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Original Article

Anaesthesia Section

Efficacy of Magnesium Sulphate in Attenuation of Succinylcholine Induced Fasciculations- A Randomised Clinical Study

S BALA BHASKAR[1], Y VEDASHREE[2], N KIRAN CHAND[3], D SRINIVASALU[4]

ABSTRACT

Introduction: Magnesium Sulphate ($MgSO_4$) pre-administration is effective in reducing Succinylcholine (Sch) induced fasciculations due to its effect at presynaptic end plate. Magnesium competes with calcium at the presynaptic end plate of neuromuscular junction and inhibits the release of Acetylcholine (Ach) from the motor nerve terminal and to a lesser extent, decreases the sensitivity of the postjunctional membrane and reduces the excitability of the muscle fibre.

Aim: To evaluate three doses of $MgSO_4$ in reducing the incidence and severity of fasciculations.

Materials and Methods: This prospective, randomised clinical trial was conducted at Vijayanagar Institute of Medical Sciences (VIMS), Ballari, India. Ninety consenting adult patients aged 20-50 years scheduled for elective surgeries with endotracheal intubation under general anaesthesia were randomly allocated into three groups- Group 1, Group 2 and Group 3, to receive Injection (Inj.) $MgSO_4$ 20 mg/kg, 30 mg/kg and 40 mg/kg, respectively, before induction. Induction with Inj. propofol (2 mg/kg) was followed by administration of Inj. Sch (1.5 mg/kg). The main outcome parameters were the incidence of fasciculations and grading of the severity. Haemodynamic responses from the basal levels and after intubation, and adverse effects to the study drugs were noted. Chi-square test was used to find the significance of study parameters on categorical scale among the groups. Probability values at <0.05 was considered as significant.

Results: The incidence of fasciculations was 90%, 53.4% and 43.4% in groups 1, 2 and 3, respectively. Greater number of patients had grade 3 fasciculations in group 1 (20%), compared to group 2 and group 3 (3.4% and nil), respectively. The fall in blood pressure after $MgSO_4$ was comparable among the three groups. Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) increased by 23.5% and 18.5%, 7.9% and 4.1% and 2.8% and 2.7% in groups 1, 2 and 3, respectively at one minute. The SBP and DBP at 3rd and 5th minute stayed at statistically significant greater levels in group 1 as compared to groups 2 and 3, but were similar in groups 2 and 3 overall. The Heart Rate (HR) changes followed similar trend in all 3 groups. Incidence of feeling of warmth was highest in group 3 as compared to other groups.

Conclusion: $MgSO_4$ at 40 mg/kg can be the optimal dose to suppress Sch-induced fasciculations, with better attenuation of intubation associated haemodynamic changes.

Keywords: Anaesthesia, Blood pressure, Calcium, Heart rate, Intubation, Propofol

INTRODUCTION

Despite more than seven decades of use, Succinylcholine (Sch) continues to be a popular agent because of excellent neuromuscular relaxation, it produces for endotracheal intubation [1]. However, its use is associated with adverse effects and fasciculations are observed frequently, with an incidence of 95% [2]. Fasciculations occur due to prejunctional depolarising action of Sch. The uncoordinated muscle contractions manifest because of repetitive firing of the motor nerve terminals and antidromic discharges [3].

Various pre-treatment modalities have been advocated to reduce the incidence and severity of these fasciculations including use of a self-taming dose of Sch, precurarising doses of Non Depolarising Neuromuscular Relaxants (NDMR), anaesthetic agents, lignocaine, $MgSO_4$, opioids, pregabalin and gabapentin [2,4,5]. Among these, only use of Non Depolarising Neuromuscular Blockers (NDMRs), lignocaine and $MgSO_4$ have been associated with significant reductions in fasciculations [2]. Magnesium competes with calcium at the presynaptic end plate of neuromuscular junction and inhibits the release of Acetylcholine (Ach) from the motor nerve terminal and to a lesser extent, decreases the sensitivity of the postjunctional membrane and reduces the excitability of the muscle fibre [6].

