

EFFECT OF PRETREATMENT WITH MAGNESIUM SULPHATE ON SUCCINYLCHOLINE-INDUCED FASCICULATIONS AND MYALGIA

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ABSTRACT

BACKGROUND

Succinylcholine, a depolarising muscle relaxant possesses a unique property of rapid onset and short duration of action, but is accompanied by side effects such as fasciculations and myalgia. A prospective randomised-controlled trial was designed to assess the effect of a combination of magnesium sulphate with propofol for induction of anaesthesia on succinylcholine-induced fasciculations and myalgia.

MATERIALS AND METHODS

60 adult patients of ASA status I and II of both sexes for elective surgery under general anaesthesia were randomly allocated into two equal groups, group MG and group NS. The patients of MG group were pretreated with magnesium sulphate 40 mg/kg body weight in 10 mL volume, while patients of NS group were given isotonic saline 0.9% in the same volume (10 mL) intravenously slowly over a period of 10 mins. Anaesthesia was administered with pentazocine 0.6 mg/kg and propofol 2 mg/kg, followed by administration of succinylcholine 2 mg/kg intravenously. Muscle fasciculations were observed and graded as nil, mild, moderate or severe. Postoperative myalgia was assessed after 24 hrs. of surgery and graded as nil, mild, moderate or severe. Observations were made in double blind manner where the observer and the patient were blinded.

RESULTS

Demographic data and baseline parameters of both groups were comparable ($P > 0.05$). Muscle fasciculations occurred in 66.7% patients of MG group versus 100% patients of NS group with a significant difference ($P < 0.001$). After 24 hrs. of surgery, 12 patients of MG group and 28 patients of NS group had myalgia with a significant difference ($P < 0.001$). Statistically significant difference was found in MAP and heart rate at various intervals between the two groups ($P < 0.001$).

CONCLUSION

Magnesium sulphate 40 mg/kg intravenously maybe used with propofol for induction of anaesthesia to control succinylcholine-induced fasciculations and myalgia.

KEYWORDS

Propofol, Magnesium Sulphate, Succinylcholine, Fasciculations and Postoperative Myalgia.

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BACKGROUND

Succinylcholine, a depolarising muscle relaxant was introduced in 1952 by Sleff and Foldes and has a unique

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place in clinical practice, because it causes quick and excellent skeletal muscle relaxation for few minutes followed by spontaneous recovery. It possesses a unique property of rapid onset and short duration of action, but is accompanied by side effects like muscular fasciculations, myalgias, masseter spasm, hyperkalaemia, rhabdomyolysis, etc. It also increases intracranial pressure, intraocular pressure and intragastric pressure.¹ The pathophysiology of fasciculations is unclear, but it may be induced by axonal depolarisation caused by connection between succinylcholine and presynaptic and cholinergic nicotinic receptors.² 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 sulphate,⁹ thiopentone sodium,¹⁰ d-tubocurarine¹¹ and vecuronium.¹² Intravenous induction agents, thiopentone and propofol, modify succinylcholine-induced side effects. Propofol has been reported to be better than thiopentone in controlling myalgia¹⁰ though with variable results. Magnesium sulphate reduces negative effects caused by succinylcholine and avoids the increase of potassium concentration. It is also effective in reducing pain after the administration of succinylcholine. Magnesium sulphate along with thiopentone for induction of anaesthesia has been used to reduce succinylcholine-induced fasciculations and myalgia. Aldrete et al observed no fasciculations following thiopentone and succinylcholine in four out of six patients who were given magnesium sulphate in the dose of 40 mg/kg body weight IV.¹³ DeVore et al reported no fasciculations in any patients following thiopentone and succinylcholine administration in parturients on magnesium sulphate therapy.¹⁴ Chestnutt and Dundee reported that after induction of anaesthesia with thiopentone, magnesium sulphate controlled succinylcholine-induced fasciculations, but not myalgia.¹⁵ McClymont observed that incidence of myalgia with use of propofol was lower than that with thiopentone (19% vs. 63%).¹⁰

AIMS AND OBJECTIVES

To study the effect of pretreatment with magnesium sulphate on succinylcholine-induced fasciculations and postoperative myalgia.

