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Original Article

Anaesthesia Section

Efficiency of Magnesium Sulphate as a Sole Muscle Relaxant for General Anaesthesia with Vecuronium Bromide for Tracheal Intubation: A Prospective Interventional Study

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ABSTRACT

Introduction: Neuromuscular blocking drugs are the standard for tracheal intubation; however, misuse can cause allergies, intraoperative awareness and prolonged blockage. As a result, intubation without these drugs is being explored, with magnesium sulphate as an alternative.

Aim: To assess the effect of magnesium sulphate on intubating conditions after the induction of anaesthesia without a neuromuscular blocking drug.

Materials and Methods: This was a prospective interventional study at the Department of Anaesthesiology, Armed Forces Medical College and Hospital in Pune, Maharashtra, India from June 2012 to June 2014 involving 200 patients, divided into two groups of 100 each: Group M and Group V. The study included both male and female patients with an American Society of Anaesthesiologists (ASA) physical status of I or II, Mallampati Class I or II, aged between 18 and 50 years. All patients were scheduled for elective surgery under General Anaesthesia (GA) with endotracheal intubation. In Group M, patients received a 40 mg/kg magnesium infusion over five minutes, followed by a 2.5 mg/kg injection of propofol intravenously. Laryngoscopy was performed after two minutes and then a 0.5 mg/kg intravenous injection of atracurium was administered one minute after intubation. In Group V, patients were given 100 mL Normal Saline (NS) over five minutes, followed by induction with 2.5 mg/kg propofol intravenously and a 0.1 mg/kg intravenous injection of vecuronium, with laryngoscopy performed after three minutes. Intubation conditions were evaluated using the Copenhagen Consensus Conference and Mean Arterial Pressure (MAP) and pulse rates were also recorded during the study. Demographic data were compared using t-tests and Chi-square tests.

Results: The mean ages for these groups were 39.78±8.42 years for Group V and 38.91±7.63 years for Group M. In terms of clinically acceptable intubation conditions, Group V had 100 patients (100%), while Group M had 78 patients (78%) ($p>0.05$). In the Copenhagen scoring system for intubating conditions, Group V (94 patients) scored significantly better than Group M (21 patients). Pulse rate and MAP were comparable until laryngoscopy, but were significantly higher in Group M after T5 ($p<0.05$). The duration of intubation was shorter in Group V, averaging 18.73±2.26 seconds, compared to 22.71±4.70 seconds in Group M ($p<0.01$).

Conclusion: The administration of magnesium sulphate before the induction of anaesthesia significantly lowers intubating conditions without requiring neuromuscular blocking agents. Magnesium sulphate serves as an alternative to a non depolarising muscle relaxant to avoid the side-effects caused by muscle relaxants, but it is inferior to a non depolarising muscle relaxant.

Keywords: Intubating condition, Laryngoscopy, Mallampati classification, Non depolarising muscle relaxant

INTRODUCTION

Although neuromuscular blocking medications are the gold standard for facilitating tracheal intubation, inappropriate use may lead to adverse consequences, including allergies, intraoperative awareness and issues resulting from persistent neuromuscular block. Therefore, the concept of intubation without using a neuromuscular blocking drug has been developed, with magnesium sulphate being used as an alternative. Very few studies are available in which magnesium sulphate is used solely as an agent for tracheal intubation [1,2].

Magnesium is a crucial cation in the body, involved in various physiological processes, such as neuronal activity, muscular contraction and the control of vasomotor tone. It competes with calcium for membrane channels and has muscle-relaxing, antinociceptive and anaesthetic effects. Magnesium also affects Central Nervous System (CNS) function, neuromuscular transmission and cardiac activity by influencing the movement of calcium, potassium and sodium in and out of cells, thus stabilising the excitable membrane [3].

Although neuromuscular blocking drugs are commonly used to facilitate tracheal intubation, their inappropriate use can lead to side-effects. Intubation without neuromuscular blockers has been developed as an alternative approach [4]. During GA, it is important to monitor neuromuscular function by stimulating a peripheral motor nerve and evaluating the muscular response. Electric nerve stimulation is used in the Train-of-Four (TOF) method.

