Original Article

Effect of magnesium sulfate with propofol induction of anesthesia on succinylcholine-induced fasciculations and myalgia

Mahendra Kumar, Nalin Talwar, Ritu Goyal, Usha Shukla, AK Sethi

Department of Anaesthesiology and Critical Care, University College of Medical Sciences and GTB Hospital, Shahdara, Delhi, India

Abstract

Background: Magnesium sulfate and propofol have been found to be effective against succinylcholine-induced fasciculations and myalgia, respectively, in separate studies. A prospective randomized double blind controlled study was designed to assess the effect of a combination of magnesium sulfate with propofol for induction of anesthesia on succinylcholine-induced fasciculations and myalgia.

Materials and Methods: Randomly selected 60 adult patients scheduled for elective surgery under general anesthesia were allocated to one of the two equal groups by draw of lots. The patients of MG Group were pretreated with magnesium sulfate 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 min. Anesthesia was induced with fentanyl 1.5 mcg/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 h of surgery and graded as nil, mild, moderate, or severe. Observations were made in double blind manner.

Results: Demographic data of both groups were comparable ($P > 0.05$). Muscle fasciculations occurred in 50% patients of MG group versus in 100% patients of NS group with a significant difference ($P < 0.001$). After 24 h of surgery, no patient of MG group and 30% patients of NS group had myalgia with a significant difference ($P < 0.002$).

Conclusion: Magnesium sulfate 40 mg/kg intravenously may be used with propofol for induction of anesthesia to control succinylcholine-induced fasciculations and myalgia.

Key words: Anesthetic agent: propofol, drug: magnesium sulfate, muscle relaxant: succinylcholine, side effects: fasciculations and postoperative myalgia

Introduction

Fasciculations and postoperative myalgia are well-known disadvantages of succinylcholine. Many attempts have been made to control these undesired effects caused by succinylcholine, which include pretreatment with nondepolarizing muscle relaxants,[1] lignocaine,[2] calcium gluconate,[3] nonsteroidal antiinflammatory drugs (NSAIDs),[4,5] diazepam,[6] etc., with variable results. Induction of anesthesia with magnesium sulfate and thiopentone has been tried for this purpose also.[7] Propofol has also been identified to be a better agent than thiopentone sodium to control succinylcholine-induced myalgia.[8] We studied induction of anesthesia with propofol, after pretreatment with magnesium sulfate, to assess their effects on incidence and severity of succinylcholine-induced fasciculations and postoperative myalgia.

Address for correspondence: Dr. Mahendra Kumar,
47-D, Pocket –A, MIG, GTB Enclave, Shahdara, Delhi – 110 093, India.
E-mail : mahendramohit@yahoo.com

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Materials and Methods

After clearance from institutional ethical committee, 60 adult patients of ASA class I, aged between 18 and 60 years, of either sex, scheduled for elective surgery under general anesthesia were selected at random. Informed consent was obtained from each patient to participate in the study. Patients, taking any medication in the form of analgesics or a combination of analgesics and muscle relaxant or having any systemic disease, were excluded from the study.

The patients were allocated to either of the two groups (MG or NS group) by draw of lots. Monitoring for continuous electrocardiogram (ECG), heart rate, noninvasive blood pressure (NIBP), and pulse oximetry (SpO_2) was started and a neuromuscular monitoring device was attached to the free hand of the patients. Before induction of anesthesia, the patients of MG group were given magnesium sulfate 40 mg/kg body weight in 10 ml (water for injection was used to make 10 ml), while patients of NS group were given isotonic saline (0.9%) in same volume (10 ml) intravenously (IV) slowly over a period of 10 min under monitoring. After administration of magnesium sulfate or saline, anesthesia was induced with fentanyl 1.5 mcg/kg and propofol 2 mg/kg body weight, followed by succinylcholine 2 mg/kg IV. Following administration of succinylcholine, fasciculations were observed and 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), or severe (vigorous, sustained, and widespread fasciculations).[5] Oral endotracheal intubation was performed after assessing complete muscular relaxation by single twitch neuromuscular monitoring and anesthesia 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, under train of four (TOF) neuromuscular monitoring, to maintain normocapnia. At the end of surgery, neuromuscular blockade was reversed by neostigmine and atropine. Postoperative myalgia was assessed after 24 h 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 of by the patient spontaneously requesting analgesia), or severe (incapacitating generalized muscle stiffness or pain).[5] 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 by using Student's *t* test and Fisher's exact test.

