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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 proorrecedures. Magnesium (Mg) sulfate is proposed to reduce the negative effects caused by succinylcholine.

Aim: we aimed to assess how different dosages of Mg sulfate affect muscle fasciculation, myalgia, hyperkalemia and hemodynamic responses due to intubation by succinylcholine.

Patients and methods: This randomized trial included 60 patients scheduled to undergo elective surgery under general anesthesia. Participants were assigned at random to three equal groups of 20 patients. Group 1,2 and 3 received intravenous Mg sulfate at a dose of 20, 30 and 40 mg/kg, respectively. In all groups, Mg sulfate was administered intravenously to all groups 10 minutes before anesthesia was induced. Patients were monitored for occurrence of fasciculation, myalgia or hyperkalemia.

Results: Of the sixty patients, males accounted for a 53.3% and females accounted for 46.7% of the cohort, with a mean age of 41.1±10 years. The incidence of fasciculation was 80%, 55% and 30% in groups 1, 2 and 3, respectively. Myalgia occurred in 25% of group 1 patients, while just 15% and 10% of groups 2 and 3 developed myalgia. The three groups showed significant fall in the hemodynamics 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: Among the doses studied, intravenous Mg sulfate at 40 mg/kg was the most efficient in decreasing succinylcholine-induced fasciculations, attenuating the hemodynamic response to intubation, and limiting the rise in serum potassium associated with succinylcholine administration.

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Introduction

Succinylcholine remains widely used for endotracheal intubation because of its rapid onset, potent neuromuscular blockade, and very short duration of action. These characteristics make it particularly useful when rapid sequence induction is required, in anticipated difficult airway management, and during surgical procedures where optimal intubating conditions are needed. Despite these advantages, its use may be associated with several adverse effects, including muscle fasciculations, rhabdomyolysis, masseter muscle spasm, postoperative myalgia, hyperkalemia, and elevations in intraocular, intracranial, and intragastric pressures [1].

The development of postoperative muscle injury and myalgia has been linked to several proposed mechanisms, including elevated intracellular calcium levels, alterations in membrane phospholipids, increased release of free fatty acids, and oxidative stress mediated by free radicals [2]. Several pharmacological strategies have been investigated to minimize these adverse effects [3-10].

Magnesium (Mg) sulfate was extensively studied as a potential agent for minimizing these adverse responses [11]. Its pharmacological effects include antagonism of adrenergic activity and inhibition of catecholamine release. Consequently, Mg sulfate may attenuate the cardiovascular and other physiological responses associated with laryngoscopy and tracheal intubation, including tachycardia, hypertension, and increased intraocular pressure [12].

Magnesium sulfate has also been reported to attenuate several adverse effects associated with succinylcholine, including the rise in serum potassium that may follow its administration. In addition, Mg sulfate may help alleviate succinylcholine-related postoperative pain [13]. Its analgesic properties have been attributed, at least in part, to its antagonistic action on N-methyl-D-aspartate receptors within the central nervous system [14].

Accordingly, the present trial targeted examining the effects of different dosages 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 enrolled 60 patients from eighteen to sixty years-age who were classified as American Society of Anesthesiologists (ASA) physical status I or II and were set to undergo elective surgery under general anesthesia. Ethical approval was granted by the Ethics Committee of Menoufia University, and written informed consent was secured from all participants before enrollment. Patients were excluded if they had pre-existing musculoskeletal disease; significant renal, cardiovascular, respiratory, or central nervous system disorders; hypo- or hypermagnesemia; contraindications to, or known hypersensitivity to, any of the study medications. Patients who had received analgesics within the 24 hours preceding surgery or were taking beta-adrenergic blockers or calcium-channel blockers were also 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

A comprehensive pre-anesthetic assessment was carried out one day before surgery, including resting Electrocardiography (ECG) and measurement of serum Mg and potassium levels. Upon arrival at the operating room, vital signs, peripheral oxygen saturation (SpO_2), and ECG were documented before induction using non-invasive monitoring as a baseline.

Before anesthesia induction, patients in groups 1, 2, and 3 received I.V. Mg sulfate at doses of 20, 30, and 40 mg/kg, respectively, administered slowly over 10 minutes using a syringe pump. Following preoxygenation, 2 mg/kg Propofol was administered to induce anesthesia. Venous sample was subsequently obtained from the other forearm to determine serum Mg and potassium concentrations, followed by I.V. administration of succinylcholine at 1.5 mg/kg.