Primary Objective

- To study the effect of pretreatment with magnesium sulphate on the incidence of succinylcholine-induced fasciculations.

Secondary Objective

- To study the effect of pretreatment with magnesium sulphate on the incidence of succinylcholine-induced myalgia.
- To study the effect on haemodynamic parameters.
- To study the associated side effects.

MATERIALS AND METHODS

After obtaining approval from the Institutional Ethics Committee and informed consents from the patients, a prospective randomised-controlled trial was performed on a total of 60 patients of ASA grade I and II of either sex undergoing surgeries under general anaesthesia.

Power based sample size calculation was done. Incidence of fasciculations was reported to be 90% and hence the value of p_1 was taken as 0.9. Considering a reduction in incidence of fasciculations from 90% to 60% as significant with the α value of 0.05 and β value of 0.1, the sample size was calculated using the following formula.

$$\begin{aligned} n &= \frac{p_1(1-p_1) + p_2(1-p_2)}{(p_1-p_2)^2} * f(\alpha, \beta) \\ &= \frac{0.9(1-0.9) + 0.6(1-0.6)}{(0.9-0.6)^2} * 7.9 \\ &= \frac{(0.9*0.1) + (0.6*0.4)}{0.3^2} * 7.9 \\ &= \frac{0.09 + 0.24}{0.09} * 7.9 \\ &= \frac{0.33}{0.09} * 7.9 \\ &= 28.96 \end{aligned}$$

The sample size calculated as 28.96 was rounded off to 30 for each group and taken in the study.

Inclusion Criteria

1. ASA grade I and II.
2. Age- 18-60 years.
3. Weight- 40-70 kg.

Exclusion Criteria

1. Patients with renal diseases, hepatic diseases, neurological disorders and neuropathies, cardiovascular diseases and respiratory problems.
2. Patients with known neuromuscular disorders.
3. Patients undergoing emergency surgery.
4. Patients with psychiatric disorders or on antipsychotic medication.
5. Pregnant patients.
6. Patients with morbid obesity.
7. Patients with malignant hypertension.
8. Patients with hypomagnesemia/hypermagnesemia.
9. Patients with anticipated airway difficulties.
10. Those with any known allergy to study drugs.
11. Patients taking any medication in the form of analgesics or a combination of analgesics and muscle relaxant.

The patients were randomly allocated into two groups of thirty patients each using a random number table; Group MG who received magnesium sulphate (40 mg/kg body weight in 10 mL water for injection)¹⁶ and Group NS who received isotonic saline (0.9%) in the same volume (10 mL) intravenously slowly over 10 minutes before the induction of anaesthesia. Allocation concealment was done using sealed opaque envelope technique. Monitoring for continuous Electrocardiogram (ECG), heart rate, Noninvasive Blood Pressure (NIBP) and pulse oximetry (SpO₂) was started. After administration of magnesium sulphate or saline, anaesthesia was administered with pentazocine 0.6 mg/kg and propofol 2 mg/kg body weight followed by succinylcholine 2 mg/kg IV. Following administration of succinylcholine, the patients were observed for fasciculations, which were graded as nil (absent), mild (fine fasciculation of the eyes, face, neck or fingers without

