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Original Research Article

A COMPARATIVE STUDY TO ASSESS THE EFFICACY OF TWO DOSES OF INTRAVENOUS MAGNESIUM SULPHATE IN ATTENUATING THE HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION

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Abstract

Background: Hemodynamic response to laryngoscopy and intubation is a known phenomenon. Numerous pharmacological and non-pharmacological methods have been employed in an attempt to blunt such responses. However, the search for a perfect agent still continues. A study was conducted in order to compare and assess the efficacy of two doses of magnesium sulphate in blunting this hemodynamic response. **Materials and Methods:** This prospective, double-blind, randomized, Helsinki protocol-compliant clinical study was conducted after written informed consent and approval from the Institutional Ethical Committee. Two groups of 40 subjects each were constituted. Group A (20mg/kg, IV Magnesium sulphate) and Group B (30 mg/kg, IV magnesium sulphate). Study drugs were administered over 10 minutes. Anaesthesia protocol was standardised. Hemodynamics were observed following study drug administration (5, 10 min), following induction and following induction and at intubation and 1,2,4,6,8,10 minutes following laryngoscopy and intubation. Side effects were also noted. **Result:** Both groups were comparable demographically and at baseline, following study drug administration . The difference between the two groups was clinically significant at 1 min, 2 min, 4 min, 6 min post intubation (p=0.005,0.001,0.004,0.006). Maximum observed heart rate in group B was at immediately post intubation which was lower than the baseline. In terms of mean arterial pressure significant intergroup difference was also observed at immediately post intubation and at 1min, 2 min, 4 min, 6 min and 8 min post intubation (p=0.04, 0.02, 0.02, 0.08). **Conclusion:** Intravenous magnesium sulphate 30mg/kg was more efficacious than 20mg/kg in attenuating hemodynamic response to laryngoscopy and intubation.

INTRODUCTION

In modern anaesthesia practice, rigid laryngoscopy and tracheal intubation are still considered the gold standard for airway care. More than 50 years ago, researchers recognised the effect of airway manipulation on heart rate and blood pressure levels.[1] It is now widely accepted that laryngoscopy and endotracheal intubation always result in hemodynamic alterations such as increased heart rate, increased blood pressure, and sometimes cardiac rhythm abnormalities.[2,3] These hemodynamic alterations occur as a result of the sympathoadrenal response and the release of norepinephrine and, to a lesser extent, epinephrine.[4] In normotensive patients, these hemodynamic alterations are transient and likely of little relevance.[5] However, these hemodynamic changes pose a risk to patients with hypertension, ischemic heart disease, or cerebrovascular illness.[6] Elevation of blood pressure and heart rate typically starts within 5 seconds of laryngoscopy, peaks in 1 to 2 minutes and return to baseline level within 5-10 minutes.

Many pharmacological and non-pharmacological techniques have been attempted to reduce the pressor reaction that occurs when the endotracheal intubation

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is attempted.[7] Magnesium sulphate has been used to lessen the adrenergic reaction during tracheal intubation and laryngoscopy. However, the number of trials evaluating various intravenous magnesium sulphate dosages as a pressor response attenuating drug is quite few.

In this study an attempt has been made to observe, assess and compare the efficacy of magnesium sulphate (20 mg/kg body weight) and magnesium sulphate (30 mg/kg body weight) intravenous bolus over 10 mins, in attenuating the haemodynamic response following laryngoscopy and endotracheal intubation in patients in undergoing various elective surgeries under general anaesthesia.

MATERIALS AND METHODS

This prospective, double-blind, randomized, Helsinki protocol-compliant clinical study was conducted after written informed consent and approval from the Institutional Ethical Committee. A total of 80 patients aged 18-60 years of either sex with the American Society of Anaesthesiologists (ASA) physical status classes I and II undergoing elective surgeries under general anaesthesia were enrolled in the study. Patient refusal; history of known allergy to anaesthetic agents used in our study or with comorbidities such as compromised renal, hepatic, pulmonary, and cardiac status; suffering from diabetes and or hypertensive illness; or having anticipated difficult intubation, duration of laryngoscopy more than 15 secs.

Enrollment of patients commenced from 1st of September 2022 and was completed in 28 of February 2024.

Patients were randomized to two groups; Group A (20 mg/kg Magnesium sulfate), Group B (30 mg/kg Magnesium sulphate).

Based on the study conducted by Misganaw et al,[8] sample size was calculated as 36 patients per group with power of study 80% and type 1 error < 0.05%.[9-11] Considering the probability of attrition during follow up (attrition of 10%) exclusions due to difficult laryngoscopy etc 40 patients per group were enrolled.

