



Effect of Different Doses of Intravenous Magnesium Sulphate in Succinylcholine Induced Fasciculations, Myalgias and Hyperkalemia

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Abstract

Introduction: Succinylcholine induced fasciculation, myalgia and hyperkalemia are common complications in surgical procedures. Magnesium (Mg) sulfate is proposed to reduce the negative effects caused by succinylcholine.

Aim: we aimed to assess the effects of different doses of Mg sulfate on muscle fasciculation, myalgia, hyperkalemia and hemodynamic responses due to intubation by succinylcholine.

Patients and methods: This randomized clinical trial was conducted on 60 patients, scheduled for elective surgeries under general anesthesia, allocated into three groups; 20 patients each. In group 1; the patients received intravenous (I.V.) Mg sulfate 20 mg/kg. In group 2; the patient received I.V. Mg sulfate 30 mg/kg and in group 3; the patients received 40 mg/kg I.V. Mg sulfate, over 10 minutes before induction. Patients were monitored for occurrence of fasciculation, myalgia or hyperkalemia.

Results: Of the sixty patients, 53.3% were males and 46.7% were females, their mean age was 41.1±10 years. The incidence of fasciculation was 80%, 55% and 30% in groups 1, 2 and 3, respectively. The highest incidence of myalgia occurred in group 1 (25% of patients), while just 15% and 10% of groups 2 and 3 developed myalgia. The three groups showed significant fall in the heart rate and blood pressure immediately after induction of anesthesia ($P < 0.05$). After one minute of induction, there was significant increase in blood hemodynamic measures, patients in group 1 showed the highest rise. The dose of Mg sulfate had significant positive correlation with the serum Mg level ($r = 0.887$, $P < 0.05$) and significant negative correlation with the serum Potassium level after injection of Mg sulfate ($r = -0.512$, $P < 0.05$).



Conclusion: Intravenous Mg sulfate in dose of 40 mg/kg was the most effective dose in reducing succinylcholine induced fasciculation, attenuation of the haemodynamic responses after intubation, and attenuating the increase in serum K associated with Succinylcholine administration.

Introduction

Succinylcholine is considered by many clinicians, to be the best drug for providing ideal intubating conditions for surgical procedures, anticipated difficult airways and rapid sequence induction and intubation due to its fast onset of action, profound neuromuscular blockade and an ultra-short duration of action. Because of these qualities many clinicians believe it is still a good choice for routine intubation in adults. Unfortunately, is accompanied by some side effects like muscular fasciculation, myalgia, masseter muscle spasm, rhabdomyolysis, hyperkalemia, increase intracranial, intraocular and intragastric pressure [1].

Postoperative muscle damages and myalgia are attributed to different mechanisms including increased myoplasmic calcium concentration, changes in membrane phospholipids, releasing free fatty acids and the involvement of free radicals [2].

Therefore, Many attempts have been made to avoid these undesirable effects, which include pretreatment with rocuronium [3], atracurium [4], lignocaine [4], calcium [5], ketorolac [6], diclofenac sodium [7], diazepam[8], Magnesium (Mg) sulfate [9], thiopentone sodium [10], d-tubocurare and vecuronium [9].

Mg sulfate is one of the drugs that has been investigated largely [11]. Mg acts as an adrenergic antagonist and inhibits the release of catecholamines. So it probably controls the undesirable effects of laryngoscopy for tracheal intubation such as tachycardia, hypertension, and increased intraocular pressure [12].

On the other hand, Mg sulfate reduces the negative effects caused by succinylcholine and avoids the increase of potassium (K) concentration after administration of succinylcholine. Mg sulfate is also effective in reducing pain after the administration of succinylcholine [13]. The analgesic effects of Mg are based on acting as an antagonist of N-methyl-D-aspartate (NMDA) receptors in central nervous system [14].

Therefore, this study is planned to assess the effects of different doses of Mg sulfate on muscle fasciculation, myalgia, hyperkalemia and hemodynamic responses due to intubation by succinylcholine.

Patients and methods

Study population and ethical considerations

This randomized clinical trial was conducted on 60 patients (aged 18-60 years and American Society of Anesthesiologists (ASA) physical status grade I and II) scheduled for elective surgeries under general anesthesia. The study was approved by the Ethics Committee of Menoufia University. A written informed consent was obtained from the patient before participation in the study. Patients with pre-existing musculoskeletal disorders, history of significant systemic disorders (renal, cardiovascular, respiratory or central nervous system), hypo or hypermagnesemia, contraindications or known hypersensitivity to study drugs, patients who had received analgesics within 24 hour before scheduled surgery and patients with beta-adrenergic or

calcium channel blockers usage were excluded.