Patients were monitored for the development of fasciculations, which were graded according to severity as follows: Grade 0, absence of fasciculation; Grade 1 represented mild, fine fasciculations limited to areas such as the eyes, face, neck, or fingers, without associated limb movement. Grade 2 was defined as moderate fasciculations involving more than two anatomical sites and/or accompanied by visible limb movement. Grade 3 denoted severe, sustained, and generalized fasciculations.

The patients were subsequently intubated. Maintenance of anesthesia was done by 50% air, 50% oxygen and 1% sevoflurane and bispectral index was maintained at 40-50. Controlled mechanical ventilation was maintained with atracurium, administered at an initial dose of 0.3 mg/kg followed by intermittent boluses of 0.1 mg/kg when clinically indicated.

End-Tidal Carbon dioxide ($EtCO_2$) levels were maintained within the range of 35–45 mmHg throughout the procedure. Episodes of hypotension were initially managed by adjusting the depth of anesthesia and, when necessary, by administering incremental I.V. doses of ephedrine (6 mg). Bradycardia with a continued downward trend over one minute, was managed with incremental I.V. doses of atropine (0.5 mg).

Vital signs and SpO_2 were documented at 1, 3, and 5 minutes following intubation and subsequently at 10-minute intervals throughout the surgical procedure until its completion. At the end of the procedure, residual neuromuscular blockade was reversed using neostigmine (0.03–0.07 mg/kg) administered in combination with glycopyrrolate (0.01–0.02 mg/kg). Once the patient was awake and able to follow commands, extubation was performed, followed by transfer to the recovery unit and subsequently to the ward. The occurrence of intraoperative bradycardia, arrhythmias, and hypotension was documented.

During the first 24 postoperative hours, vital signs, SpO_2, ECG findings, and urine output, and any additional complications were recorded. Postoperative myalgia was graded on a four-point scale: Grade 0, no pain; Grade 1, represented mild muscle stiffness or discomfort that was elicited only upon specific questioning, typically affecting the neck, shoulders, or lower chest and becoming noticeable during deep inspiration.; Grade 2, moderate muscle stiffness or pain reported spontaneously by the patient and requiring analgesic treatment; and Grade 3, severe, generalized muscle pain or stiffness that was incapacitating.

Outcome measures

The primary outcome measures included the occurrence 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 reported.

Sample size calculation

The required number of participants was estimated using the anticipated variation in the occurrence of succinylcholine-related fasciculations across the three magnesium sulfate dosing regimens, which was considered the primary outcome. Based on previously reported fasciculation rates reported form different magnesium sulfate regimens in a previous randomized study [15], the study was designed to include at least 20 participants in each treatment arm, with a 5% significance level used for statistical testing.

Statistical analysis

Data analysis was conducted using SPSS software, version 20. Numerical variables were summarized as mean ± Standard Deviation (SD), whereas categorical variables were reported as numbers and percentages. Normality was assessed before analysis. Categorical variables were compared using the chi-square or Fisher's exact test, as appropriate, whereas one-way ANOVA with Tukey's post-hoc test was used for continuous variables across the three groups. Paired t-tests were applied to related measurements, and correlation analysis was used to assess associations between continuous variables. A P value <0.05 was considered statistically significant.

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.

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 did not differ significantly among the 3 groups (Table 1) (P>0.05).

The occurrence of fasciculations was 80% in Group 1, 55% in Group 2, and 30% in Group 3. The highest severity of fasciculations was observed in Group 1. sixty percent of patients had grade 2 and 3 fasciculation. Group 3 patients showed mild forms of fasciculation. Concerning myalgia, the highest incidence (25% of patients) occurred in group 1, while just 15% and 10% of groups 2 and 3 developed myalgia (P>0.05) (Table 2).

Significant decrease in Heart Rate (HR) and Systolic (SBP) and Diastolic (DBP) blood pressure was observed in the three groups after Mg sulphate administration and immediately after anesthesia being induced (P<0.05). After one minute of induction, significant rise in blood hemodynamic measures occured. 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 concentration (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 experienced warmth feeling after the administration of Mg sulfate. While just three in the second group had the feeling of warmth and none of group 1 developed it. Two patients in the third group complained of nausea while none in group 1 and 2 complained of PONV.