Every patient who was scheduled for surgery was subjected to a comprehensive pre-anesthesia examination day before the scheduled surgery. A comprehensive general, systemic, and airway examination was completed. All necessary investigations were carried out, and the results were analysed. Age, sex, height, weight, and BMI were among the demographic details recorded. The patients' anaesthesia protocol was standardised. In accordance with the American Society of Anaesthesiologists' fasting recommendations, patients were kept at nil per oral.

In the pre-operative area, standard 18G iv access was achieved and patients were preloaded with ringer's lactate solution 2ml/kg/hr. All Standard monitors like ECG, Pulse oximeter, NIBP connected to the patients and baseline Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MBP) noted.

All patients were pre-medicated with midazolam 0.02 mg/Kg. Drugs and hemodynamic parameters were recorded at 5 minutes interval from beginning of administration till the end of study drugs administration. Induction was commenced with intravenous Injection Fentanyl (2mcg/kg) followed by Injection Propofol (2mg/kg) till loss of verbal response was achieved. Muscle relaxation was accomplished with Vecuronium 0.1 mg/kg following which a swift smooth laryngoscopy and intubation was done by a trained anaesthesiologist. No surgical or any other stimulation was permitted during 10 minutes of study period. Further anaesthesia management was as per institutional protocol.

The patients were monitored every hour for 24 hours in the postoperative period for any complications.

RESULTS

A total of 80 patients were recruited in the study. None of the patients were excluded from the analysis. Both groups were comparable demographically.

The primary Outcome, measures haemodynamic parameters including HR, MAP and oxygen saturation levels which were recorded 5 minutes and 10 minutes after starting of administration of study drugs, following induction and at intubation and 1,2,4,6,8,10 minutes following laryngoscopy and intubation. The secondary outcome measures included the side effects attributed to study drugs were monitored and recorded in the peri-operative period.

Both groups were comparable in terms of baseline heart rate, mean arterial pressures and oxygen saturation levels.

Both groups displayed mild reduction of heart rate but no significant intergroup difference following administration of study drugs (p=0.833, p=0.639). There was no significant intergroup difference in heart rate between the two groups following induction as well (p=0.822, p=0.329). There was increase in Heart rate following intubation which reached the peak at 2 minutes in group A while no such response to laryngoscopy and intubation was observed in group B. The difference between the two groups was clinically significant at 1 min, 2 min, 4 min, 6 min post intubation (p=0.005,0.001,0.004,0.006). Maximum observed heart rate in group B was at immediately post intubation which was lower than the baseline. Difference between the two groups was non-significant at 8- and 10-minutes post intubation.

In terms of mean arterial pressure both groups were comparable with each other at baseline, at 5- and 10-minutes post drug administration and at 1 minute post induction. A significant drop in MAP was observed in group B resulting into significant intergroup difference (p=0.008). Significant intergroup difference was also observed at immediately post

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intubation and at 1min, 2 min, 4 min, 6 min and 8 min post intubation (p=0.04, 0.02, 0.02, 0.08). The intergroup difference was not significant at 10 minutes post intubation (p=0.14).

Both groups were comparable at all time frames during the peri-operative period.

The only complication exhibited amongst the two groups was hypotension. While in group A; 1/40 patients had hypotension the corresponding number in group B was 2/40 with no significant difference between the two group. No other adverse events were observed.

Table 1: Demographic profile.

	Group A	**Group B**	**p value**
	Mean ± SD	Mean ± SD	
Age	28.23 ± 9.45	28.40 ± 4.29	0.917
Weight	65.03 ± 5.41	66.25 ± 7.16	0.392
Height	159.20 ± 8.67	161.70 ± 8.67	0.201
BMI	25.70 ± 3.38	25.30 ± 3.50	0.604