movements of the limbs), moderate (obvious muscle twitching at more than one sites or movement of limb) and severe (vigorous, sustained and widespread fasciculations).¹⁷ Oral endotracheal intubation was performed after assessing complete muscle relaxation clinically over 60s and anaesthesia was maintained with a mixture of nitrous oxide and oxygen (2:1) and halothane (0.5%) using a Bain's coaxial circuit. Controlled ventilation was facilitated by using vecuronium bromide. Vitals such as SBP, DBP, heart rate and SpO₂ were recorded at regular intervals, i.e. immediately after intubation, just after intubation and 3 minutes and 5 minutes after intubation and monitoring was continued at 15 minutes interval intraoperatively. At the end of surgery, neuromuscular blockade was reversed using neostigmine and glycopyrrolate. Postoperative myalgia was assessed after 24 hrs. of surgery in all patients and graded as nil (absence of pain), mild (muscle stiffness or pain on specific questioning in nape of neck, shoulders and lower chest on deep breathing), moderate (muscle stiffness and pain complained by the patient spontaneously requesting analgesia) and severe (incapacitating generalised muscle stiffness or pain).⁷ The person who injected the drug and observers for fasciculations and postoperative myalgia (separate observer for each parameter) were blinded for the pretreatment drug. The statistical analysis of the observed data was done using

SPSS version 20. Continuous data were analysed by Student's t-test while the categorical data by the chi-square test.

RESULTS

The demographic data and the vital parameters between the two groups were comparable (Table 1). Significant difference was noted in the mean arterial pressure at different intervals after induction just after intubation and 3 minutes and 5 minutes after intubation (P<0.01) (Table 2). Statistically significant difference was also observed in heart rate at various intervals just after 3 minutes and 5 minutes after intubation (P<0.01) (Table 3). The overall incidence of muscle fasciculations was 66.7% in MG group against 100% in NS group with a statistical significant difference between two groups (P<0.001) (Table 4). In MG group, 40%, 30% and 6.7% patients developed mild, moderate and severe fasciculations, respectively (Table 4). Observation of NS group revealed mild, moderate and severe fasciculations in 13.3%, 13.3% and 73.3% patients, respectively. 12 patients (40%) of MG group while 28 patients (86.7%) of NS group had postoperative myalgia after 24 hrs. with statistically significant difference between two groups (P<0.001) (Table 5). Patients of group MG developed myalgia only of mild intensity while it varied from mild (20%) to moderate (46.7%) to severe (20%) in NS group (Table 5).

Parameter	MG	NS	P Value	Significance
Gender: Male/Female	10/20	14/16	0.430 ^a	Not significant
ASA: I/II	18/12	18/12	1 ^a	Not significant
Age (yrs.)	27.30±9.03	30.80±11.60	0.198 ^b	Not significant
Weight (kg)	51.10±7.31	54.60±7.80	0.078 ^b	Not significant
Height (cm)	157.20±5.64	157.93±7.31	0.665 ^b	Not significant
SBP	118.40±12.72	124.06±11.44	0.075 ^b	Not significant
DBP	73.26±7.85	77.20±9.60	0.088 ^b	Not significant
MAP	88.31±9.14	92.82±9.89	0.072 ^b	Not significant
HR	93.26±7.68	95.60±8.52	0.270 ^b	Not significant
SpO ₂	97.66±0.80	97.86±0.89	0.367 ^b	Not significant

Table 1. Demographic Data and Baseline Characteristics of the Two Groups

a- chi-square test, b- Student's t-test

MAP	MG	NS	P Value	Significance
Baseline	88.31±9.14	92.82±9.89	0.072	Not significant
After induction	76.77±7.29	91.56±9.86	0.000	Significant
After intubation	95.08±10.51	109.11±10.24	0.000	Significant
3 mins. after intubation	89.07±7.96	99.68±6.34	0.000	Significant
5 mins. after intubation	85.02±7.72	91.02±9.99	0.012	Significant