Previous studies attempting to study the effects of $MgSO_4$ in reducing the incidence of fasciculations, included doses of 40 to 60 mg/kg. At 40 mg/kg doses, the reported reductions in incidence have been 50%, 65% and 92%, respectively [7-9]. One study that used 60 mg/kg, showed only 35% reduction in incidence, probably attributable to faster rate of administration. The studies cited had drawbacks in terms of methodologies and confounders which could affect the outcomes- in terms of the induction agents, duration of administration of $MgSO_4$, non assessment of preoperative Mg levels, and poor sample sizes. Hence, it was decided to assess effectiveness of smaller dose of 20 mg/kg and compare with 30 mg/kg and 40 mg/kg of $MgSO_4$ in 3 groups in a better designed and implemented randomised trial.

The primary objective of the study was to assess the reduction in the incidence of Sch induced fasciculations. Secondary objectives included assessment of severity of the fasciculations, the attenuation of haemodynamic responses after intubation, the changes in the serum Magnesium (Mg) and Calcium (Ca) levels, Electrocardiogram (ECG) changes, urine output and respiratory rate.

MATERIALS AND METHODS

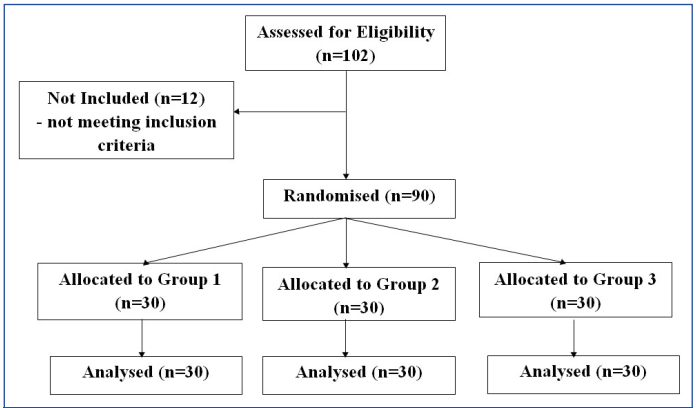
This randomised clinical trial was conducted from September 2017 to August 2018, at Vijayanagar Institute of Medical Sciences (VIMS), Ballari, India. The study was approved by Institutional Ethics Committee (No. VIMS/PG/IEC/17/2017-18/dt.8.6.17), and registered in the Clinical Trials Registry of India (CTRI Reg No: CTRI/2018/ 01/011484).

Inclusion criteria: After informed and written patient consent, 90 patients aged 20-50 years of either sex belonging to American Society of Anaesthesiologists (ASA) physical status grade I and II and modified Mallampati Airway (MMA) (Samsoon Young) class I and II, scheduled for elective surgeries under general anaesthesia participated in this trial.

Exclusion criteria: Patients with history of significant systemic disorders (cardiovascular, respiratory, central nervous system or renal system), pre-existing musculoskeletal disorders, hypo/hypermagnesemia with a diagnosed condition or with altered serum values, beta-adrenergic or calcium channel blocker usage and refusing for procedure were excluded from the study.

Sample size calculation: The incidence of fasciculations after administration of Sch was taken as 95%, based on a previously published meta-analysis of randomised controlled trials [2]. A reduction in incidence of fasciculations by 30% (effect size) was assumed in group 1 as compared to this 'control' value. Previous studies showed an average reduction of 40% in fasciculations using $MgSO_4$ at 40 mg/kg. Hence, a 30% reduction in this figure in group 2 (30 mg/kg) was assumed in the current study as effect size [7,8]. With 95% confidence interval, α error of 0.05 and power of 80%, sample size was calculated as 28 in each group. To account for possible dropouts during recruitment and study, 30 patients were included in each group.

The patients were randomly allocated to three groups of 30 each, based on computer generated random numbers [Table/Fig-1]. The randomisation was implemented by allocation concealment using Sequentially Numbered Opaque Sealed Envelope (SNOSE) technique for the three groups. The envelop was opened in the morning of the surgery and the test drug administration and the monitoring was performed by different anaesthesiologists, with participant also blinded to allotment. Group 1 patients received Inj. $MgSO_4$ 20 mg/kg, Group 2 patients received Inj. $MgSO_4$ 30 mg/kg and Group 3 patients received Inj. $MgSO_4$ 40 mg/kg, intravenously over 10 minutes before induction.