Table 2: Intergroup comparison of heart rate

HR	**Group A**	**Group B**	**P value**
	Mean ± SD	**Mean** ± SD	
BASELINE	80.18 ± 13.98	80.63 ± 10.46	0.870
AT 5MIN	79.4 ± 15.56	78.8 ± 9.03	0.833
AT 10 MIN	79.6 ± 15.31	78.2 ± 10.97	0.639
POST INDUCTION 1MIN	80.63 ± 15.33	79.90 ± 13.56	0.822
POST INDUCTION 2MIN	81.78 ± 14.67	78.60 ± 14.32	0.329
IMMEDIATE POST INTUBATION	84.33 ± 18.86	78.55 ± 14.67	0.130
POST INTUBATION 1 MIN	87.13 ± 18.46	76.53 ± 14.08	0.005
POST INTUBATION 2 MIN	88.53 ± 17.49	76.75 ± 13.84	0.001
POST INTUBATION 4 MIN	87.65 ± 18.72	76.60 ± 14.28	0.004
POST INTUBATION 6 MIN	86.38 ± 18.64	76.10 ± 13.37	0.006
POST INTUBATION 8 MIN	80.03 ± 17.8	76.00 ± 13.14	0.252
POST INTUBATION 10 MIN	79.45 ± 14.87	76.22 ± 14.2	0.323

Table 3: Intergroup comparison of mean arterial pressure

MAP	**Group A**	**Group B**	**p value**
	Mean ± SD	**Mean ± SD**	
BASELINE	86.08 ± 12.16	86.85 ± 15.67	0.806
AT 5MIN	82.1 ± 11.38	80.28 ± 14.67	0.537
AT 10 MIN	80.55 ± 10.37	77.47 ± 14.19	0.271
POST INDUCTION 1MIN	76.75 ± 10.86	73.8 ± 13.87	0.292
POST INDUCTION 2MIN	72.93 ± 10.33	67.2 ± 11.18	0.01
IMMEDIATE POST INTUBATION	78.38 ± 14.94	71.83 ± 11.07	0.02
POST INTUBATION 1MIN	79.45 ± 13.09	72 ± 11.52	0.008
POST INTUBATION 2MIN	84 ± 15.94	77.72 ± 11.27	0.04
POST INTUBATION 4MIN	82.3 ± 12.94	76.05 ± 11.35	0.02
POST INTUBATION 6MIN	81.73 ± 12.49	75.28 ± 11.87	0.02
POST INTUBATION 8MIN	79.13 ± 13.76	74.18 ± 11.6	0.08
POST INTUBATION 10MIN	78.95 ± 12.97	74.88 ± 11.42	0.14

Table 4: Intergroup comparison of mean spo2

SPO2	**Group A**	**Group B**	**p value**
	Mean ± SD	**Mean ± SD**	
BASELINE	98.80 ± 0.41	98.78 ± 0.48	0.802
AT 5MIN	98.28 ± 14.67	99.1 ± 11.38	–
AT 10 MIN	100.00 ± 0.00	100.00 ± 0.00	–
POST INDUCTION 1MIN	100.00 ± 0.00	100.00 ± 0.00	–
POST INDUCTION 2MIN	100.00 ± 0.00	100.00 ± 0.00	–
IMMEDIATE POST INTUBATION	99.88 ± 0.42	99.98 ± 0.40	0.283
POST INTUBATION 1MIN	99.35 ± 0.22	100.00 ± 0.00	0.156
POST INTUBATION 2MIN	100.00 ± 0.00	100.00 ± 0.00	–
POST INTUBATION 4MIN	100.00 ± 0.00	100.00 ± 0.00	–
POST INTUBATION 6MIN	100.00 ± 0.00	100.00 ± 0.00	–
POST INTUBATION 8MIN	100.00 ± 0.00	100.00 ± 0.00	–
POST INTUBATION 10MIN	100.00 ± 0.00	100.00 ± 0.00	–

Table 5: Intergroup comparison of common complications

	Group A		**Group B**	
	Frequency	**%**	**Frequency**	**%**
Hypotension	1	2.5%	2	5.0%
Bradycardia	0	0.0%	0	0.0%
PONV	0	0.0%	0	0.0%

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Allergic Reaction	0	0%	0	0%
Desaturation/Bronchospasm	0	0%	0	0%

DISCUSSION

Laryngoscopy and endotracheal intubation are linked to significant changes in hemodynamics and autonomic reflex activity, including an increase in heart rate, blood pressure, and sporadic disruptions in cardiac rhythm, during the induction of anaesthesia.[2,3] These potentially harmful changes start as soon as the laryngoscopy/intubation is performed, peaking after two minutes, and then starting to decline and return to baseline after ten minutes. Preventing perioperative morbidity and mortality requires effective attenuation (<20% of baseline) of the hemodynamic response to laryngoscopy and tracheal intubation.

Multiple variables impact the cardiovascular response linked to laryngoscopy and intubation, including the patient's age, the drugs employed, the kind and length of the procedures, the depth of anaesthesia, any instances of hypoxia or hypercarbia, etc. Of these, the length of the laryngoscopy is the most important factor affecting cardiovascular responses.[9,10] The force used during a laryngoscopy barely makes a difference. The laryngoscopy and intubation times in our trial were restricted to less than 15 seconds, and all of the procedures were carried out by skilled anaesthesiologists.