Computer based randomization had allocated the patients into three groups; 20 patients each. In the first group, the patients received intravenous (I.V.) Mg sulfate 20 mg/kg (group 1), the second group received I.V. Mg sulfate 30 mg/kg (group 2) and group 3 patients received 40 mg/kg I.V. Mg sulfate, over 10 minutes before induction.

Anesthetic workup

Thorough pre-anesthetic evaluation was performed one day prior to the surgery including; resting ECG, serum Mg, and K levels. On shifting the patients to the operation theatre; pre-operative vital signs were recorded before induction of anesthesia with non-invasive monitoring [Heart rate (HR), systolic and diastolic blood pressure (SBP & DBP), oxygen saturation (SpO₂) and Electrocardiogram (ECG)]

Before induction of anesthesia, the patients of group 1, group 2 and group 3 were given Mg sulfate 20, 30 and 40 mg/kg; respectively I.V. slowly over a period of 10min via a syringe pump. After pre-oxygenation, induction of anesthesia was performed with propofol 2mg/kg body weight then a blood sample was drawn from the forearm from the opposite side of infusion of study drug for measuring serum Mg and K levels, followed by administration of I.V. succinylcholine 1.5 mg/kg.

Patient was monitored for appearance of fasciculation and graded as Grade 0: no fasciculation, Grade 1: fine fasciculation at eyes, neck, face or fingers without limb movement, Grade 2: moderate fasciculation occurring at more than two sites or obvious limb movement and Grade 3: severe sustained and wide-spread fasciculation.

Oral endotracheal intubation was performed. Maintenance of anesthesia was done by 50% air, 50% oxygen and 1% sevoflurane and bispectral index was maintained at 40-50. Controlled ventilation was facilitated by using atracurium 0.3mg/kg as induction dose and intermittent 0,1mg/kg bolus as per requirement and EtCO₂ was maintained at 35-45 mmHg.

The episodes of hypotension (MAP < 20% of baseline) was managed with re-balance of anesthesia and if necessary, treated with incremental doses of ephedrine 6mg I.V. Bradycardia (HR <50 bpm and trend of further fall over one minute) was treated with incremental I.V. doses of 0.5mg of atropine.

HR, SBP, DBP and SpO₂ readings were recorded at 1 minute, 3 minutes and 5 minutes after intubation and every 10 minutes thereafter till the end of surgery.

At the completion of surgery, neuromuscular blockade was reversed by neostigmine 0.03-0,07 mg/kg and glycopyrolate 0.01-0,02mg/kg. After patient started obeying commands patient was extubated and shifted to recovery room and thereafter to the ward.

Incidence of bradycardia, arrhythmias, hypotension during intraoperative period was noted. During the postoperative period, patient HR, SBP, DBP, SpO₂, ECG, respiratory rate and urine output were monitored for 24 hours after surgery. Any other intraoperative and postoperative complications were noted.

Postoperative myalgias were assessed after 24 hours of surgery in all patients and graded on scale of 0 to 3 with 0 =nil (absence of pain), 1 = mild (muscle stiffness or pain on specific questioning in nape of neck, shoulders and lower chest on deep

breathing), 2 = moderate (muscle stiffness and pain complained of by the patient spontaneously requesting analgesia), 3 = severe (incapacitating generalized muscle stiffness or pain).

Outcome measures

The primary outcome measures included the incidence of fasciculations and myalgia and the secondary outcome measures (serum Mg and K levels, attenuation of hemodynamic responses to intubation, vital signs measures, ECG changes and urine output) were noted from the time of injection of test drugs till the surgery was completed.

Statistical analysis

All data was entered and analyzed using the Statistical software Statistical Package for Social Sciences (SPSS) 20. Continuous variables were recorded as Mean ± SD and categorical variables as numbers and percentages. The normal distribution of dependent variables was checked before statistical analyses. Chi-square/Fisher’s-exact test was used to find the significance of study parameters on categorical scale among three groups. Analysis of Variance (ANOVA) was used to find the significance of numeric study parameters among three groups of patients. Tukey Post-Hoc test was used to find the significance of study parameters on continuous scale between two groups (Inter group analysis). Paired sample t-test was used to compare the mean of pairs of observations. Correlation analysis was used to assess the association between 2 continuous variables. Probability (P) values at <0.05 were considered as significant for the various tests.

Results

The study included sixty (60) patients divided into 3 groups. 53.3% of our patients were males and 46.7% were females, their mean age was 41.1±10 years with no significant difference among the 3 groups as regard the sex and age (P > 0.05). The mean of the weight was 76.1± 12.7 kg. Seventy-two percent of the patients were ASA-I and 28% were ASA-II.