Table 2. Comparison of MAP at Different Intervals between Two Groups

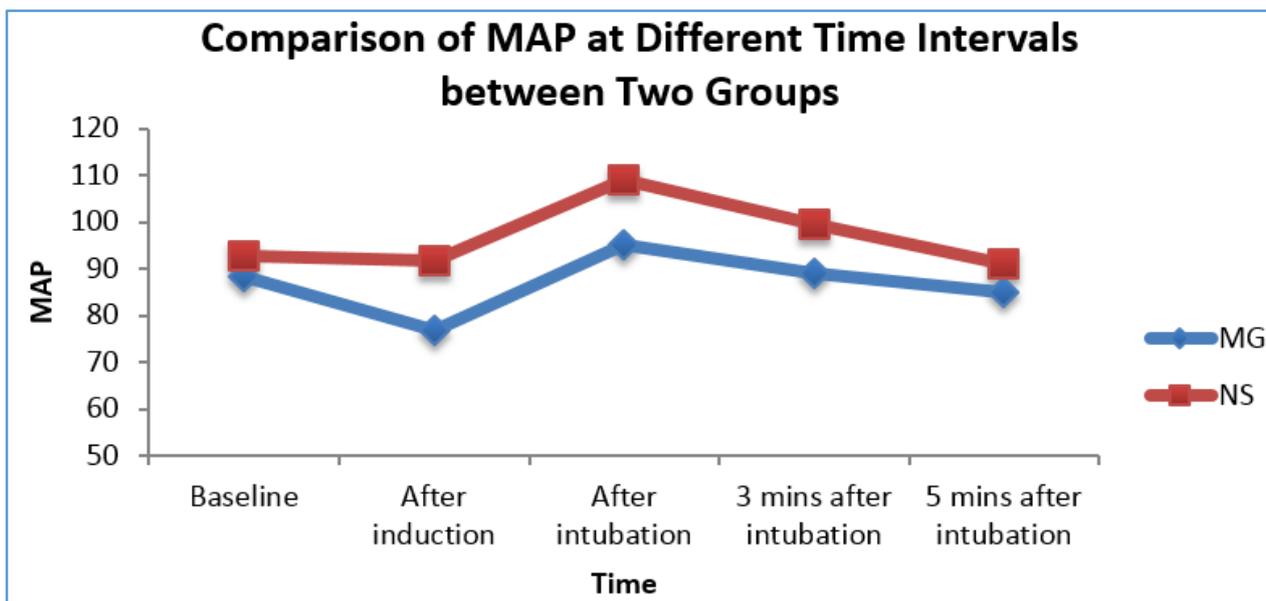


Figure 1. Difference in MAP between the Two Groups at Different Time Intervals

HR	MG	NS	P Value	Significance
Baseline	93.26±7.68	95.60±8.52	0.270	Not significant
After induction	86.83±6.48	88.53±6.57	0.318	Not significant
After intubation	109.10±8.66	116.36±7.93	0.001	Significant
3 mins. after intubation	100.20±5.12	105.60±4.68	0.000	Significant
5 mins. after intubation	88.73±8.34	94.36±5.79	0.004	Significant