Results

The demographic data of patients of the two groups were comparable [Table 1]. The overall incidence of muscle fasciculations was 50% in MG group against 100% in NS group with a statistical significant difference between two groups ($P < 0.001$) [Table 2]. The different grades of muscle fasciculations observed are also shown in the same table. In MG group, 23.3% and 26.7% patients developed mild and moderate fasciculations, respectively. Observation of NS group revealed mild, moderate, and severe fasciculations in 33.3%, 60%, and 6.7% patients, respectively. No patient of MG group, while 9 (30%) patients of NS group had postoperative myalgia after 24 h with statistically significant difference between two groups ($P < 0.002$) [Table 2]. No patient of any group showed prolonged neuromuscular blockade.

Table 1: Demographic data of patients of two groups

	MG group (n = 30)	NS group (n = 30)	*P* value
Mean age ± S.D (y)	33.57 ± 9.26	34.20 ± 11.61	0.54*
Mean body weight ± S.D. (kg)	50.27 ± 7.12	51.50 ± 7.26	0.50*
Duration of surgery (min)	111.96 ± 18.17	109.73 ± 21.29	0.59*
Sex ratio (M:F)	13:17	15:15	

*P value < 0.05 significant. * .– no significant difference between two groups*

Table 2: Total number of patients and their distribution with percentage having different grades of fasciculations and postoperative myalgia in both groups

	MG group (n = 30) No. of patients (percentage)	NS group (n = 30) No. of patients (percentage)	*P* value
Fasciculations: Nil	15 (50)	0 (0)	
Mild	7 (23.3)	10 (33.3)	
Moderate	8 (26.7)	18 (60)	
Severe	0 (0)	2 (6.7)	
Total number of patients who had fasciculations	15 (50)	30 (100)	<0.001
Myalgia: Nil	30 (100)	21 (70)	
Mild	0 (0)	6 (20)	
Moderate	0 (0)	3 (10)	
Severe	0 (0)	0 (0)	
Total number of patients who had post operative myalgia	0 (0)	09 (30)	<0.002

P < 0.05 shows significant difference between two groups

All patients remained hemodynamically stable. There was no statistically significant difference between two groups for their heart rate and systolic blood pressure at any point of time ($P > 0.05$) [Figure 1].

Discussion

Succinylcholine, a depolarizing muscle relaxant, has a unique place in clinical practice because it causes quick and excellent skeletal muscles relaxation for few minutes followed by spontaneous recovery. Unfortunately, its use is associated with muscular fasciculations and postoperative myalgia. Pretreatment with various drugs such as rocuronium,[1] atracurium,[2] lignocaine,[2] calcium,[3] ketorolac,[4] diclofenac sodium,[5] diazepam,[6] magnesium sulfate,[7] thiopentone sodium,[8] small dose of succinylcholine (self-taming),[9] d-tubocurare,[10] and pancuronium,[11] vecuronium[12] have been tried to reduce these side effects. Intravenous induction agents, thiopentone and propofol, modify succinylcholine-induced side effects. Propofol has been reported to be better than thiopentone to control myalgia.[8] Magnesium sulfate along with thiopentone for induction of anesthesia 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 sulfate 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 sulfate therapy.[14] Chestnut and Dundee[15] reported that after induction of anesthesia with thiopentone, magnesium sulfate controlled succinylcholine induced fasciculations but not myalgia. McClymont[8] observed that incidence of myalgia with use of propofol was lower than that with thiopentone (19% vs. 63%).

In our study, incidence and severity of fasciculations were significantly lower in patients who received magnesium sulfate as compared to those patients who received normal saline. On comparison of our results with those of Stacey *et al.*,[16] who used magnesium sulfate 40 mg/kg body weight with thiopentone induction, we found no fasciculations in 50% patients receiving magnesium sulfate as against 40% in their study; and after 24 h, no patient of MG group had myalgia, while 9 patients of NS group had myalgia, as against no difference in the incidence of myalgia between control and magnesium groups in their study. No prolonged muscular relaxation was observed in either of the studies. Our results were possibly better because propofol was used as induction agent.

Fasciculations following succinylcholine administration are associated with muscle damage with a rise in serum concentration of creatinine kinase and myoglobin.[17,18] Literature, however, shows no correlation between fasciculations and postoperative myalgia.[19,20] Laurence[17] observed no correlation between myalgia and rise in creatine kinase, an indicator of muscle damage. Collier observed a transient fall in serum calcium levels at 1 min, following succinylcholine administration in patients who had postoperative myalgia and postulated that influx of calcium in to muscle cells caused an increase in muscle damage and pains.[21] Magnesium affects the neuromuscular junction and competes with calcium at prejunctional site. These both ions antagonize each other—high magnesium concentrations inhibit release of acetylcholine, while high calcium concentration increases the release of acetylcholine from the presynaptic nerve terminals.[22] This may explain

