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Original Research Article

To Compare Effects of Nebulised Lignocaine and Nebulised Magnesium Sulfate on Tracheal Intubation Induced Pressor Response: A Randomized Control Trial

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Conflict of interest: Nil

Abstract:

Background and Aims: Laryngoscopy and tracheal intubation produces pressor and sympathoadrenal response leading to increase in heart rate, blood pressure, myocardial oxygen demand, and consequently potential dysrhythmias and myocardial ischemia/infarction. This study aimed to compare nebulized magnesium sulfate and lignocaine to attenuate the hemodynamic response to tracheal intubation and the incidence of POST.

Materials and Method: Following ethics committee approval, a double-blinded randomized controlled trial assigned patients into two groups using computer-generated randomization. Vital signs (HR, SBP, DBP, MAP) were recorded, and ten minutes before anesthesia induction, Group B received 2% nebulised lignocaine (2mg/kg), while Group A got 250mg of nebulised magnesium sulfate. Vitals were checked post-intubation at 0, 2, 4, 6, and 10 mins along grading of POST.

Results: Both groups (30 patients each), had similar baseline characteristics. Group B exhibited higher HR(87.50 ± 12.62), systolic(127.40 ± 13.20) and diastolic BP (83.27 ± 10.34), MAP(104.79 ± 8.35) compared to Group A [HR(80.33 ± 14.19), SBP(115.50 ± 14.18), DBP (74.20 ± 8.39) MAP(88.37 ± 8.70)](p<0.001) at time of intubation. Conclusion: Nebulised $MgSO_4$ is better than nebulised lignocaine in reducing the pressor response with no apparent side effects.

Keywords: Pressor Response, Nebulised Magnesium Sulfate, Nebulised Lignocaine 2%, Post-Operative Sore Throat (POST).

Introduction

Laryngoscopy and tracheal intubation after induction of general anesthesia produces pressor and sympathoadrenal responses because of somatovisceral reflexes that arise from the stimulation of the epipharynx and laryngopharynx [1]. These reflexes can lead to heightened levels of circulatory catecholamines, as well as an increase in heart rate (HR), blood pressure, myocardial oxygen demand, and potential dysrhythmias. The surge in HR and blood pressureis typically temporary, irregular, and difficult to anticipate. Studies have shown an average increase in HR and a rise in blood pressure, resulting in a decrease in the left ventricular ejection fraction [2,3]. This can have detrimental consequences for patients especially those with cardiovascular diseases, intracranial aneurysm, or mass lesions.

Various methods and drugs have been used in attenuating this response like intravenous and nebulised lignocaine, short acting opiates, short acting beta blockers like esmolol and intravenous and nebulised magnesium sulfate and dexmedetomidine [4,5]. Nebulisation allows higher mucosal bioavail-

ability and greater ease of administration while ensuring lesser systemic side effects [6–8].Magnesium sulfate has been reported to be effective in perioperative pain treatment and in blunting somatic, autonomic and endocrine reflexes in response to noxious stimuli [9,10]. Magnesium sulfate is administered as gargles, lozenges or nebulization before surgery for control of postoperative sore throat (POST) [11].Lignocaine, the first aminoamide local anesthetic, has been commonly used to suppress airway reflexes, reduce bronchial hyper-reactivity, and attenuate hemodynamic responses from intubation due to its analgesic and anti-inflammatory properties [12].

There is a gap in literature comparing nebulised magnesium sulphate and nebulised lignocaine for attenuating pressor responses due to laryngoscopy and intubation. This study aims to bridge this gap.

The primary aim of this study was to observe the alteration in Heart rate, Mean arterial pressure from baseline pre-nebulisation to the time of intubation (T_0), 2 Min (T_2), 4 min (T_4), 6 min (T_6), 8 min (T8), 10 mins (T_{10}). The secondary aim was to study the severity of Post operative sore throat (POST).