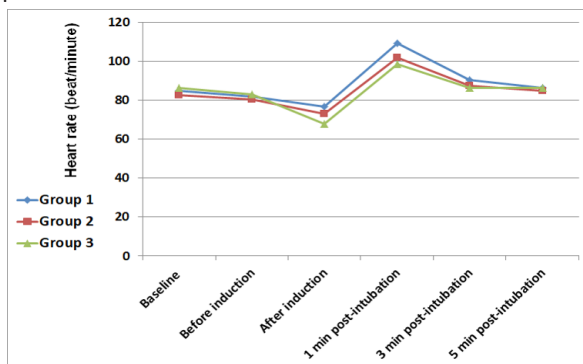


Figure 1: Heart Rate changes in the three groups.

The patient hemodynamics were comparable among three groups before induction of anesthesia (**Figure 1 and 2**) (P > 0.05). The base lines of Mg and K levels showed no significant difference among the 3 groups (**Table 1**) (P > 0.05).

The incidence of fasciculation was 80%, 55% and 30% in groups 1, 2 and 3, respectively. Group 1 showed the most intense forms of fasciculation, 60% of patients had grade 2 and 3 fasciculation. Group 3 patients showed mild forms of fasciculation (**Table 2**).

The highest incidence of myalgia occurred in group 1 (25% of patients), while just 15% and 10% of groups 2 and 3 developed myalgia, with no significant difference between the 3 groups (P > 0.05) (**Table 2**).

The 3 groups showed significant fall in the HR, SBP and DBP after Mg sulphate administration and immediately after induction of anesthesia (P<0.05). After one minute of induction, there was significant increase in blood hemodynamic measures. Patients in group 1 showed the highest rise in HR, SBP and DBP.

The HR, SBP and DBP tended to decrease again at 3 and 5 minutes with nearly comparable values between the 3 groups (P>0.05) except for the fall of DBP at 3 minutes, group 2 and 3 showed significantly more decrease in DBP than group 1 (P<0.05).

The serum Mg and K levels changed significantly after injection of Mg sulfate (P< 0.05) (Table 1). The dose of Mg sulfate had significant positive correlation with the serum Mg level (r = 0.887, P< 0.05) and significant negative correlation with the serum K level after injection of Mg sulfate (r = - 0.512, P< 0.05).

All patients in the 3 groups did not develop any significant changes in the ECG, the respiratory rate nor the urine outputs (P > 0.05). Nearly half of the patients in group 3 complained of warmth feeling after the administration of Mg sulfate. While just 3 patients in group 2 complained of the feeling of warmth and none of group 1 developed it. None of the patients in group 1 and 2 complained of PONV and only 2 in group 3 complained of nausea.

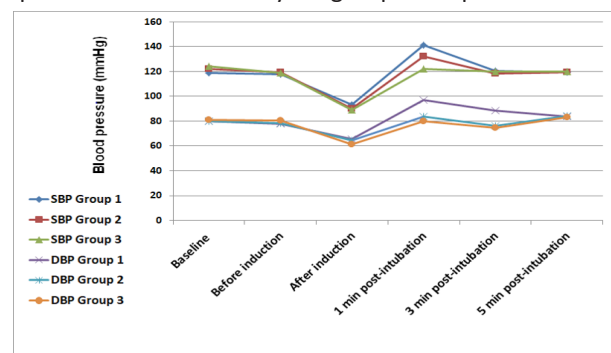


Figure 2: The Systolic and Diastolic blood pressure changes in the three groups.

Table 1: The serum Mg and K levels before and after Mg administration among the studied groups.

	Group 1	Group 2	Group 3	F	P-value
	N=20	N=20	N=20		
	Mean ± SD	Mean ± SD	Mean ± SD		
Baseline Mg level (mmol/L)	0.93 ± 0.11	0.90 ± 0.09	0.91 ± 0.11	0.565	0.572
Mg level after Mg administration (mmol/L)	1.72 ± 0.16	2.44 ± 0.30	2.91 ± 0.25	117	<0.0001
Baseline K level (mmol/L)	3.86 ± 0.31	3.78 ± 0.32	3.86 ± 0.30	0.488	0.616
K level after mg administration (mmol/L)	4.4 ± 0.37	4.03 ± 0.352	3.87 ± 0.32	12.09	<0.0001

K: potassium; Mg: Magnesium.

Table 2: The incidence of fasciculation and myalgia among the studied groups.