[Table/Fig-1]: CONSORT flowchart.

Study Procedure

The primary outcome parameter (incidence of fasciculations) and secondary parameters (severity of fasciculations, attenuation of haemodynamic responses to intubation, serum Magnesium (Mg) and Calcium (Ca) levels, ECG changes, urine output and respiratory rate) were noted from the time of injection of test drugs till the surgery was completed. Patients were followed-up for 24 hour in the postoperative period.

Preoperative procedure: Thorough pre-anaesthetic evaluation was performed one day prior to the surgery. Preoperative investigations as per the surgical indication was obtained including resting ECG. The serum Mg and Ca levels were obtained in the evening prior to the day of surgery. The procedure of general anaesthesia and study was explained to the patients and written consent was obtained. The patients were advised overnight fasting and advised tablet alprazolam 0.5 mg and tablet ranitidine 150 mg on the night before surgery.

Intraoperative procedure: On shifting the patients to the operation theatre and after preinduction check of machine, monitoring for continuous ECG, heart rate, Non Invasive Blood Pressure (NIBP), and Pulse Oximetry (SpO_2) was established and baseline values were noted. The study solution was prepared before anaesthesia procedure by a resident not involved in patient management or monitoring intra and postoperatively, as per group allocation, revealed by opening sealed envelope in the morning of surgery. The calculated dose was drawn from the 2 mL (50%) ampoules of Inj. $MgSO_4$ and diluted to 20 mL with normal saline. This solution was administered over a period of 10 minutes via a syringe pump and patients were asked for their subjective feeling of warmth while receiving the drug or for any other complaints.

This was followed by administration of Inj. midazolam 30 µg/kg and Inj. fentanyl 2 µg/kg intravenously. Preoxygenation was performed with 8 lpm of oxygen flow rate using closed circuit followed by induction with Inj. propofol 2 mg/kg. After induction, a blood sample was drawn from the forearm from the opposite side of infusion of study drug for measuring serum magnesium and calcium levels, followed by administration of inj. succinylcholine 1.5 mg/kg. Patient was monitored for appearance of fasciculations and graded as Grade 0: no fasciculations, Grade 1: Fine fasciculations at eyes, neck, face or fingers without limb movement, Grade 2: Moderate fasciculations occurring at more than two sites or obvious limb movement and Grade 3: Severe sustained and widespread fasciculations [10].

Oral endotracheal intubation was performed after assessing complete muscular relaxation. If laryngoscopy time exceeded 30 seconds or multiple attempts were required for intubation, patients were excluded from the study. Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), SpO_2 and End Tidal Carbon Dioxide ($EtCO_2$) readings were recorded at 1 minute, 3 minutes and 5 minutes after intubation and every 10 minutes thereafter till the end of surgery. Anaesthesia was maintained with oxygen, nitrous oxide (33:66) and isoflurane 1-2% and vecuronium. Intermittent positive pressure ventilation was balanced to maintain $EtCO_2$ at 35-45 mmHg. The episodes of hypotension (MAP >20% of baseline) was managed with re-balance of anaesthesia and if necessary, treated with incremental doses of mephentermine 3 mg i.v. Bradycardia (HR <50 bpm and trend of further fall over one minute) was treated with incremental intravenous doses of 0.3 mg of atropine.

Postoperative procedure: At the end of surgery, neuromuscular blockade was reversed with Inj. neostigmine 0.05 mg/kg and Inj. glycopyrrolate 0.02 mg/kg and trachea extubated after adequate recovery of muscle power. Normal saline was maintained as the intravenous fluid from the beginning and only changed after sampling of blood was done for Mg and Ca. Incidence of bradycardia, arrhythmias, hypotension during intraoperative period was noted. During the postoperative period, patient HR, NIBP, SpO_2, ECG, respiratory rate and urine output were monitored. Any other intraoperative and postoperative complications were noted.