Methods:

After receiving approval from the institute ethics committee, this double-blinded randomized controlled trial was conducted in the pre-operative room and operating rooms (OR).Written informed consent was obtained from all the study participants for the purpose of this study.

Patients aged between 18 and 60 years of American society of anesthesiologists (ASA) physical status 1 and 2 and Mallampati grade 1 and 2, undergoing elective surgery lasting upto to 2 hours, requiring endotracheal intubation were included in the study.

Patients with drug allergies, BMI≥35 kg/m^2, history of head injury, ischemic heart disease (IHD), neuromuscular diseases, pregnancyand those taking more than 15 seconds to intubate were excluded from the study.

Each patient was randomly assigned to one of the two groups: Group A (Magnesium suphate group) and Group B (Lignocaine group), using computer software. The patient and the primary investigator were blinded to group allocation. The patient name with assigned group was enclosed in a sealed envelope handed over to the trained nursing officer who was responsible for administering the mentioned drug in respective patient. The nursing staff did not further participate in the study.

Nebulisation with magnesium sulphate 250 mg (Group A) or lignocaine 2mg/kg (Group B) for 15 minutes in sitting position using a fitting face mask with Comp Air Compressor Nebulizer NE-C28 model of OMRON healthcare. The primary investigator observed the side effects of the nebulised drug, like sedation or bradycardia. Post-nebulisation HR, systolic blood pressure (SBP), diastolicblood pressure (DBP), and mean arterial pressure(MAP) were recorded, following which the patient was shifted to the OR.

Upon arrival in theOR, standard monitoring devices were connected to the patient, including NIBP, ECG, pulse oximetry. Patient was premedicated with intravenous (IV) glycopyrrolate (4µg/kg), IV ondansetron (0.1 mg/kg), IV Midazolam (0.03 mg/kg) and IV fentanyl (2µg/kg). After adequate preoxygenation, general anaesthesia was induced withIV propofol (2mg/kg) and IV vecuronium (0.1 mg/kg). Laryngoscopy and intubation was done by an experienced anaesthesiologist who was also blinded to treatment group allocation.

Anaesthesia was maintained with oxygen and nitrous oxide (in a ratio of 1:1) and sevoflurane to achieve a minimum alveolar concentration (MAC) of 1.2. Neuromuscular blockade was maintained with boluses of IV vecuronium. The HR, SBP, DBP, and MAP at the time of intubation (0 minutes), 2, 4, 6, 8, 10 minutes after intubation (T_0, T_2, T_4, T_6, T_8, T_{10}) were recorded. Any noxious stimulus was avoided during the time of recording of parameters. During the surgery, any fall in SBP >30% from the baseline for >60 s was treated with IV Mephentermine 3 mg and bradycardia (HR <45/min) was treated with IV atropine 0.6 mg.

At the end of surgery, sevoflurane and nitrous oxide were discontinued, and neuromuscular blockade was reversed with intravenous neostigmine (50µg/kg) and glycopyrrolate (8µg/kg). Patients were extubated if extubationcritera was fulfilled.

The severity of postoperative sore throat (POST) was assessed by a four-point scale,(at the time of extubation, 2 hours,4 hours ,6 hours following ex-tubation), as follows(13):

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 hoarse-ness, associated with throat pain).

The sample size was calculated based on a study by Elmeligy et al. (6). Assuming 80% power and 95% confidence interval, the minimum sample size required was 25 in each group. Considering the dropout rate of 20%, 30 patients were recruited ineach group.

Statistical package for social science (SPSS) software, version 15 for Microsoft Windows (SPSS Inc., Chicago, iL, USA) was used for data analysis. Categorical data were expressed as frequency (%) and analysed using the X^2 test or the Fisher's exact test as appropriate. Continuous data were tested for normality using the Shapiro-Wilk test and were presented as either mean (standard deviation), or median (inter-quartile range). Continuous data were analysed using unpaired t-test (for normally distributed data) or Mann–Whitney U test (for skewed data). A p-value of 0.05 was considered statistically significant.