Table 3. Comparison of Heart Rate at Different Intervals between Two Groups

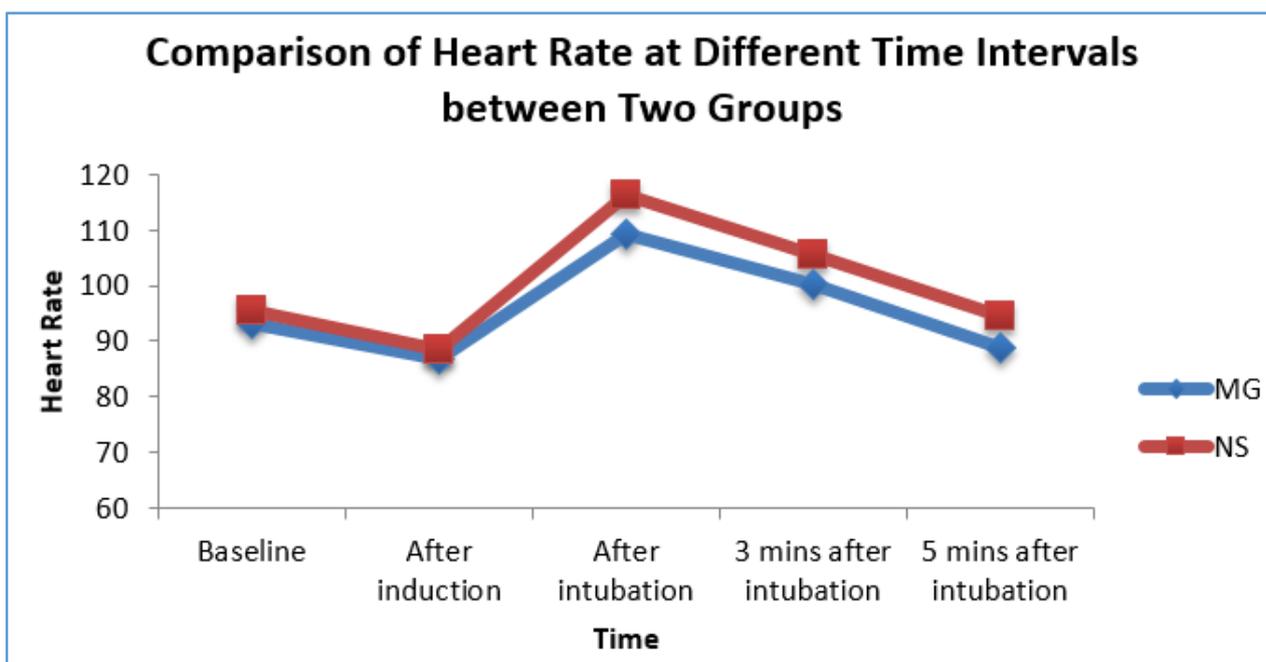


Figure 2. Distribution of Heart Rate between the Two Groups at Different Time Intervals

Fasciculations	MG	NS	P Value	Significance
Nil	10 (33.3%)	0 (0%)	<0.01	Very significant
Mild	12 (40%)	4 (13.3%)		
Moderate	6 (30%)	4 (13.3%)		
Severe	2 (6.7%)	22 (73.3%)		
Total	20 (66.7%)	30 (100%)		

Table 4. Comparison of Severity of Fasciculations between Two Groups

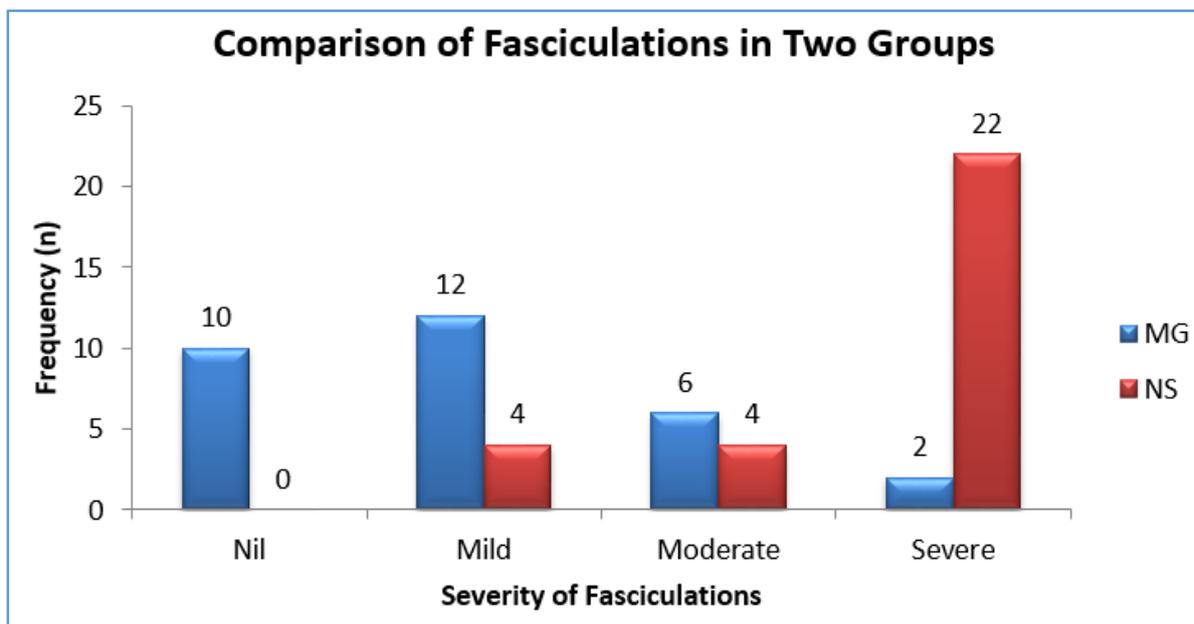


Figure 3. Incidence and Severity of Succinylcholine-Induced Fasciculations between the Two Groups

