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Research Article

Comparison between perioperative infusion of magnesium sulfate and placebo in cases undergoing upper abdominal surgery

[1]Saadia Khaleeq, [2]Sahir Shafiq

and [3]Sadia Yaqoob

[1]Assistant professor of Anaesthesia, Services hospital Lahore
[2]Assistant Professor Anesthesia, Children Hospital Institute of Child Health Faisalabad
[3]Woman Medical Officer, Department of Anesthesiology, Jinnah hospital Lahore

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ABSTRACT

Objective: To compare mean duration of postoperative analgesia between perioperative infusion of magnesium sulfate versus placebo in patients undergoing upper abdominal surgery.

Material and methods: This randomized controlled trial was conducted at Department of Surgery, Services Hospital, Lahore from January 2018 to June 2018. Total 100 patients undergoing upper abdominal surgery were selected for this study and divided into two group A and B randomly. Comparison of mean duration of postoperative analgesia between perioperative infusions of magnesium sulfate versus placebo was done.

Results: Mean age of the patients of study group A and B was 42.77 $\pm$ 9.48 years and 39.42$\pm$ 8.87 years and mean weight of study group A was 59.50 $\pm$ 12.35 kg and group B was 53.74 $\pm$ 11.07 kg. Mean duration of analgesia was 138.45 $\pm$ 32.11 minutes and 84.32 $\pm$ 23.84 minutes respectively in study group A and B. Mean duration of analgesia of study group A was significantly higher as compared to study group B with p value 0.001.

Conclusion: Results of present study showed significantly higher mean duration of analgesia in treatment group as compared to placebo group. Mean duration of analgesia was also significantly higher in treatment group for gender, age, weight and type of surgery.

Keywords: Magnesium sulfate, Postoperative analgesia, placebo

INTRODUCTION

Magnesium sulphate has been used as an adjuvant for perioperative analgesia.[1]Many clinical studies have demonstrated that i.v. magnesium infusion during general anesthesia reduced anesthetic requirement and postoperative analgesic consumption.[2] Relatively few studies have been investigated on the effects of magnesium sulphate infusion during spinal anesthesia.[3]

Postoperative pain falls in category of acute pain which is sharp, lacerating in character. Commonly employed methods for treating postoperative pain are conventional use of opioids, NSAIDS & paracetamol through various routes, central neuraxial blocks, peripheral nerve blocks, local anesthetic infiltration of wound.[4-8] Moreover, nonconventional therapy for postoperative pain

includes use of adjuncts to conventional therapy like $MgSO_4$, Clonidine, Reserpine, Neostigmine, use of antidepressants and anticonvulsants, transcutaneous electrical nerve stimulation (TENS), acupuncture, radiofrequency ablation (RFA), cryoanalgesia and rhizotomy.[9-11] In addition to relieve pain, $MgSO_4$ is also used in treatment of torsade de pointes, quinidine induced arrhythmias, as a bronchodilator in severe asthmatic attacks, as anticonvulsant in eclampsia, to delay preterm birth, to prevent cerebral palsy in preterm babies, calcium channel blocker over dosage and migraine and is recommended in various text books of different specialties.

Purpose of present study was to evaluate the mean duration of postoperative analgesia between perioperative infusion of magnesium sulfate versus placebo in patients undergoing upper abdominal surgery. Results of present study may help us in decrease in morbidity related to post-operative pain.

MATERIAL AND METHODS

This randomized controlled trial was conducted at Department of Surgery, Services Hospital, Lahore from January 2018 to June 2018. Total 100 patients of ASA grade I and II, who had to undergo different types of elective surgery for upper abdomen like chyolecystectomy, gastrostromy, liver abscess, right hemicolectomy, having age 18-50 years either male or female were selected.

Patient with prior surgery, major systemic illness, on calcium channel blocker, renal dysfunction, history of neuropathy, myopathy were excluded from study.Selected patients were randomly divided into two groups A & B. Group A received 50 mg/kg I/v of $MgSO_4$ in 0.9% N/S at induction and 15 mg/kg $MgS0_4$/hr, 6 hours postoperatively. While group B received 100 ml of 0.9% N/S at induction and 500 ml of 0.9% N/S 6 hours postoperatively.All the patients received injNalbuphine (0.1 mg/kg) inj Midazolam (0.1 mg/kg) for premedication, InjPropofol (2 mg/kg) injAtracurium (0.5 mg/kg) for induction, N_2O & O_2 (60:40) and Sevoflurane titrated to keep B.P + 20% of baseline value for maintenance, inj Atropine (0.02 mg/kg) and inj Neostigmine (0.05 mg/kg) postoperatively for reversal of neuromuscular blockade.

All the observations were recorded and entered in theproforma. Time for requirement of first rescue analgesia, which was provided by Inj. Tramadol 2–3 mg/kg iv was noted on the proforma. The outcome variable i.e. duration of analgesia was calculated and entered in the proforma.

All the collected was entered in SPSS version 18 and analyzed. Mean and SD was calculated for numerical data and frequencies were calculated for categorical data.