Results

Eighty two patients were assessed for the eligibility of the study. Twelve patients could not meet the inclusion criteria, while 10 patients denied consent. Finally 60 patients were randomised to receive one of the two interventions and were available for final analysis (Figure 1). No exclusion was done post-randomisation and each group contained 20 patients each.

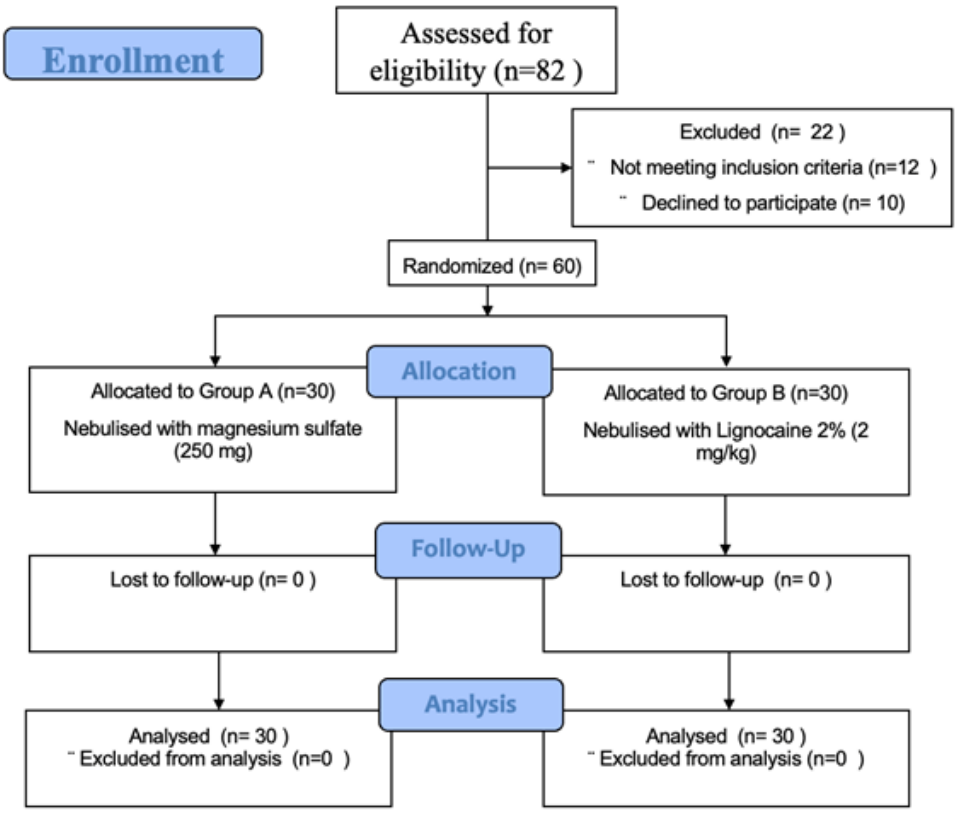

Figure 1: Consolidated Standards of Reporting Trails (CONSORT) diagram of the participants in the study.

Table 1: Demographic details

Parameters	Group		p
	A (n = 30)	B (n = 30)	
Age (Years)	35.80 ± 12.21	33.97 ± 11.55	0.5531
Gender			0.7743
Male	9 (30.0%)	8 (26.7%)	
Female	21 (70.0%)	22 (73.3%)	

Both groups were similar with respect to demographic characteristics like age and gender (Table 1). The mean age of group A patients was 35.80 ± 12.21 and that of group B was 33.97 ± 11.55 (p=0.55). The number of males in group A and B was 9 (30%) and 8 (26.7%) respectively and that of females was 21 (70%) and 22 (73.3%) respectively (p = 0.77).