Myalgia	MG	NS	P Value	Significance
Nil	18 (60%)	4 (13.3%)	<0.001	Very significant
Mild	12 (40%)	6 (20%)		
Moderate	0 (0%)	14 (46.7%)		
Severe	0 (0%)	6 (20%)		
Total	12 (40%)	26 (86.7%)		

Table 5. Comparison of Severity of Myalgia between Two Groups

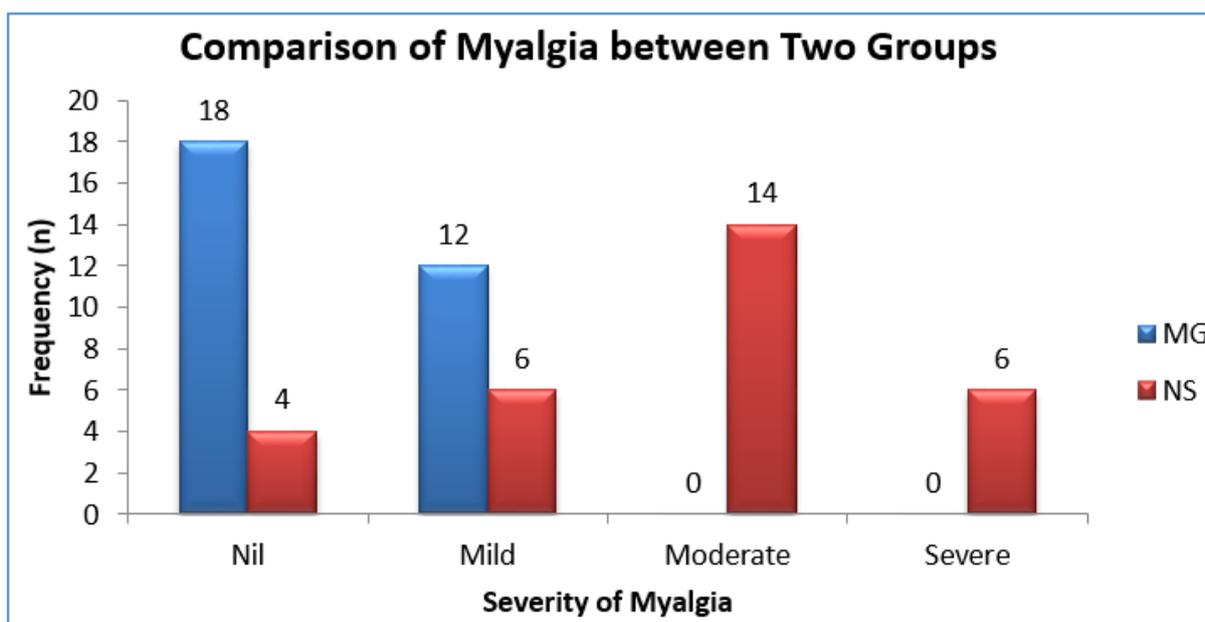


Figure 4. Incidence and Severity of Succinylcholine-Induced Postoperative Myalgia between the Two Groups