In investigating ways to enhance anaesthetic methods for tracheal intubation without muscle relaxants, we hypothesised that the combined administration of magnesium sulphate, propofol and an opioid could potentially synergistically improve intubating conditions [5]. This prospective interventional study was conducted to assess the effectiveness of magnesium sulphate in facilitating intubation conditions during the induction of GA without using neuromuscular blocking drugs. The study aimed to compare the efficacy of magnesium sulphate with that of the gold standard neuromuscular blocking agent, vecuronium bromide.

MATERIALS AND METHODS

The present prospective interventional study was conducted at the Armed Forces Medical College and Hospital in Pune, Maharashtra, India from June 2012 to June 2014 after obtaining clearance from

the Institutional Ethical Committee. Written informed consent was obtained from the patients to participate in the study.

Sample size calculation: The number of participants included in the study was determined using information from a previous study [6]. The main focus was on the intubation conditions, aiming to achieve a study power of over 80% with a 5% margin of error.

Inclusion criteria: Both male and female patients with ASA physical status I and II, Mallampati Class I or II, aged between 18 and 50 years and scheduled for elective surgery under GA with endotracheal intubation were included in the study.

Exclusion criteria: Individuals under 18 or over 50 years of age, obese patients with a Body Mass Index (BMI) over 30 kg/m^2, those with a history of reactive airway disease, an increased risk of regurgitation, anticipated difficult airway, allergy to any of the study drugs, patients with hepatic, renal, cardiovascular, or respiratory diseases, individuals being treated with calcium channel blockers and pregnant individuals were excluded.

Study Procedure

The patients were divided into two groups: Group M and Group V, each comprising 100 patients. This resulted in almost equal cohorts with minimal internal bias regarding all the above variables. They were assigned to the groups based on odd and even dates, respectively. A different anaesthesiologist carried out the administration of magnesium and normal saline and the data was observed by anaesthesiology residents who were not involved in the study.

In Group M, patients received a 40 mg/kg magnesium infusion over five minutes, followed by a 2.5 mg/kg injection of 1% propofol intravenously. Laryngoscopy was performed after two minutes and then a 0.5 mg/kg intravenous injection of atracurium was administered one minute after intubation [7].

In Group V, patients were given 100 mL of NS over five minutes, followed by induction with 2.5 mg/kg of 1% propofol intravenously and a 0.1 mg/kg intravenous injection of vecuronium, with laryngoscopy performed after three minutes [8].

The individuals fasted for 10 hours and received a 0.25 mg oral dose of alprazolam the evening before the operation. In the operating room, each patient was connected to a multichannel monitor displaying electrocardiography, Heart Rate (HR), non invasive blood pressure, pulse oximetry (SpO_2) and Respiratory Rate (RR). Peripheral venous access was established with an 18 G cannula.

Premedication involved the intravenous injection of glycopyrrolate (0.2 mg), ondansetron (4 mg), midazolam (50 micrograms/kg) and fentanyl (2 mcg/kg). Induction was achieved with the injection of propofol (2.5 mg/kg) in both groups. The first laryngoscopy was performed in Group M two minutes after the administration of propofol. In Group V, laryngoscopy was carried out three minutes after the injection of vecuronium bromide (0.1 mg/kg). Tracheal intubation was performed using a properly sized cuffed endotracheal tube and the cuff was adequately inflated. An experienced anaesthetist performed and scored laryngoscopy and tracheal intubation in both groups.

Intubating conditions were evaluated using the Copenhagen scoring system [Table/Fig-1] [9,10]. The duration of laryngoscopy was recorded as the time from the start of laryngoscopy until tracheal intubation and the removal of the laryngoscope blade from the mouth. Anaesthesia was maintained with 50% nitrous oxide in oxygen and 1% isoflurane. At various time points, we measured MAP and HR: T1 (baseline), T2 (after the infusion of the study drug or normal saline), T3 (30 seconds after the bolus injection of propofol for anaesthetic induction), T4 (1 minute after tracheal intubation) and T5 (5 minutes after tracheal intubation).