		Group			X ²	P-value
		Group 1	Group 2	Group 3		
		N=20	N=20	N=20		
Fasciculation	Occurred	16 (80%)	11 (55%)	6 (30%)	10.1	0.006
	Not occurred	4 (20%)	9 (45%)	14 (70%)		
Fasciculation grade	Grade 0	4 (20%)	9 (45%)	14 (70%)	16.9	0.01
	Grade 1	4 (20%)	3 (15%)	5 (25%)		
	Grade 2	6 (30%)	6 (30%)	1 (5%)		
	Grade 3	6 (30%)	2 (10%)	0 (0%)		
Myalgia in 1 st 24 hours	Occurred	5 (25%)	3 (15%)	2 (10%)	1.68	0.432
	Not occurred	15 (75%)	17 (85%)	18 (90%)		
Myalgia grade	Grade 0	15 (75%)	17 (85%)	18 (90%)	2.88	0.824
	Grade 1	1 (5%)	1 (5%)	1 (5%)		
	Grade 2	3 (15%)	1 (5%)	1 (5%)		
	Grade 3	1 (5%)	1 (5%)	0 (0%)		

Discussion

The current study assessed the effect of increasing doses of Mg sulfate in succinylcholine induced fasciculation, myalgia, hyperkalemia and hemodynamic response after intubation.

The increasing dose of Mg sulfate inversely affected the incidence of fasciculation. The lowest dose of Mg sulfate seems to be ineffective in attenuation of fasciculation. Fasciculation occurred in 80% of the patients received Mg sulfate in a dose of 20 mg/kg, most of them were of high grades. Higher doses were more effective in prevention of occurrence of fasciculation as nearly half of the patients who received 30 mg/kg Mg sulfate developed fasciculation and nearly one third of patients in the 3rd group experienced low grades of muscle fasciculation.

Concomitant with our results; Bhaskar et al., assessed the effect of different doses of Mg sulphate in attenuation of succinylcholine induced fasciculation, the incidence of fasciculation was 90%, 53.4% and 43.4% in 20, 30 and 40 mg/kg groups, respectively. Greater number of patients had grade 3 fasciculation in group 1 (20%), compared to group 2 and group 3 (3.4% and nil), respectively [15].

In our study myalgia was tested by asking about muscle pain at 24th hour after surgery in the postoperative ward and found that as in fasciculation, the incidence of myalgia was increasing with lowering the dose of Mg sulfate, despite the difference in incidence among the 3 different doses were non-significant. Kousar et al., 2021 revealed that use of Mg sulphate 40mg/kg before induction of anesthesia significantly reduces the incidence and severity of myalgia [16].

The pathophysiology of occurrence of fasciculation and myalgia is not clear and the exact mechanism of succinylcholine induced myalgia is still to be unknown. However, according to the most proposed mechanisms, succinylcholine is a quaternary ammonium depolarizing muscle relaxant; it produces sustained depolarization of pre-junctional membrane of neuromuscular junction without repolarization resulting in initially fasciculation followed by muscle relaxation [17].

Magnesium attenuates succinylcholine induced muscle fasciculation by decreasing the amount of Acetylcholine liberation and action and by depressing the excitability of the muscle fiber

membrane [15] Mg, as compared to all other interventions to prevent fasciculation, is an endogenous electrolyte without the risks attributable to the sedatives, anesthetic agents or relaxants when pre-administered before succinylcholine [18].

The hemodynamic response to induction of anesthesia was variable among the different groups. Intense reduction in HR, SBP and DBP occurred with higher doses of Mg sulfate. On the other side the sharp rising of blood hemodynamics after 1 minute of induction was lower in the patients who received the highest dose of Mg sulfate.

Raman et al., 2016 studied that effect of pretreatment with Mg sulphate on succinylcholine induced fasciculation and myalgia. They found that Mg sulphate acts in blunting the intubation response during induction of general anesthesia [19]. The administration of Mg sulphate produces vasodilatation by direct effect on blood vessels and by indirectly sympathetic blockade and inhibition of catecholamine release [20].

The serum K level after injection of Mg sulfate inversely correlated with the dose of Mg sulfate in our study. Concomitant with our results; Danladi et al., 2006 showed that pretreatment with Mg Sulphate significantly reduce succinylcholine induced hyperkalaemia by an average of 0.3mmol/L despite he used a dose of 60mg/kg [21].

No significant complications were recorded in our study and only 2 patients in group 3 complained of nausea.

Conclusion

Intravenous Mg sulfate in dose of 40 mg/kg was the most effective dose in reducing the degree of succinylcholine induced fasciculation, attenuation of the haemodynamic responses after intubation, and attenuating the increase in serum K associated with succinylcholine administration with no significant adverse effects. Mg sulfate in dose of 20 mg/kg is not recommended.

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