DISCUSSION

Kumar M et al (2012) reported fasciculations in 100% of placebo group and 50% in magnesium sulphate group.¹⁶ We observed fasciculations in 66.7% cases in magnesium sulphate group and 100% cases in control group. Our findings are supported by the findings of Sakuraba S et al (2007) who also reported no fasciculations in 33% of magnesium sulphate group.¹⁷ Behzad Ahsan et al (2014)

reported fasciculations in 8% of magnesium sulphate group and 90% in placebo group.² Aldrete JA et al (1970) also observed fasciculations in 70% of the patients receiving 1 g of magnesium sulphate/sodium thiopental/succinylcholine. They found fasciculations to be mild and brief in 40% of the patients.¹³ We also had a similar finding. Though, they reported 30% of the patients developing fasciculations having the usual intensity and duration in our study, 20% of

patients had moderate intensity and 2 (6.7%) patients had severe intensity. These variations maybe due to different drugs used for the induction purpose. In the above study, thiopentone sodium 4 mg/kg was used for induction while we used propofol 2 mg/kg in our study. This variation may also be due to variation in criteria for fasciculation. They observed the onset and intensity of muscle fasciculations only in the upper half of the body whereas we noted fasciculations in the entire body. Kararmaz A et al (2003) studied the effect of propofol on succinylcholine-induced fasciculations and found that 20% of the propofol group did not experience any type of fasciculation and none of them experienced severe fasciculations.¹⁸ We also found that 33.3% propofol, magnesium sulphate, succinylcholine group had no fasciculations and only 2 (6.7%) developed severe fasciculations. Thus, both propofol as well as magnesium sulphate have an additive role in controlling the frequency as well as intensity of the fasciculations.

The choice of induction agent and premedication affects the incidence of myalgia. Manataki AD et al (1999) used continuous propofol infusion to control succinylcholine-induced postoperative myalgia. Postoperative myalgia is an annoying complication associated with the use of succinylcholine. No correlation has been established between the incidence of fasciculations and myalgia. Fasciculations are due to agonistic action of succinylcholine to acetylcholine on postsynaptic acetylcholine receptors resulting in rapid firing. Asynchronous action of muscle spindles leads to fasciculations and myalgia. A comparatively larger dose of succinylcholine results in synchronous activation of muscle spindles resulting in less myalgia.¹⁹ We observed the incidence of myalgia to be 12 (40%) in magnesium sulphate group as compared to 26 (86.6%) in the control group. These differences were found to be significant. Our findings are supported by findings of Mahendra Kumar et al (2012) who reported 30% postoperative myalgia in control group compared to none in magnesium sulphate group.¹⁶ Our study is in contrast to the findings of R Ursekar et al (2016) who reported no significant difference in postoperative myalgia between control group and the group receiving magnesium sulphate.²⁰ Our study is also supported by the study of McClymont C (1994) who found significantly lower incidence of suxamethonium myalgia (19%) compared with thiopentone group (63%) ($P < 0.05$).¹⁰ Stacey MR et al (1995) noticed no significant difference in the effect of magnesium sulphate on succinylcholine-induced myalgia. Incidences were similar in both the groups.²¹ The difference may be due to the fact that in the above study, thiopentone sodium was used as an induction agent, whereas in our study, propofol was used. The lower incidence of myalgia maybe due to synergistic effect of propofol and magnesium sulphate.

In our study, we found that majority of the patients (50%) receiving magnesium sulphate had a strange feeling of warmth, which was very annoying to the patients and was felt initially in the throat passing to the body before it either disappeared or radiated to the peripheries. It was associated with tachycardia, mild hypotension along with occasional

sweating. Chestnutt WN et al (1985) also found similar distressing side effects in their study.¹⁵ Peck and Meltzer (1916) in their study also reported a feeling of hot sensation and flushing of the face.²² Flushing of face was not observed in our study. The difference was probably due to difference in dose of magnesium sulphate. The sensation of warmth maybe explained by the peripheral dilation and pooling of blood in extremities.

CONCLUSION

Magnesium sulphate is an effective drug in reducing the incidence and severity of both fasciculations and myalgia associated with succinylcholine administration. It also acts in blunting the intubation response during induction of general anaesthesia. Propofol has a synergistic action on these effects when given along with magnesium sulphate. However, magnesium sulphate is also associated rarely with some bothersome effects such as the feeling of warmth and flushing in the body along with sweating.

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