ORIGINAL ARTICLE

Effect of Intavenous Magnesium Sulphate Vs Placebo in Reduction of Succinylcholine Induced Fasciculations and Myalgias

RAFIA KOUSAR[1], MUHAMMAD ABDUL AZIZ[2], SAJID FAROOQ[3], ATHAR PARVAIZ[4], SYED AUSHTAR ABBAS NAQVI[5], HAQ DAD DURRANI[6]

[1]*Senior Registrar Anesthesia, Sahara Medical College Narowal.*
[2]*Associate Professor Anesthesia, Sahara Medical College Narowal*
[3]*Assistant Professor Cardiac Anesthesia and ICU CCB/QAMC Bahawalpur*
[4]*Registrar Medicine, Sahara Medical College Narowal.*
[5]*Assistant Professor & HOD Anesthesia, Pain and Intensive Care DG Khan Medical College, DG Khan.*
[6]*Professor of Anesthesia, Pain and Intensive Care Sahara Medical College Narowal.*
Correspondence to Dr Rafia Kousar, Email: drrafi2010@ymail.com. Mobile. 03468789572

ABSTRACT

Background: Magnesium sulphate inhibits the release of acetylcholine at nerve terminal and decreases the excitability of muscle fiber. Recently it has been shown to decrease fasciculations and myalgias caused by succinylcholine. Therefore this study was planned to investigate its effects on succinylcholine induced fasciculations and myalgias.
Study design: Randomized control trial
Methodology: 70 Patients were randomly divided into two groups i.e. Magnesium Sulphate 40mg/kg (Group A) and Normal Saline 0.9% (Group B). The patients of Group A were pretreated with magnesium sulphate 40mg/kg body weight in 10 mL volume, while patients Group B were given isotonic saline 0.9% in the same volume (10mL) intravenously slowly over a period of 10 minutes. Fasciculations were assessed and graded. Postoperative myalgias were assessed after 24hr of surgery and graded. All the data was collected using case report form and analyzed using SPSS version 20.
Results: In group-A, 17(48.6%) cases had no fasciculation and myalgias, 18(51.4%) had mild fasciculation and myalgias. In group-B all had moderate fasciculation, 7(20%) had mild and 28(80%) had moderate Myalgias. The mean hospital stay in group A and group B was 1.63 ± 0.60 and 2.11±1.13 days respectively
Conclusion: Use of Magnesium Sulphate 40mg/kg before induction of anesthesia significantly reduces the incidence and severity of fasciculations and myalgias and decreases the hospital stay.
Keywords: Magnesium Sulphate, Succinylcholine, Fasciculations, Myalgias, Postoperative, Graded, excitability.

INTRODUCTION

Succinylcholine is short acting and depolarizing neuromuscular blocker, because of its rapid onset with complete and predictable paralysis. It is superior in providing Ideal intubating conditions[1]. It is concomitantly used with non-depolarizing blocking agents having a slight effect on tracheal intubation[2]. By far it is regarded as most suitable method for rapid sequence intubation[3]. In case of minor operations and ambulatory anesthesia it serves as unique muscle relaxant despite of high rate of minor to fatal complications.[4]The temporary fasciculation after injection is one of the side effects which is also related to various other complications of succinylcholine.[5] The fasciculation and myalgia are not so major side effects of succinylcholine but these are most commonly observed and are very distressing for the patients. The incidence of myalgias with succinylcholine is 20-80% and more commonly seen in Females[6,7]. Myalgia can persist for many days in some cases along with muscle tenderness and considerable distress.[8] The level of serum potassium are also augmented by this causing serious arrhythmia[9].

The fasciculation pathophysiology is not clear yet and it is thought to be induced by axonal depolarization. The link between succinylcholine and presynaptic and cholinergic nicotinic receptors causes this axonal depolarization. Myalgia as well as postoperative muscle damages are suggested to have various mechanisms, such as rise in the concentration of myoplasmic calcium, Alternation in membrane phospholipids, liberation of free fatty acids and free radicals[10]. The increase in phosphokinase is most likely to take part in development postoperative myalgia[11].

Several drugs have been used to reduce the undesired effects like Fasciculations and Myalgias. Pretreatment with Diclofenac, Ketorolac, Calcium, Diazepam, Lignocaine, Gabapentin, small dose of succinylcholine itself, Atracurium, rocuronium, cisatracurium, Remifentanil, d-tubocurare, Pancuronium, vecuronium, dexmeditomidine have been used for reducing or preventing succinylcholine induced fasciculation and myalgias but the results were not satisfactory [7,12,13,14,15,16].