Neuromuscular blockade was monitored with the help of a neuromuscular monitor (Organon's TOF watch) in Train-of-Four (TOF) [11] mode, 30 seconds after administration of magnesium or vecuronium and one and five minutes after intubation in both groups. A TOF value of zero indicates the use of a neuromuscular blocker (atracurium), suggesting complete relaxation, while values between 85% to 92% after five minutes of tracheal intubation were recorded because a muscle relaxant was not given to these patients as per surgical requirements.

Variables	Clinically acceptable		Clinically not acceptable
Laryngoscopy	Easy	Fair	Difficult
Vocal cords position	Abducted	Intermediate/ moving	Closed
Reaction to insertion of the tracheal tube and cuff inflation (Diaphragmatic movement/coughing)	None	Slight 1-2 weak contractions or movement for less than 5 seconds.	Vigorous/sustained More than two contractions and/ or movement for longer than 5 seconds.
Intubation conditions	Excellent	All qualities were excellent.	
	Good	All qualities were either excellent or good.	
	Poor	The presence of a single quality listed under poor.	
Laryngoscopy*	Easy	Jaw relaxed, no resistance to blade insertion.	
	Fair	Jaw not fully relaxed, slight resistance to blade insertion.	
	Difficult	Poor jaw relaxation, active resistance of the patient to laryngoscopy.	
Cormack and Lehane grading [9]	Grade 1	The entire aperture visible.	
	Grade 2	Posterior arytenoids visible, some of glottic aperture.	
	Grade 3	Only epiglottis is visible.	
	Grade 4	No visible structures (only can see the soft palate).	

[Table/Fig-1]: Copenhagen scoring system for intubating conditions [9,10].

STATISTICAL ANALYSIS

The data were analysed using Statistical Package for Social Sciences (SPSS) version 20.0. Demographic data were compared using t-tests and Chi-square tests. A p-value of less than 0.05 was considered significant.

RESULTS

The two groups were comparable with regard to age, sex, weight, height, BMI, ASA grade and Mallampati class (p>0.05) [Table/Fig-2].

Variables	Group V (n=100)	Group M (n=100)	p-value
Age (years) (Mean±SD)	39.78±8.42	38.91±7.63	p=0.445
Gender (M/F)	48/52	46/54	p=0.887
Weight (Kg) (Mean±SD)	63.09±8.14	61.17±7.21	p=0.079
Height (cm) (Mean±SD)	164.57±6.83	165.01±5.80	p=0.624
BMI (Kg m^{-2}) (Mean±SD)	23.33±2.28	22.82±1.85	p=0.087
ASA grade (I/II)	59/41	59/41	p=1
MPCL (1/2) (Mallampati class)	39/61	41/59	p=0.885

[Table/Fig-2]: Patients' characteristics.
Data are expressed as mean±SD or count number. F: Female; M: Male; BMI: Body mass index; ASA: American society of anaesthesiologists classification

A comparison of intubating conditions between both groups is shown in [Table/Fig-3]. The pulse rate and MAP were comparable at baseline (T1) in both groups. After the infusion of magnesium at T2, the pulse rate was significantly higher in the magnesium group (85.56±8.41 vs. 78.69±6.88) and the MAP was significantly lower in the magnesium group (93.65±5.64 vs. 95.97±5.71) (p<0.01).

At T3, 30 seconds after propofol induction, there was a significant fall in pulse rate and MAP in the saline group compared to the magnesium group (74.88±6.25 vs. 79.18±6.4) and (81.76±5.69 vs. 84.6±4.52) (p<0.01). At T4 and T5, one minute and five minutes

Parameters	Group V (n=100)	Group M (n=100)	p-value
Laryngoscopy			
Easy, n	94	92	p>0.05
Fair, n	6	8	p>0.05
Difficult, n	0	0	
Vocal cords position			
Excellent (abducted) n	100	68	p<0.05
Good (intermediate/ moving), n	0	32	p<0.05
Poor (closed), n	0	0	
Intubating conditions			
Excellent, n	94	21	p<0.05
Good, n	6	57	p<0.05
Poor, n	0	22	p<0.05
Clinically acceptable, n	100	78	p>0.05
Cormack-Lehane score			
Grade 1, n	75	61	p>0.05
Grade 2, n	22	32	p>0.05
Grade 3, n	3	7	p>0.05
Reaction to insertion of the tracheal tube and cuff inflation (diaphragmatic movement/coughing), n			
Coughing	n (%)		
Yes, n	0	23	p<0.01
No, n	100	77	p<0.05
Movement of limbs			
Yes, n	0	11	p<0.01
No, n	100	89	p<0.05
Heating sensation			
Yes, n	0	29	p<0.01
No, n	100	71	p<0.05
Additional drug for intubation			
Yes, n	0	22	p<0.01
No, n	100	78	p<0.05
Duration of achievement of intubation (In sec) (Mean±SD)	18.73±2.26	22.71±4.70	p<0.01