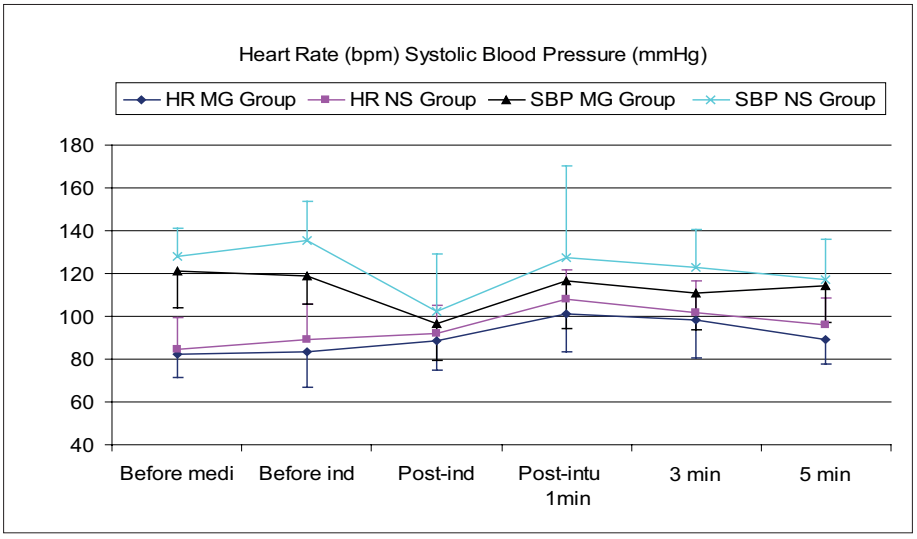

Figure 1: Mean with SD of heart rate (beats per minute) and systolic blood pressure (mm of Hg) in two groups at different points of time (medi = medication, ind = induction, intu = intubation)

the control of succinylcholine-induced fasciculations by magnesium.

Serum magnesium levels were not done in this study and this was a limitation of our study. However, no patient showed any clinical sign of hypermagnesemia. Many studies have shown the use of magnesium sulfate in the dose of 40–60 mg/kg without any sign of hypermagnesemia or clinically significant rise in serum magnesium levels after infusion of magnesium sulfate for many hours. Tauzin-Fin *et al.*[23] used magnesium sulfate 50 mg/kg over a period of 20 min preoperatively without any rise in serum magnesium level. Tramer *et al.*[24] estimated serum magnesium level after giving a bolus of 3 g (20% 15 ml) followed by a continuous infusion of 500 mg/h for 20 h (total amount of magnesium: 13 g). In their study, pretreatment serum magnesium level was 0.74 ± 0.09 mmol/l, while after infusion for 20 h it was 1.34 ± 0.09 mmol/l (levels were not high enough to produce clinical effects of hypermagnesemia). In presence of normal renal functions, renal elimination of magnesium is rapid. Ryu *et al.*[25] injected magnesium sulfate 50 mg/kg IV as bolus and then 15 mg/kg/ hr IV infusion till the end of surgery. Serum magnesium levels were found to be significantly higher in patients who received magnesium sulfate than those who received saline only (1.5 ± 0.2 vs. 0.9 ± 0.1 mmol/l). Magnesium toxicity begins at the concentration of 2.5–5 mmol/l, which is much higher than highest level observed in their study.[26] When serum magnesium level reaches 3.1 mmol/l, depression of deep tendon reflexes occurs as a sign of toxicity.[27] We used a bolus of magnesium 40 mg/kg without infusion which is a safe dose considering the result of above studies and no patient had any sign of magnesium toxicity.

A meta-analysis found that the average incidence of myalgia at 24 h was 65.4% with propofol and 49.2% with thoipentone.[28] The result of this meta-analysis however do not tally with the findings of McClymont,[8] whose study was surprisingly not included in the meta-analysis. The analysis included 47 trials that used thiopentone sodium against only 4 trials in which propofol was used as induction agent. Although, a single-dose propofol induction has been used with conflicting results for preventing postoperative myalgia and it has no effect in preventing the increase in creatine kinase.[29] Manataki *et al.* used continuous propofol administration to control succinylcholine-induced postoperative myalgia.[30]

The findings of our study, regarding myalgia, were similar to that of McClymont's study. He observed that propofol induction was associated with a significantly lower incidence of succinylcholine-induced myalgia (19%) compared with thiopentone induction (63%) ($P < 0.05$). In our study, NS group had 30% incidence of postoperative myalgia with propofol induction of anesthesia.

To conclude, magnesium sulfate 40 mg/kg intravenously, as pre-treatment, may be used with propofol for induction of anesthesia to control succinylcholine-induced fasciculations and myalgia.

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