Magnesium competes with calcium at presynaptic nerve terminal where it Causes inhibition of calcium release from motor end terminal and to some extent It also reduces the sensitivity of postjunctional membrane and excitability of the muscle fiber[17]. Previous studies on treatment with magnesium sulphate have shown significant benefits. Mahindra et al, have concluded in their study that IV magnesium sulphate 40mg/kg When used with propofol for induction of general anesthesia significantly decreased The severity and incidence of succinylcholine induced fasciculation and myalgias[18]. Ahsan et al in 2012 conducted a clinical trial to explore the influence of

Received on 24-10-2020
Accepted on 09-01-2021

magnesium Sulphate on succinylcholine-induced fasciculation on cases undergoing general Anaesthesia and concluded that fasciculation can be prevented with the use of magnesium sulphate[10]. Sakurba et al in 2006 conducted a study which concluded Prior administration of magnesium is considered as more beneficial to arrest Fasciculation and hemodynamic alternations which is associated with tracheal intubation in comparison to vecuronium[5].

The objective of the study was to compare incidence and severity of succinylcholine induced Fasciculation's and myalgias by Magnesium sulphate with placebo and to compare difference in hospital stay in groups receiving pretreatment with Magnesium sulphate and placebo for postoperative succinylcholine induced Myalgia.

MATERIAL AND METHODOLOGY

On the basis of previous related study, thirty five patients were allocated to each group[18]. This sample size was calculated by taking zero percentage of Myalgia's in Magnesium Sulphate Group (Group A) and 30% Myalgia's in normal saline group

Group B with power of the Test 90% and level of significance 99%. This randomized controlled study was conducted in Department of Anesthesia, King Edward Medical University/Mayo Hospital, Lahore in patients Aged 18-42 years of either sex undergoing elective General surgical procedures corresponding to American society of Anesthesiologists Class I or II. Following patients were excluded from the study as per the exclusion criteria:

- Patients with preexisting musculoskeletal disorders
- Patients receiving sedatives other than those determined by the study protocol
- Patients taking calcium channel blockers
- Patients with severe renal, hepatic, respiratory or cardiac disease.
- Patients who had received analgesics within 24 hour before scheduled surgery
- Patients with known hypersensitivity or contraindications to study drugs

All patients were allocated into two equal groups by using a table generated by computer, Magnesium sulphate 40mg/kg (Group A) and Normal Saline 0.9% (Group B) with 35 patients in each group. With non-invasive monitoring (Heart rate, systolic and diastolic blood pressure, Mean arterial pressure, oxygen saturation, Electrocardiogram) pre-operative vital signs were recorded in operation theatre. Intravenous line with 18 G cannula was taken. Ringer Lactate intravenous infusion was given. Before induction of anesthesia, the patients of A group was given magnesium sulfate 40mg/kg body weight in a micro burette (distilled water was used to make 100ml), while patients of B group was given isotonic saline (0.9%) in same volume (100ml) intravenously (IV) slowly over a period of 10min.We waited for 92 seconds after administration of magnesium sulfate or saline then anesthesia was induced with propofol 2mg/kg body weight, followed by succinylcholine 1mg/kg Following administration of succinylcholine, fasciculation were assessed and graded on the scale of 0 to 3 with 0 = nil (no visible fasciculation), 1 = mild(fine fasciculation of eyes, face, neck, or fingers without movements of the limbs), 2 = moderate (obvious muscle twitching at more than one sites or movement of limb), 3 = severe (vigorous, sustained, and widespread fasciculation).Oral endotracheal intubation was performed. 50% nitrous oxide, 50% oxygen and 1% isoflorane was used for maintenance .Controlled ventilation was facilitated by using atracurium 0.5mg/kg as induction dose and intermittent 10mg bolus as per requirement. At the completion of surgery, neuromuscular blockade was reversed by neostigmine 0.05mg/kg and glycopyrolate 0.01mg/kg. .After patient started obeying commands patient was extubated and shifted to recovery room and thereafter to the ward. There was no difference in time required for return of spontaneous breathing in both groups. Postoperative myalgias were assessed after 24hr 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).As we used a bolus of magnesium sulphate 40mg/kg without Infusion which is a safe dose no patient had any signs of magnesium toxicity such as Weakness, nausea and vomiting, Impaired breathing, Low blood pressure, abnormal heart Rhythm and asystole, Decreased or absent deep tendon reflexes, Low heart rate, Dizziness, Respiratory Arrest or cardiac arrest. The patients who develop fasciculations and myalgias were treated with injection ketorolac 30mg intravenously.

