limits for all the patients, although some had upper limit of normal.

When used in clinical setting, it is important to monitor patients for minor adverse effects such as flushing, increased warmth, nausea, vomiting, headaches, muscle weakness, blurred vision, and intravenous site pain or discomfort; and serious adverse effect that would require medical intervention or admission into the intensive care unit. These adverse effects are not common when magnesium sulphate is used at low doses such as for management of Asthma and prevention of POST. In this study, no patient complained of any of these minor side effects during the postoperative period. The study by Mega et al[25] assessed the presence of adverse effects following administration of magnesium sulphate via different route and reported no serious adverse effect that required medical intervention among patients who received the drug intravenously and by nebulisation. Their findings agree with this study.

Patients' level of satisfaction plays an important role in determining the acceptability of any treatment modality or medication. Effectiveness, ease of use, and side effects are factors that determine patient's level of satisfaction following the use of medications. The more side effects recorded following the use of a medication, the lower the level of satisfaction of that medication.[9] When used for the management of preeclamptic patients, high dose magnesium sulphate according to Pritchard's regimen or its modifications is utilised. At this regimen, Smith et al[8] reported an incidence of adverse effect as low as 1.6%. Thus, at a dose of 30mg/kg intravenously or 225mg via nebulisation, incidence of side effects was found to be rare in this study. No patient in this study expressed dissatisfaction with the study medications. The satisfaction level found in this study is in keeping with studies by McDonald et al[12] and Ciarkowski et al[13] who reported that magnesium sulphate is safe when used within recommended therapeutic doses.

It is pertinent to note that although chlorhexidine in different forms have been tried in oral and pharyngeal procedures,[26,27] water-based lubricants are generally recommended for ETT lubrication rather than chlorhexidine, as the latter could cause irritation in the lower airway, and therefore is not commonly used. Besides, minimal use of chlorhexidine gel has a more localized effect compared to the use in solution form that could spread causing more irritation. In this study therefore, the ETT was minimally lubricated with chlorhexidine gel because it has no effect in preventing POST when compared to other conventional lubricants[17] which could create confounding or false negative effects.

There are some limitations in our study. Firstly, there was no baseline measurement of serum magnesium sulphate, making it difficult for an objective comparison of preoperative and postoperative serum magnesium level. Also, the use of size 7mm ID endotracheal tube for female patients and size 8mm ID ETT for males was a limitation. Different body sizes would require flexibility. And lastly, there was a variable time interval between extubation and arrival at post anaesthesia care unit (PACU).

CONCLUSION

This study has shown that intravenous and nebulised $MgSO_4$ is an effective agent for the prevention of POST. When it is used at the recommended doses for this purpose, it does not cause hypermagnesaemia, and both routes are well tolerated by patients.

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Conflicts of interest
There are no conflicts of interest

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