LiBurstein et al. discovered that the primary cause of the pressor response is an increased sympathetic response brought on by stimulation of the laryngopharynx and epi-pharynx. The afferent stimulation from the epiglottis and infraglottic region is carried by the vagus and glossopharyngeal nerves, which then activate the vasomotor centre, triggering a peripheral sympathetic adrenal response that releases noradrenaline and adrenaline.[11,12] The pressor response has been altered using a variety of methods. All of these may come with additional dangers and adverse effects, and none of them completely inhibit response.

Researchers have demonstrated Magnesium sulfate (MgSO4) inhibits catecholamine release translating to reduced serum epinephrine and norepinephrine levels manifesting as reduced cardiac contractility, bradycardia, vasodilation and hypotension.[13] It has been demonstrated that intravenous magnesium is effective in conditions with excess circulating catecholamines Moreover, MgSO4 directly lessens vascular contraction by reducing smooth muscle tonicity.[14-18] James et al also demonstrated reduction in plasma catecholamine levels in patients who were administered pre-operative magnesium sulphate and who underwent general anaesthesia/ laryngoscopy and intubation.[19] Researchers have investigated and compared effect of pre-operative magnesium sulphate administered intravenously with agents such as lignocaine and most have found magnesium sulphate better.[9] However, there has been paucity of research comparing efficacy of different doses of intravenous magnesium sulphate in blunting hemodynamic response to laryngoscopy and intubation.

While one group was administered intravenous magnesium sulphate 20mg/kg and other study group was administered 30mg/kg. In terms of heart rate, there was no intergroup difference till immediately post intubation (p>0.05). However subsequently group A (Magnesium sulphate 20mg/kg) exhibited rise in heart rate which reached its peak at 2 min post intubation and returned to baseline by 10 minutes. In contrast, the HR was relatively stable with no surges observed in group B(magnesium sulphate 30mg/kg) with heart rate lower than baseline at all time points. This can be due to magnesium sulphate preventing catecholamine surge and counteracting effect of calcium level surge.[10-13,19] Also, IV Magnesium sulphate inhibits the sinoatrial node directly and indirectly, extending the recovery period of the sinus node. Also, Following IV atropine, magnesium exerts a detrimental chronotropic impact.[20]

Findings by Kotwani et al and Nandal et al were similar to our study and they observed intravenous magnesium sulphate 30 mg/kg optimal to control heart rate surges. Higher doses exhibited compensatory tachycardia secondary to hypotension.[21,22] Honarmand et al, also conducted similar study but in their study, magnesium failed to control tachycardia. They attributed this to the overwhelming sympathetic response which could not be controlled by parasympathetic effects of magnesium sulphate.[10]

In terms of mean arterial pressure (MAP), though both groups attenuated the surge in blood pressure; group B was more effective in controlling the surge. Peak MAP in group A though lower than the baseline was higher than that after the study drug administration. Even this surge was absent in Group B. Higher baseline values can be attributed to patient anxiety and higher pre-operative catecholamines levels which was effectively countered by the study drugs. In studies conducted by Honarmund et al, kotwani et al and Nandal et al magnesium mediated vasodilation and refractoriness of catecholamines on smooth muscles resulted in blunting of incremental response of MAP.[10,21,22]

At no time did the rate-pressure product reach the critical ischemia value of 12000 in either group, thereby making magnesium sulphate an effective drug in preventing ischemia due to raised HR and MAP. Also in terms of side effects, the most common side effect was hypotension, the difference between the two groups was non-significant.

Limitations

No study is complete without limitations. Identifying limitations of a study is essential as it paves the way for future research and critical thinking. We lacked on multiple counts in our research. Firstly, even though the sample size was based on previous

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studies, but a study having a greater sample is likely to have greater accuracy. Secondly, we did not measure plasma catecholamines, magnesium and calcium levels in different stages of research. Hopefully these lacunae shall be dealt with in future research.

CONCLUSION

Hemodynamic response to intubation and laryngoscopy is a universal phenomenon, which needs to be blunted. Multiple pharmacological methods have been utilised to achieve this target. However, no satisfactory agent has been identified till date. Magnesium sulphate in a dose of 30mg/kg acts as a suitable agent to attenuate the hemodynamic response to laryngoscopy and intubation as compared to intravenous magnesium sulphate 20mg/kg.

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