Statistical analysis: Collected data was entered to SPSS version 20 and was analyzed. Tables and graphs were used to represent the results. The Quantitative variables like age was described with mean ± standard deviation. The Qualitative variables like gender, pain were described as frequencies and percentages. Fasciculations and myalgias were analyzed by chi-square test. Student t test was used to compare hospital stay in both groups. A level of 1% ($p \leq 0.01$) was used for significant testing and association.

RESULTS

A total number of 70 patients were included in this study. The patients of Group A were pretreated with magnesium sulphate while patients of Group B were given isotonic saline 0.9%. The mean age of cases in this study was 30.17 ± 6.78 years with minimum and maximum age of 18-42 years respectively. The mean age in group-A and B was 29.86±6.89 years and 30.49 ± 6.75 years (Table 1) There were 15(21.43%) male and 55(78.57%) female cases in this study. The male to female ratio was 1:3.67(Fig 1). In group-A there were 6(17.14%) male and 29(82.86%) female while in group-B there were 9(25.71%) male and 26(74.29%) female case (Fig 2). In group-A 31(88.57%) cases had ASA-I and 4(11.42%) had ASA-II and in Group-B 34(97.14%) had ASA-I and 1(2.85%) had ASA-II (Fig 3).

In group-A, 17(48.6%) cases had no fasciculation, 18(51.4%) had mild fasciculation while in Group-B all cases had moderate fasciculation. There was significant association of Fasciculation with study group. (P-value <

0.001) (Table 2). In group-A 17(48.6%) did not develop Myalgia, 18(51.4%) had mild myalgia while in Group-B, 7(20%) cases had mild and 28(80%) cases had moderate Myalgia (P-value < 0.001) (Table 3). In group-A and group-B the mean hospital stay was 1.63±0.60 days and 2.11±1.13 days with higher stay in group-B but not statistically significant (P-value=0.028) (Table 4).