STATISTICAL ANALYSIS

All data was entered in Microsoft Excel sheet; continuous variables as Mean±SD and categorical, as percentages. Data was cleaned before inferential statistical analyses and normal distribution of dependent variables was checked. Analysis of Variance (ANOVA) was used to find the significance of numeric study parameters among three groups of patients. Post-Hoc Tukey (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups (Inter group analysis). Chi-square/Fisher's-exact test was used to find the significance of study parameters on categorical scale among three groups. The Statistical software Statistical Package for Social Sciences (SPSS) 20.0 and MedCalc 9.0.1 was used for the analysis of the data. Probability values at <0.05 were considered as significant for the various tests.

RESULTS

Ninety patients were included, based on the selection criteria for the study. The patient characteristics including haemodynamic parameters were comparable among three groups [Table/Fig-2]. The

Parameter	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	p-value		
				Gr 1-Gr 2	Gr 1-Gr 3	Gr 2-Gr 3
Age (years) (Mean±SD)	33.3±11.5	32.9±9.5	33.9±11.1	0.987*	0.938*	0.912*
Gender (Male: Female)	14:16	12:18	12:18	0.833#	0.833#	0.992#
Weight (Kg) (Mean±SD)	56.2±5.4	54.1±5.3	57.6±6.7	0.915*	0.941*	0.804*
ASA physical status I/II	21:9	20:10	20:10	0.962#	0.962#	0.990#
Basal systolic blood pressure (mm Hg) (Mean±SD)	122.8±10.7	123.4±11.7	123.8±11.1	0.905*	0.939*	0.969*
Basal diastolic blood pressure (mm Hg) (Mean±SD)	74.1±7.3	76.4±8.8	75.8±9.5	0.681*	0.726*	0.834*
Basal heart rate (beats/min) (Mean±SD)	87.5±13.2	92.4±10.1	90.1±9.1	0.780*	0.883*	0.896*

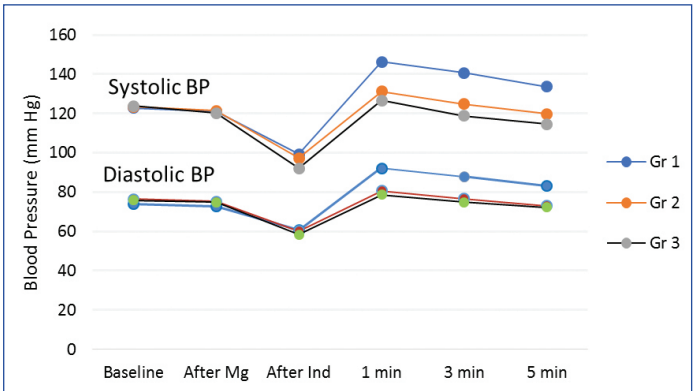
[Table/Fig-2]: Patient characteristics.
*One-way ANOVA test used; #Fischer's-exact test used; Gr: Group

incidence of fasciculations was found to be 90%, 53.4% and 43.4% in groups 1, 2 and 3, respectively [Table/Fig-3]. Group 1 patients had the most intense fasciculations. The severity of fasciculations was reduced in groups 2 and 3, with almost all of the group 3 patients having only grade 1 fasciculations [Table/Fig-3].

Groups	Incidence n (%)	Fasciculations				
		Grades of fasciculations n (%)				Percentage of patients in grades 2 and 3
		0	1	2	3	
Group 1	27/30 (90)	3 (10)	9 (30)	12(40)	6 (20)	60%
Group 2	16/30 (53.3)	14 (46.6)	9 (30)	6 (20)	1 (3.4)	23.4%
Group 3	13/30 (43.3)	17 (56.6)	12 (40)	1 (3.4)	0 (0)	3.4%
p-values (Chi-square test)						
Groups 1-2	0.0018					0.0053
Groups 2-3	0.454					0.216
Groups 1-3	0.00013					0.00002