The pre-nebulisation (baseline) HR in groups A and B were comparable (79.40 ± 13.04, 77.73 ± 9.60 resp.; p=0.86). However, the post nebulization HR of group A (74.00 ± 12.79) was significantly lower than that of group B (81.30 ± 10.88)

(p=0.01). The HR at post intubation time point (T0) was statistically significantly lower in group A (80.33 ± 14.19) compared to group B (87.50 ± 12.62) (p=0.03). Moreover, at all other time points, the mean HR in group A was lower than that in group B (all p<0.05) (Table 2). This can be confirmed from Figure 2 that HR in group A trended lower than that in group B over the period of observation

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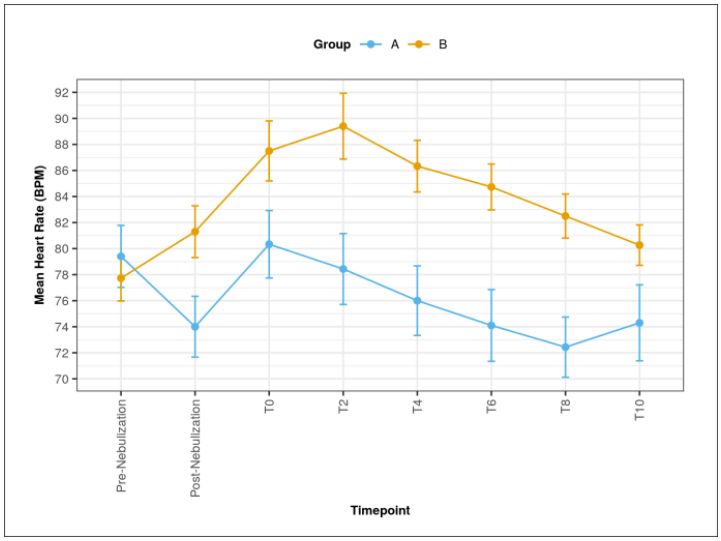

Figure 2: Trend of heart rate over time.

Table 2: Heart rate at various time points.

Heart Rate (BPM)	Group		p
	A (n = 30)	B (n = 30)	
Pre-Nebulization	79.40 ± 13.04	77.73 ± 9.60	0.865
Post-Nebulization	74.00 ± 12.79	81.30 ± 10.88	0.013
T0	80.33 ± 14.19	87.50 ± 12.62	0.033
T2	78.43 ± 14.92	89.40 ± 13.85	0.003
T4	76.00 ± 14.62	86.33 ± 10.85	0.001
T6	74.10 ± 15.08	84.73 ± 9.63	0.001
T8	72.43 ± 12.66	82.50 ± 9.27	<0.001
T10	74.30 ± 15.98	80.27 ± 8.50	0.004

A similar trend was observed in MAP values (Table 2) of groups A and B wherein the pre-nebulisation values were comparable (90.14 ± 8.78 and 90.07 ± 9.83 resp.; p=0.994) and a statistically significant difference was found in post nebulization (baseline) values (85.13 ± 9.50 and 93.21 ± 9.71 resp.; p=0.003). Furthermore, like the HR, MAP values were notably lower in group A compared to group B at all timepoints intra-operatively (all p<0.05), as depicted graphically in Figure 3.

Table3: MAP over various time point

MAP (mmHg)	Group		p
	A (n = 30)	B (n = 30)	
Pre-Nebulization	90.14 ± 8.78	90.07 ± 9.83	0.994
Post-Nebulization	85.13 ± 9.50	93.21 ± 9.71	0.003
T0	88.37 ± 8.70	104.79 ± 8.35	<0.001
T2	85.40 ± 8.20	99.09 ± 9.13	<0.001
T4	81.47 ± 8.17	95.69 ± 6.75	<0.001
T6	79.47 ± 8.29	92.39 ± 6.64	<0.001
T8	78.07 ± 8.05	88.98 ± 8.01	<0.001
T10	79.73 ± 7.49	88.64 ± 7.73	<0.001