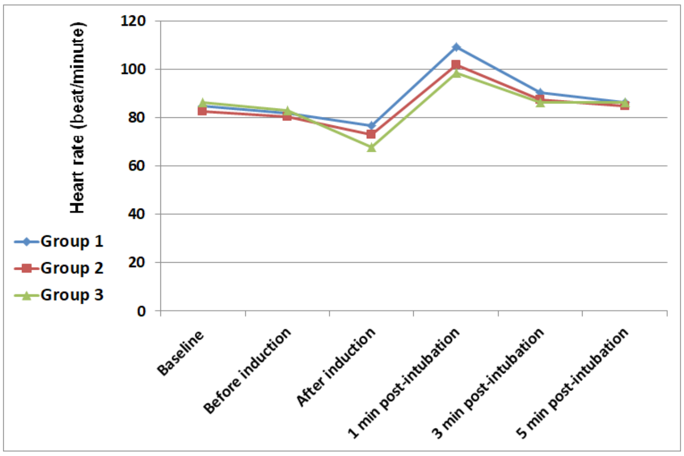

Figure 1: Heart Rate changes in the three groups.

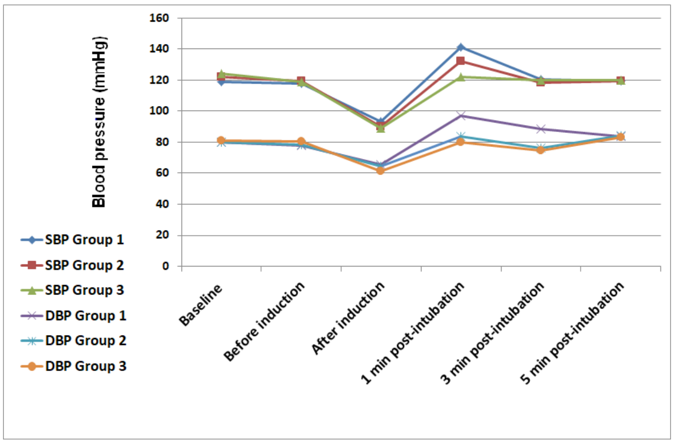

Figure 2: The Systolic and Diastolic blood pressure changes in the three groups.

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

	Group 1 N=20 Mean± SD	Group 2 N=20 Mean± SD	Group 3 N=20 Mean± SD	F	P
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

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

		Group			X2	P
		Group 1 N=20	Group 2 N=20	Group 3 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 1st 24hr	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. Fasciculations were observed in 80% of patients who received magnesium sulfate at 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 influence of different Mg sulphate doses 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. Grade 3 fasciculations were more frequent in group 1, occurring in 20% of patients, compared with 3.4% in group 2 and none in group 3 [15].

In the present study, postoperative myalgia was assessed 24 hours after surgery by asking patients about the presence of muscle pain 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 pretreatment with 40 mg/kg Mg sulfate significantly decreased postoperative myalgia [16].

The mechanism of occurrence of myalgia and fasciculation is not clear and the precise pathophysiological basis of succinylcholine-induced myalgia remains unclear. One proposed explanation is related to its action as a quaternary ammonium depolarizing neuromuscular blocker. By producing persistent depolarization of the presynaptic membrane, succinylcholine initially triggers muscle fasciculations before producing sustained neuromuscular relaxation [17].

The inhibitory effect of Mg sulfate on succinylcholine-induced fasciculations may be related to reduced acetylcholine release and activity, together with suppression of muscle fiber membrane excitability [15]. Furthermore, as an endogenous electrolyte, Mg offers a potential advantage over other pharmacological pretreatments, as it does not carry the same risks associated with sedative, anesthetic, or neuromuscular-blocking agents [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., suggested that Mg sulfate could attenuate the hemodynamic response associated with tracheal intubation during induction of general anesthesia [19]. This effect may be explained by Mg-induced vasodilation, resulting from its direct action on vascular smooth muscle as well as its sympatholytic effects 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. reported that pretreatment with Mg sulfate significantly attenuated succinylcholine-induced hyperkalemia, reducing the serum potassium increase by approximately 0.3 mmol/L, despite using a higher dose of 60 mg/kg [21].

In the current study, no significant complications were recorded and only two patients in the third group experienced nausea during the postoperative period.

Conclusion

Among the doses evaluated, I.V. Mg sulfate at 40 mg/kg demonstrated the greatest efficacy in reducing succinylcholine-induced fasciculations, reducing the cardiovascular response associated with tracheal intubation, and limiting the associated rise in serum potassium levels with no significant adverse effects. Mg sulfate in dose of 20 mg/kg is not recommended.

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