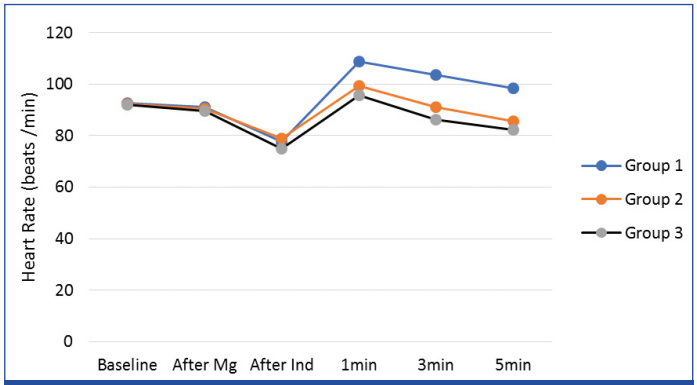
[Table/Fig-3]: Incidence and grading of severity of fasciculations.
p-value <0.05 considered significant

The relative falls in SBP and DBP after $MgSO_4$ administration and immediately after induction were comparable among the three groups [Table/Fig-4]. After one minute, there was increase by 23.5% and 18.5% in SBP and DBP, respectively in group 1 as compared to 7.9% and 4.1% in group 2 and 2.8% and 2.7% in group 3 (p=0.001 between group 1 and 2 and group 1 and 3). The increase in SBP in group 3 was statistically less as compared to group 2 (p=0.05). The observed increase in DBP did not differ significantly between groups 2 and 3. The SBP at 3rd and 5th minute stayed at statistically significant greater levels in group 1 as compared to groups 2 and 3. The SBP was maintained at a lower level in group 3 as compared to group 1 at 3rd and 5th minute (p=0.019 and 0.047, respectively). The DBP at 3rd and 5th minute stayed at statistically significant greater levels in group 1 as compared to groups 2 and 3 but there were no statistically significant differences between groups 2 and 3 during these times.



[Table/Fig-4]: Systolic (Mean) and Diastolic (Mean) blood pressure changes in the three groups.

The baseline mean heart rate was comparable amongst the 3 groups as also after $MgSO_4$ administration [Table/Fig-5]. The mean heart rate was significantly high (16.7%) at 1 minute after intubation in group 1 as compared to groups 2 and 3 (6.8% and 3.7% from baseline, respectively). The heart rate remained at a higher level in group 1 as compared to groups 2 and 3 at 3rd and 5th minute also. Between group 2 and 3, the HR was better maintained in group 3 at 3rd minute (p=0.027) but at 5th minute, there were no significant differences.



[Table/Fig-5]: Heart Rate (mean) changes in the three groups.

Baseline serum Mg levels were comparable in the 3 groups. After administration of $MgSO_4$, the increases were from 0.76±0.10 to 1.71±0.07 mmoL/l in group 1, from 0.77±0.08 to 2.41±0.06 mmoL/l in group 2 and from 0.76±0.08 to 2.82±0.10 mmoL/l in group 3 [Table/Fig-6]. The serum Ca levels (preoperative and after $MgSO_4$ administration) were 9.35±0.43 mg/dL and 9.5±0.47 mg/dL in group 1, 9.49±0.63 mg/dL and 9.5±0.49 mg/dL in group 2 and 9.69±0.49 mg/dL and 9.62±0.55 mg/dL in group 3 respectively. The p-value (2 tailed, ANOVA)- between groups: preoperative=0.11 and after $MgSO_4$=0.68, and within groups: 0.48, 0.18 and 0.53 for groups 1, 2 and 3 respectively].

Group	Serum Mg levels (mmol/l)		Grades of fasciculations (0-3) and S. Mg levels after Mg administration (mmol/l)				
			Grades	0	1	2	3
Group 1	Preoperative	0.76± 0.09	S. Mg level	1.71± 0.07	1.74± 0.09	1.69± 0.06	1.65± 0.07
	After Mg administration	1.71± 0.073	No. of patients	3	9	12	6
Group 2	Preoperative	0.76± 0.08	S. Mg level	2.46± 0.06	2.38± 0.05	2.34± 0.06	2.29*
	After Mg administration	2.41± 0.06	No. of patients	14	9	6	1
Group 3	Preoperative	0.76± 0.08	S. Mg level	2.88± 0.10	2.67± 0.11	2.57*	-
	After Mg administration	2.82± 0.106	No. of patients	17	12	1	0

[Table/Fig-6]: Serum Magnesium levels- Preoperative and After $MgSO_4$ administration (overall) and in relation to grades of fasciculations.
Values of Serum Mg are in Mean±SD except for Single value, with*

There were no significant ECG changes in any of the patients; the respiratory rate and the urinary outputs were within clinical ranges in the three groups. Feeling of warmth after $MgSO_4$ administration

was expressed by two patients, five patients and 10 patients in groups 1, 2 and 3 respectively. Two patients in group 3 complained of nausea which was not statistically significant.