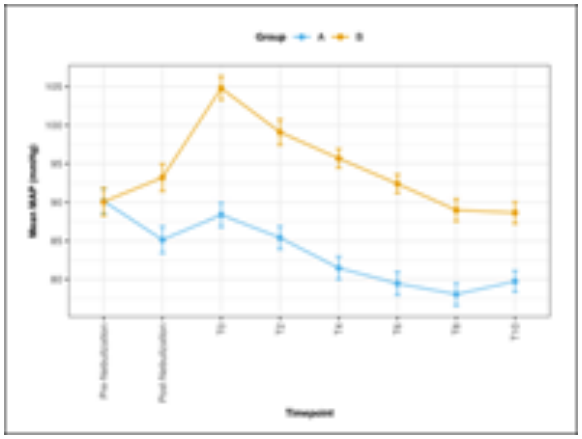

Figure 3: line diagram depicting MAP over time

Table 4: SBP over various time points

SBP (mmHg)	Group		p
	A	B	
	(n = 30)	(n = 30)	
Pre-Nebulization	119.90 ± 12.19	118.73 ± 13.17	0.723
Post-Nebulization	113.93 ± 12.38	121.57 ± 13.33	0.025
T0	115.50 ± 14.18	127.40 ± 13.20	0.001
T2	113.40 ± 15.83	125.93 ± 11.56	0.001
T4	109.33 ± 13.07	122.40 ± 9.13	<0.001
T6	105.73 ± 12.42	119.03 ± 8.57	<0.001
T8	104.07 ± 11.40	114.87 ± 10.40	<0.001
T10	105.60 ± 10.32	113.73 ± 9.39	0.002

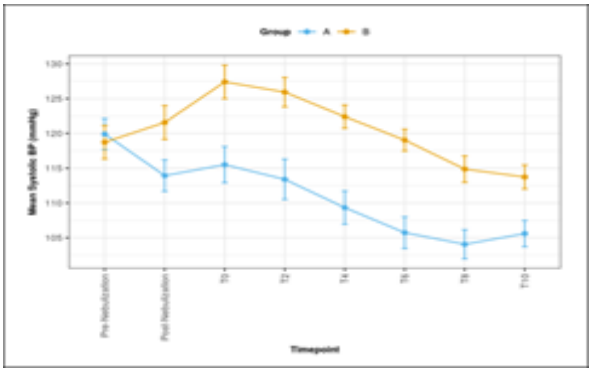

Figure 4: Line diagram depicting change in SBP (mmHg) over time.

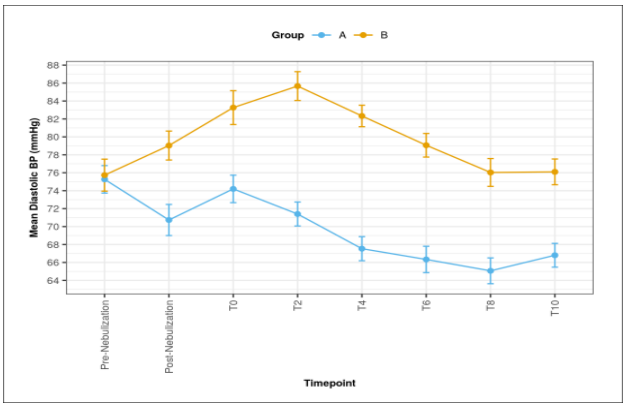

Figure 5: Line diagram depicting change in DBP over time.

Table 5: DBP over various time points.

DBP (mmHg)	Group		p
	A	B	
	(n = 30)	(n = 30)	
Pre-Nebulization	75.27 ± 8.40	75.73 ± 9.77	0.843
Post-Nebulization	70.73 ± 9.50	79.03 ± 8.84	0.001
T0	74.20 ± 8.39	83.27 ± 10.34	<0.001
T2	71.40 ± 7.32	85.67 ± 8.81	<0.001
T4	67.53 ± 7.35	82.33 ± 6.56	<0.001
T6	66.33 ± 8.05	79.07 ± 7.21	<0.001
T8	65.07 ± 7.87	76.03 ± 8.50	<0.001
T10	66.80 ± 7.25	76.10 ± 7.85	<0.001

SBP and DBP values (Table 4 and 5) of groups A and B wherein the pre-nebulisation values were comparable (SBP; p=0.723, DBP; P=0.843) and a statistically significant difference was found in post nebulization (baseline) values. Furthermore, like the HR and MAP values, SBP and DBP were notably lower in group A compared to group B at all timepoints intra-operatively (all p<0.05), as depicted graphically in Figure 4 and 5.