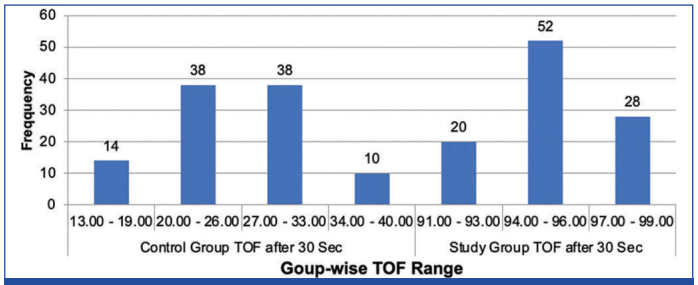
[Table/Fig-3]: Intubating Condition: Copenhagen consensus conference scoring system.
Data are expressed as mean±SD or count number, percentages (%), p<0.01=highly significant

after tracheal intubation, the stress response was significantly lower in Group M (p<0.01). The mean baseline values of pulse rate and mean arterial blood pressure were comparable in both groups (p>0.05) [Table/Fig-4].

Time	Group	Pulse rate (Mean±SD)	p-value	Mean Arterial Pressure (MAP) (Mean±SD)	p-value
T1	Group V	79.14±7.19	0.458	98±6.12	0.17
	Group M	79.95±8.19		96.74±6.18	
T2	Group V	78.69±6.88	<0.01	95.97±5.71	0.05
	Group M	85.56±8.41		93.65±5.64	
T3	Group V	74.88±6.25	<0.01	81.76±5.69	<0.01
	Group M	79.18±6.4		84.6±4.52	
T4	Group V	92.18±6.21	<0.01	102.43±5.69	<0.01
	Group M	88.78±6.47		95.83±6.21	
T5	Group V	83.87±6.43	<0.01	95.08±5.02	<0.01
	Group M	80.13±6.04		88.88±5.52	

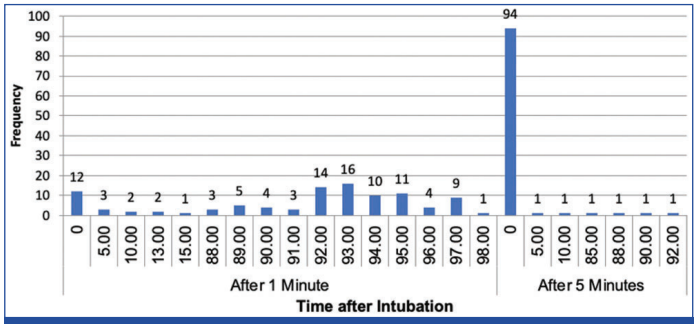
[Table/Fig-4]: Pulse rate and Mean Arterial Pressure (MAP).
Data are expressed as mean±SD, p<0.01-Highly significant

In Group V, after 30 seconds of administering vecuronium, the maximum frequency of TOF values was found to be between 20% to 33%. In the magnesium group, the maximum frequency of Train-of-Four values was found to be between 94% to 96%, indicating inadequate block in the magnesium group. The fall in Train-of-Four values was significantly greater in the control group (p-value <0.001) as shown in [Table/Fig-5].



[Table/Fig-5]: Train-of-Four profile after 30 seconds of infusion of magnesium and control group (vecuronium).

In the magnesium group, no significant fall in Train-of-Four values was observed. The maximum frequencies were recorded at one minute, ranging between 88% to 98%. A Train-of-Four value of zero, suggestive of the use of a neuromuscular blocker (atracurium), indicates complete relaxation. Four patients in the study had high Train-of-Four values (between 85% to 92%) after five minutes of tracheal intubation because a muscle relaxant was not given to these patients as per surgical requirements [Table/Fig-6].