Fig.1: Gender distribution of cases

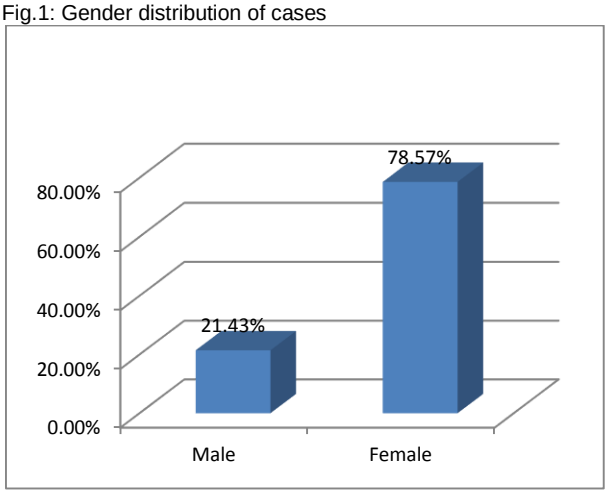

Fig. 2: Gender distribution of cases in both study groups

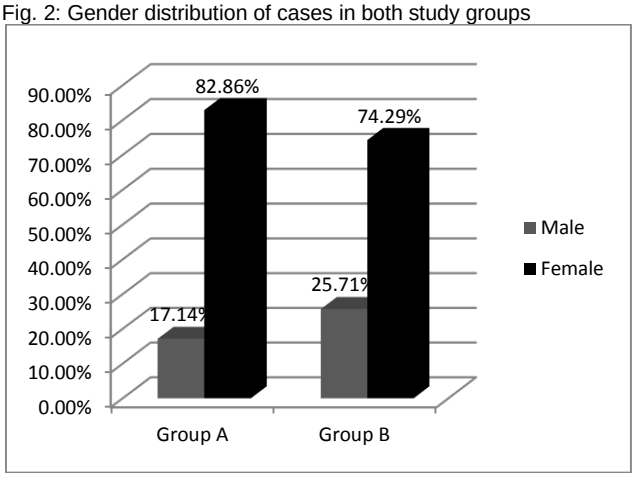

Fig. 3: Distribution of ASA classification in both groups

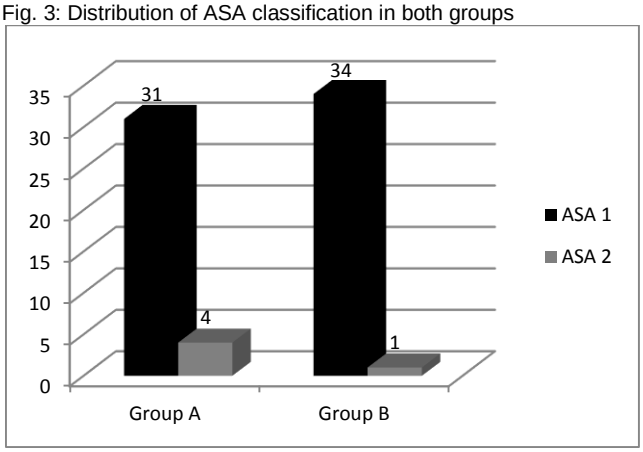

Table 1: Descriptive statistics and comparison of age in both groups

Study groups	Mean	S.D	Min.	Max.
Group A	29.86	6.89	18	42
Group B	30.49	6.75	19	40
Total	30.17	6.78	18	42

Table 2: Comparison of fasciculation in both groups

Fasciculation	Group A	Group B	Total
Nil	17(48.6%)	0(0%)	17(24.3%)
Mild	18(51.4%)	0(0%)	18(25.7%)
Moderate	0(0%)	35(100.0%)	35(50.0%)
Severe	0(0%)	0(0%)	0(0%)
Total	35(100.0%)	35(100.0%)	70(100.0%)

P-value < 0.001

Table-3: Comparison of myalgia in both groups

Myalgia	Group A	Group B	Total
Nil	17(48.6%)	0(0%)	17(24.3%)
Mild	18(51.4%)	7(20.0%)	25(35.7%)
Moderate	0(0%)	28(80.0%)	28(40.0%)
Severe	0(0%)	0(0%)	0(0%)

P-value < 0.001

Table 4: Comparison of hospital stay in both study groups

Study groups	Mean	S.D	Min.	Max.
Group A	1.63	0.60	1	3
Group B	2.11	1.13	1	6

P-value = 0.028

DISCUSSION

Results of this study demonstrated that the use of Magnesium Sulphate before induction of Anesthesia significantly reduces the incidence and severity of fasciculations and myalgias. A meta-analysis has been conducted in 1990 including 45 randomized and nonrandomized trials. The study has concluded a considerable reduction of about"30%"in myalgia incidence with atracurium, Gallamine, d-tubocurarine, lidocaine, diazepam, and pancuronium[19].

Precurarisation with nondepolarising muscle relaxants are used to prevent the SCC-induced side effects excluding arrhythmia. Though, partial paralysis can occur, that can lead to delays in the onset of SCC.[20] Alternatively, SCC-induced fasciculation are prevented by magnesium sulphate (MgSO4) due to its Precurarisation-effects and level of serum potassium is increased without any delay in the onset or continuation of SCC-induced effects.[21]Moreover, hemodynamic response is reduced by administrating MgSO4 before tracheal intubation. Vasodilatation and antiarrhythmic effects are produced by MgSO4 via inhibiting vasoconstricting elements.[11]Consequently; it should inhibit SCC-induced side effects and hemodynamic reactions to tracheal intubation. Though, distressing warm feeling can be sensed by conscious patients when inducing quick or slow (2 min) injection, while hypertension is suppressed in hypertensive proteinuric pregnant females.[22] This distressing sensation are eluded by providing MgSO4 between sedatives and SCC administration and it do not subjugate hypertension and raise heart rate (HR) prompted by rapid sequence induction.[20]The catecholamine release is inhibited by magnesium as it works like an adrenergic antagonist. Hence, the unwanted consequences of laryngoscopy for

tracheal intubation are controlled by magnesium like rise in heart rate, rise in blood pressure and rise in intraocular pressure. However, the SCC adverse effects are lessened by magnesium sulphate and it may prohibit rise in the level of potassium.[5] The SCC induced myalgia is also effectively managed by magnesium sulphate. Nonetheless, it has not been regularly implemented as data regarding this drug is short. For that reason, this study was designed to evaluate the magnesium sulphate effects on muscle fasciculation induced by SCC in subjects during the induction of anesthesia[23].