Ten (33.3%) patients in group A and 7 (23.3%) in group B reported no POST (Table 3). Out of the 20 patients who reported sore throat post operatively in group A, majority (19) had grade 1 POST, while 1 patient reported moderate (grade 2) POST. No patient in group A reported severe POST. On the other hand, of the 23 patients in group B who reported POST, majority had moderate (grade 2) POST (14) while 8 reported mild (grade 1) POST. One patient in group B reported severe (grade 3) POST.

Table 4: POST over various time points.

Highest Post Grade	Group		p
	A	B	p
None	10 (33.3%)	7 (23.3%)	<0.001
Grade 1	19 (63.3%)	8 (26.7%)	
Grade 2	1 (3.3%)	14 (46.7%)	
Grade 3	0 (0.0%)	1 (3.3%)	

Discussion

Mitigating the pressor response to laryngoscopy and endotracheal intubation in patients with comorbidities is a challenge. Multiple researches have been conducted to study the drugs like lignocaine, fentanyl, dexmedetomidine, clonidine and magnesium sulphate that blunt somatic and sympathoadrenal reflexes [2,4–7,14].

Magnesium is the fourth most common cation in the body and has a key role in hundreds of physiologic processes [15]. Calcium has a major role in the release of catecholamines from the adrenal medulla and adrenergic nerve terminals. Magnesium competes with calcium for binding to the membrane channels [16]. Magnesium by acting as a calcium antagonist, blocks release of catecholamine stores and decrease responses to adrenergic stimulation [17]. In addition to this, centrally mediated anti-nociceptive action of magnesium sulphate by antagonising N-methyl-D-aspartate (NMDA) has also been described [18,19].Lignocaine is a local anaesthetic agent that acts by inhibiting sodium channels on the axons of neurons and prevents propagation of action potential [20]. It is also an antiarrhythmic agentused in ventricular arrythmias [21].

Administering drugs through nebulization results in fewer side effects compared to the IV route due to reduced systemic absorption. Nebulized drug delivery avoids issues such as cough, vocal cord irritation, and laryngospasm commonly associated with the intranasal route [8]. Additionally, nebulization offers advantages like increased bioavailability and simplified administration [6].

We observed in our study that post nebulisation HR and MAP in magnesium sulphate group were lower than those in the lignocaine group. This can be attributed to a mild anxiolytic and sedative effect of magnesium sulphate owing to its action of blocking NMDA receptors as discussed earlier.

We found that nebulised magnesium sulfate was found to effectively mitigate the sympathoadrenal stimulation in response to laryngoscopy and intubation which is in agreement with Puri et al. who found that IV magnesium sulfate is an effective means to attenuate intubation response in a cohort of patients undergoing CABG [6,22]. Our results were also comparable to Elmeligy et al. who found that nebulized magnesium sulfate had significant

effect in attenuating pressor responseand Grover et al. who compared nebulised dexmedetomidine, magnesium sulfate and fentanyl , and found that dexmeditomidine and magnesium sulfate had significant effect on stress response as compared to fentanyl [23].

Our results were consistent with the conclusions of Mendonça et al., Nooraei et al. and Kiaee et al for intravenous administration of these drugs [24,25].

Our study was in agreement with Neogi et al. and Sharma et al who compared nebulised magnesium sulphate and lignocaine for POST and found that nebulised magnesium sulphate was superior to lignocaine in reducing incidence and severity of POST [26,27].

Conclusion

Nebulised magnesium sulfate (250mg/kg) is better than nebulised lignocaine (2%) in reducing the pressor response and severity of POST with no apparent side effects.

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