DISCUSSION

$MgSO_4$ is among few drugs with proven benefit in reducing the incidence of fasciculations but the previous studies using different dosages of $MgSO_4$ (40 mg/kg to 60 mg/kg) have shown inconsistent results and differing methodologies in terms of duration of administration and use of induction agents [7-9]. The study compared three different doses (lower doses of 20 mg/kg and 30 along with the 40 mg/kg) of $MgSO_4$ over 10 minutes before premedication and induction, along with assessment of serum Mg levels.

A dose of 20 mg/kg of $MgSO_4$ was not at all beneficial, with fasciculations observed in 90% of patients, with 2/3^{rds} of them being of moderate to severe grades. Doses of 30 mg/kg and 40 mg/kg reduced the incidence to nearly half. The dose of 40 mg/kg was most effective in reducing severity of fasciculations, with 92% having only mild grades, whereas at 30 mg/kg, only 60% had mild grades of fasciculations. The intubation responses were found to be best attenuated in groups 2 and 3 but not much in group 1. The serum Mg levels were found to reach therapeutic levels in groups 2 and 3 but not in group 1, after administration of $MgSO_4$.

Mg attenuates Sch induced muscle fasciculations by decreasing the amount of Ach liberation and action and by depressing the excitability of the muscle fiber membrane [11] Magnesium, as compared to all other interventions to prevent fasciculations, is an endogenous electrolyte without the risks attributable to the sedatives, anaesthetic agents or relaxants when preadministered before Sch. The onset of action of $MgSO_4$ (i.v.) is immediate and the duration lasts for about 30 minutes. Normal range of serum magnesium concentration is 0.7-1.1 mmoL/l (therapeutic: 2-4 mmoL/l) [6]. The current study attempted to correlate the serum levels with the degree of fasciculations unlike other studies and observed that serum levels above 2.38±0.05 mmoL/l were associated with absent to mild grade fasciculations [Table/Fig-6].

Serum calcium levels were within normal ranges in all the groups, before and after administration of $MgSO_4$. There were no intraoperative or postoperative effects attributable to Mg administration (hypotension, bradycardia, ECG changes, respiratory rate and urine output). It was observed that the patients receiving $MgSO_4$ had a strange feeling of warmth, which may be explained by the peripheral dilation and pooling of blood in extremities. This feeling is dependent on the amount of $MgSO_4$ administered in time unit and can be attenuated by injecting the drug over longer time period [12]. Hence, in the present study $MgSO_4$ was diluted to 20 mL with saline and administered over 10 minutes.

In a study on patients aged 18-60 years, using 2 mg/kg of Sch and $MgSO_4$ at 40 mg/kg, the incidence of fasciculations was 50%, but half of them had moderate grades of fasciculations [8]. In the present study, author uses similar doses, only mild grades of fasciculations were observed in 92% of cases. The routinely used doses of 1.5 mg/kg of Sch could be associated with greater incidence of fasciculations as compared to smaller or larger doses, but the relationship is variable with no strong and recent evidences being available [2,13].

In a three group study comparing $MgSO_4$ at 40 mg/kg with precurarising dose of vecuronium and saline, the incidence of fasciculations in Mg group was least at 65%, higher than that in the present study at same doses but nearly 77% of them had minimal grade [7]. Tracheal intubation induced hemodynamic responses were attenuated significantly in Mg group.