[Table/Fig-6]: TOF profile after 1 minute and 5 minutes.

DISCUSSION

Magnesium is an agent with anaesthetic, analgesic and muscle relaxant effects. Its analgesic effect is mediated by interference with calcium channels and N-methyl-D-aspartate receptors. This antinociceptive agent has been used as an adjuvant for intraoperative and postoperative analgesia [12]. Magnesium is considered to be a 'muscle relaxant'-like agent. Indeed, neuromuscular transmission is altered by a preponderant presynaptic effect, which reduces the release of acetylcholine at motor nerve terminals [13]. Moreover, it is known that magnesium sulphate potentiates the effect of non depolarising neuromuscular blocking agents [14]. A rapid infusion of magnesium sulphate (50 mg/kg) can re-establish a relevant degree of muscle paralysis in patients who have just recovered from non depolarising neuromuscular blocking agents.

Various techniques have been investigated to improve intubating conditions when neuromuscular blocking drugs are not used. Propofol, which has a depressant effect on laryngeal reflexes, is usually combined with a rapid-onset and short-acting opioid (such as alfentanil or remifentanil) [15].

The authors found that in Group M, both the mean HR (88.78±6.47 and 80.13±6.04 per minute) and the MAP (95.83±6.21 and 88.88±5.52 mm Hg) at one and five minutes after tracheal intubation were lower compared to Group V. This finding aligns with the results of Park SJ et al., which noted that no hypertensive episodes occurred in the magnesium group (p-value <0.01) [16].

In the present study, the intubating conditions were less favourable in Group M compared to Group V, which correlates well with the

findings of Aissaoui Y et al., [5]. The dosage of magnesium sulphate used in the present study (40 mg/kg) was selected based on previous trials that investigated magnesium as an adjuvant for perioperative analgesia. At a dose of 50 mg/kg, the serum concentration of magnesium was increased by an average of 30% to 80% [17]. No side-effects related to hypermagnesemia were observed in the present study. Only minor symptoms of short duration, such as a feeling of heat or a burning sensation (probably due to peripheral vasodilation caused by magnesium), were experienced by 29% of the patients, as compared to the vecuronium group, where there were no such symptoms. Coughing (23%) and limb movement (11%) observed in the magnesium group could be attributed to inadequate neuromuscular blockade.

There was a decrease in the consumption of remifentanil and vecuronium during intravenous anaesthesia with magnesium sulphate, likely due to the inhibition of catecholamine release associated with tracheal intubation by intravenous magnesium sulphate [18]. In laparoscopic cholecystectomy, systolic and diastolic arterial pressures were controlled, resulting in lower levels of epinephrine or nor epinephrine in patients who received magnesium preoperatively [19].

In the present study, the baseline MAP was comparable in both groups. After intubation, the rise in MAP was significantly higher in the vecuronium group in comparison to the magnesium group. The MAP remained more stable in the magnesium group even after intubation. In the present study, the TOF ratio was 94% to 96% 30 seconds after the infusion of magnesium; however, the degree of neuromuscular blockade was greater in the vecuronium group (TOF ratio 20% to 33%) after 30 seconds following the injection of vecuronium. The TOF ratio at intervals of 20 seconds after induction with propofol showed significantly longer times with magnesium [20].

Limitation(s)

The present study results cannot be applied to emergency surgery, elderly patients, or ASA class III/IV patients, as their haemodynamic tolerance may be poor. Therefore, the present findings should not be recommended for a large patient population. Selected patients (as described above) may benefit from the use of relaxant-free intubation optimised with the addition of magnesium sulphate. Magnesium sulphate will be used as the sole agent, along with fentanyl and propofol, in ASA I/II patients.

CONCLUSION(S)

Acceptable intubating conditions can be achieved with magnesium as the sole agent for tracheal intubation in a haemodynamically stable patient. Magnesium sulphate is well-established in reducing the intubation stress response and minimising the need for reversal agents. However, using it as the only agent is less effective compared to a neuromuscular blocking agent.

Authors' contribution: All authors contributed to manuscript preparation.

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