Kumar M et al in 2012 studied that the magnesium sulphate effects with propofol for anesthesia induction on SCC-induced fasciculations and myalgia. The result of the study showed that demographic data and baseline parameters of both groups were comparable (P>0.05). Muscle fasciculations was reported in “66.7%” patients of MG group versus 100% patients of NS group with a significant difference (P<0.001). After 24 hours of surgery, “12”cases of MG group and “28” cases of NS group reported 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). Thus, the study concluded that magnesium sulphate“40mg/kg” intravenously may be utilized with propofol for anesthesia induction to prevent succinylcholine-induced fasciculations and myalgia.[18] This study is comparable with our study.

Ahsan et al in 2012 conducted a clinical trial that had similar results to our study. He Investigate the magnesium sulphate effects on SCC-induced fasciculation on patients undergoing general anesthesia. Their study results demonstrated significant difference between the 2 groups in terms of the degree of fasciculation and muscle fasciculation (p0.05), but it was significant after anesthesia (p< 0.001). Hence, the fasciculation after anesthesia can be prevented by using magnesium sulphate. Therefore it can be used to prevent fasciculation[10].

Sakurba et al in 2006 conducted a study to assess the efficacy of pretreatment with magnesium and Precurarisation of vecuronium on SCC-induced fasciculation. Their results were in consistent with our study. They found significantly lower fasciculation scores and mean percent changes of heart rate, systolic blood pressure and rate pressure product between baseline and after induction in Magnesium group. Hence the study result concluded that pretreatment with magnesium is quite beneficial to render SCC-induced fasciculation.[5]

Jan-Uwe Schreiber et al in 2005 studied that non depolarizing muscle relaxants, lidocaine, or magnesium prevented fasciculation. Best prevention of myalgia was with nonsteroidal anti-inflammatory drugs and with rocuronium or lidocaine. A decrease in myalgia is proved with “1.5mg/kg” succinylcholine in comparison to“1mg/kg”. There was no effect of opioids. Like the results of our study, they reported that the SCC-induced fasciculation is ideally rendered by using magnesium, lidocaine or muscle relaxants[24].

In 1980 Jay S Devore et al found magnesium sulphate to be used as a primary treatment for the succinylcholine induced fasciculation and myalgias that is in accordance with our study[9].

M. R .Stacey et al in 1995 studied effects of Magnesium sulphate on suxamethonium-induced complications. They concluded that considerably low incidence of fasciculations in the magnesium group; during rapid-sequence induction of anesthesia this is same as in our study[20].

Astha Raman et al in 2016 studied that effect of pretreatment with magnesium sulphate on succinylcholine induced fasciculations and myalgia. They found that Magnesium sulphate is an effective drug in decreasing the frequency and degree of fasciculations as well as myalgia induced by succinylcholine. It also acts in blunting the intubation response during induction of general anaesthesia.[25] Result of this study is consistent with our study.

Danladi et al in 2007 studied that the severity of fasciculations were significantly reduced by pretreatment with magnesium sulphate[26]. This study is comparable with our study.

Aldrete et al found no fasciculation subsequent to succinylcholine in 4 out of 6cases who were provided magnesium sulphate in the dose of 40mg/kg same as our study.[27]

In contrast to our study James and colleagues reported no significant difference in frequency of fasciculations among magnesium and control groups. The reason for this may be due to the use of higher dose of magnesium sulphate (60 mg/kg)[28]

Stacey MRW study revealed that magnesium sulphate group had no statistically noteworthy decline in myalgia as compare to control group. The difference may be due to different induction agent i.e., thiopentone and higher dose of succinylcholine[20].

The findings of R Ursekar et al (2016) were different from our study results .They reported no significant difference in postoperative myalgia between control group and the group receiving magnesium sulphate which may be due to the use of low dose of Magnesium sulphate (30mg/kg) or due to higher dose of succinylcholine (2mg/kg)[29]

CONCLUSION

Results of this study demonstrated that the use of Magnesium Sulphate before induction of Anesthesia significantly reduces the incidence and severity of fasciculations and myalgias but not the hospital stay.

Limitations of study: The Serum magnesium levels were not done. But, no clinical sign of hypermagnesemia was manifested in any patient. Future studies can be done to investigate serum magnesium levels and side effects of magnesium sulphate.

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