One of the studies using higher dose of $MgSO_4$ (60 mg/kg) after fentanyl-thiopentone induction was still associated with nearly 65% incidence of fasciculations. The study did not reveal fall of the BP from the baseline in the $MgSO_4$ group, which is contradictory to the expectations at this dose. The short duration of administration of the drug (30 secs) may have contributed to this outcome [14]. In a study of 50 patients administered $MgSO_4$ at 40 mg/kg before fentanyl-propofol induction (followed by 2 mg/kg of Sch), as compared to the group not receiving $MgSO_4$, there was a reduction in incidence of fasciculation to the extent of 92% in the $MgSO_4$ group [9]. The confounders in other studies include the type of induction agent used, inadequate or poorly defined sample sizes, the rate and duration of administration of $MgSO_4$ before administration of Sch and correlation of serum levels of Mg with the grades of fasciculations. The onset of fasciculations was within 30-45 seconds after Sch administration in the present study. The duration of administration of $MgSO_4$ in different studies was 10 seconds, 30 seconds, 60 seconds, 5 minutes and 10 minutes. Thus, the onset with adequate serum level of Mg may not have been reached to coincide with the onset of fasciculations with fast rates of administration [7,8,14-16]. It was found that when administered in 20 mL volume over 10 minutes, the serum levels of Mg were achieved in the therapeutic range with 30 mg/kg and 40 mg/kg dosage of $MgSO_4$ (but not 20 mg/kg).

Mg has been shown to inhibit catecholamine release during tracheal intubation, the decrease in blood pressure associated with peripheral vasodilatation. Studies purely targeting benefits of Mg towards attenuation of haemodynamic responses to intubation have suggested 30 mg/kg to be the optimum dose, with reduced risk of hypotension [12,17]. In the current study, decreases in SBP and DBP after induction were observed in groups 2 and 3, with the SBP fall being statistically significant in group 3 as compared to group 2. The SBP increased above basal levels at one minute after intubation in all the groups. The authors feel that this brief fall can be attenuated with judicious fluid loading before induction so that the maximum benefits related to attenuation of fasciculations can be better exploited at 40 mg/kg of $MgSO_4$.

The amount of transmitter liberated at the nerve terminals varies directly with the logarithm of the Ca concentration, without affecting the sensitivity of the end-plate region to Ach. Thus, an excess of Ca could increase the amount of transmitter liberated and antagonise the effect of Mg on the motor nerve endings, the neuromuscular block being thereby relieved. So, the serum Ca levels were measured before and after administration of $MgSO_4$, which did not change much within and between groups and hence, no inference could be drawn on potential role of Ca in interfering with the attenuating effect of Mg on the fasciculations [11,18].

Limitation(s)

The presence and degree of fasciculations in the present study was graded with the widely used and valid scale (0 to 3 grades), but it carries risks of misinterpretation attributable to the observational skills of the recorder. Electromyography based maximum muscle action potential amplitude is a better means of quantifying the severity of visible muscle fasciculations, which was not utilised in the study.

CONCLUSION(S)

Preadministration of intravenous $MgSO_4$ in doses of 30 mg/kg and 40 mg/kg was effective in reducing the incidence of succinylcholine induced fasciculations by nearly 50% whereas, it was ineffective at 20 mg/kg. However, at 40 mg/kg, 90% of those affected had only mild grades. The dose of 40 mg/kg could also be better in attenuating the haemodynamic responses to laryngoscopy and intubation, without any other significant adverse effects. Therapeutic levels of serum Mg levels were achieved at 30 mg/kg and 40 mg/kg doses and not 20 mg/kg dose of $MgSO_4$.

REFERENCES

[1] Huang L, Sang CN, Desai MS. A Chronology for the identification and disclosure of adverse effects of Succinylcholine. J Anaesth Hist. 2019;5(3):65-84.
[2] Schreiber JU, Lysakowski C, Fuchs-Buder T, Tramèr MR. Prevention of succinylcholine- induced fasciculation and myalgia: A meta-analysis of randomised trials. Anaesthesiology. 2005;103(4):877-84.

[3] Hartman GS, Fiamengo SA, Riker WFJ. Succinylcholine: Mechanism of fasciculations and their prevention by d-tubocurarine or diphenylhydantoin. Anaesthesiology. 1986;65(4):405-13.
[4] Pandey CK, Karna ST, Tandon M, Pandey VK, Singh A. Comparative evaluation of prophylactic use of pregabalin, gabapentin and diclofenac sodium for prevention of succinylcholine-induced myalgia: A randomised, double-blinded study. J Postgrad Med. 2014;60(1):16-20.
[5] Joshi GP, Hailey A, Cross S, Thompson-Bell G, Whitten CC. Effects of pretreatment with cisatracurium, rocuronium, and d-tubocurarine on succinylcholine-induced fasciculations and myalgia: A comparison with placebo. J Clin Anaesth. 1999;11(8):641-45.
[6] Herroeder S, Schönherr ME, De Hert SG, Hollmann MW. Magnesium-Essentials for Anaesthesiologists. Anaesthesiology. 2011;114:971-93.
[7] Sakuraba S, Serita R, Kosugi S, Eriksson LI, Lindahl SG, Takeda J. Pretreatment with magnesium sulphate is associated with less succinylcholine-induced fasciculation and subsequent tracheal intubation-induced hemodynamic changes than precurarization with vecuronium during rapid sequence induction. Acta Anaesthesiol Belg. 2006;57(3):253-57.
[8] Kumar M, Talwar N, Goyal R, Shukla U, Sethi A. Effect of magnesium sulfate with propofol induction of anaesthesia on succinylcholine-induced fasciculations and myalgia. J Anaesthesiol Clin Pharmacol. 2012;28(1):81-85.
[9] Najeeb R, Tajamul S, Sofi AA. Role of magnesium sulphate in attenuating succinylcholine induced fasciculations and postoperative myalgia. Saudi J Med Pharm Sci. 2019;5(10):901- 06.
[10] Kahraman S, Ercan S, Aypar U, Erdem K. Effect of preoperative I.M. administration of diclofenac on suxamethonium-induced myalgia. Br J Anaesth.1993;71:238-41.
[11] Del Castillo J, Engbaek L. The nature of neuromuscular block by magnesium. J Physiol. 1954;l24:370-84.
[12] Montazeri K, Falah M. Dose-response study: MGSO4 in cardiovascular responses after laryngoscopy & endotracheal intubation. Can J Anaesth. 2005;52:A129. https://doi.org/10.1007/BF03023167
[13] McLoughlin C, Leslie K, Caldwell JE. Influence of dose on suxamethonium-induced muscle damage. Br J Anaesth.1994;73(2):194-98.
[14] Das MK, Yasmin R, Khatun UHS, Alam MT, Akhtaruzzaman AKM, Debnath H. Effects of pretreatment with magnesium sulphate on suxamethonium induced complications during induction of general anaesthesia- A placebo-controlled study. Journal of the Bangladesh Society of Anaesthesiologists. 2013;26(1):27-32.
[15] Stacey MR, Barclay K, Asai T, Vaughan RS. Effects of magnesium sulphate on suxamethonium-induced complications during rapid-sequence induction of anaesthesia. Anaesthesia. 1995;50(11):933-36.
[16] James MF, Cork RC, Dennett JE. Succinylcholine pretreatment with magnesium sulfate. Anaesth Analg. 1986;65(4):373-76.
[17] Panda NB, Bharti N, Prasad S. Minimal effective dose of magnesium sulfate for attenuation of intubation response in hypertensive patients. J Clin Anaesth. 2013;25(2):92-97.
[18] Jenkinson DH. The nature of the antagonism between calcium and magnesium ions at the neuromuscular junction. J Physiol. 1957;138:43-44.

PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Anaesthesiology, Vijayanagar Institute of Medical Sciences, Ballari, Karnataka, India.
2. Assistant Professor, Department of Anaesthesiology, Shridevi Institute of Medical Sciences and Research Hospital, Tumkur, Karnataka, India.
3. Associate Professor, Department of Anaesthesiology, Vijayanagar Institute of Medical Sciences, Ballari, Karnataka, India.
4. Professor, Department of Anaesthesiology, Vijayanagar Institute of Medical Sciences, Ballari, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
S Bala Bhaskar,
Professor, Department of Anaesthesiology, Vijayanagar Institute of Medical Sciences (VIMS), Ballari-583104, Karnataka, India.
E-mail: sbalabhaskar@gmail.com

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