RESULTS

Mean age of the patients of study group A and B was 42.77 $\pm$ 9.48 years and 39.42$\pm$ 8.87 years and mean weight of study group A was 59.50 $\pm$ 12.35 kg and group B was 53.74 $\pm$ 11.07 kg. Mean duration of analgesia was 138.45 $\pm$ 32.11 minutes and 84.32 $\pm$ 23.84 minutes respectively in study group A and B. Mean duration of analgesia of study group A was significantly higher as compared to study group B with p value 0.001. (Table 1)

Comparison of mean duration of analgesia was done between male and female patients of both groups was done. Total 29 patients of study group A and 26 patients of stud group B were male and 21 patients of group A and 24 patients of group B were female. Mean duration of analgesia in male patients of group A was 134.77 $\pm$ 30.94 minutes and in male patients of group B was 85.78 $\pm$ 20.15 minutes. Statistically significant difference of mean duration of analgesia between the male patients of both groups was observed with p value 0.001. In female patients of group A, mean duration of analgesia was 139.65 $\pm$ 36.77 minutes and in group B was 87.91 $\pm$ 26.45 minutes. Difference of mean duration of analgesia was statistically significant with p value 0.001 (Table 2). Selected patients were divided into two age groups i.e. age group $\leq$ 35 years and age group >

35 years. Total 30 patients of study group A and 32 patients of study group B belonged to age group ≤ 35 years while 20 patients of study group A and 18 patients of study group B belonged to age group >35 years. In age group ≤ 35 years, mean duration of analgesia was 127.74 ± 24.45 minutes and 86.49 ± 28.58 minutes respectively in study group A and B. In study group A, mean duration of analgesia was significantly higher as compared to study group B with p value 0.001.

In Age > 35 years, mean duration of analgesia in study group A was 146.34 ± 36.33 minutes while in study group B was 85.55 ± 23.78 minutes and the difference was statistically significant with p value 0.001. (Table 3)

Stomach surgery was performed in 12 patients of group A while in 8 patients of group B. Mean duration of analgesia was 156 ± 32.68 minutes and 86.48 ± 20.75 minutes respectively in study Group A and B. difference of mean duration of analgesia was statistically significant with p value 0.001. Total 16 patients of study group A and 18 patients study group B undergone gallbladder surgery. Mean duration of analgesia in study group A was 138.11 ± 34.72 minutes and in study group B was 82 ± 24.41 minutes. Mean duration of analgesia was significnalty higher in study group A as compared to study group B with p value 0.001. Liver surgery was performed in 7 patients of group A and in 10 patients of group B. mean duration of analgesia was 130 ± 46.77 minutes and 89.25 ± 20.78 minutes respecitvley in group A and B and the difference was significant with p value 0.001. Colon surgery was performed in 15 patients and 14 patients respectively in study group A and B. mean duration of anlages in group A was 134.79 ± 16.33 minutes and in group B was 85.48 ± 22.88 minutes and the difference was statistically significant. (Table 4)

Patients were divided into two groups according to weight i.e. weight group <55kg and weight group ≥ 55 kg. In weight group <55kg, total 15 patients belonged to study group A while 28 patients belonged to study group B. In ≥ 55 kg group, total 35 patients belonged to study group A while 22 patients belonged to study group B. In weight group <55kg, mean duration of analgesia was 115.55 ± 20.45 minutes and 82.78 ± 24.33 minutes respectively in study group A and B. Mean duration of analgesia was significantly higher in stud group as compared to study group B. In weight group ≥ 55 kg, mean duration of analgesia was 150.47 ± 28.51 minutes in study group A while 89.72 ± 20.88 minutes in study group B and the difference was statistically significant with p value 0.001. (Table 5)

Table 1: Comparison of mean duration of analgesia between group A and B

Group	Mean duration of analgesia	P value
A	138.45 ± 32.11	0.001
B	84.32 ± 23.84	

Table 2: Comparison of mean duration of analgesia between male and female patients of both groups.

Group	Mean duration of analgesia	P value
Male patients		
A (N = 29)	134.77 ± 30.94	0.001
B (N = 26)	85.78 ± 20.15	
Female patients		
A (N = 21)	139.65 ± 36.77	0.001
B (N = 24)	87.91 ± 26.45	

Table 3: Comparison of mean duration of analgesia between both groups for age

Group	Mean duration of analgesia	P value
Age group ≤ 35 years		
A (N = 30)	127.74 ± 24.45	0.001
B (N = 32)	86.49 ± 28.58	
Age > 35 years		
A (N = 20)	146.34 ± 36.33	0.001
B (N = 18)	85.55 ± 23.78	

Table 4: Comparison of mean duration of analgesia between both groups for type of surgery

Group	Mean duration of analgesia	P value
Stomach Surgery		
A (N = 12)	156± 32.68	0.001
B (N = 8)	86.48± 20.75	
Gallbladder Surgery		
A (N = 16)	138.11± 34.72	0.001
B (N = 18)	82± 24.41	
Liver Surgery		
A (N = 7)	130± 46.77	0.001
B (N = 10)	89.25± 20.78	
Colon surgery		
A (N = 15)	134.79± 16.33	0.001
B (N = 14)	85.48± 22.88	

Table 5: Comparison of mean duration of analgesia between both groups for weight

Group	Mean duration of analgesia	P value
Weight < 55 kg		
A(n = 15)	115.55± 20.45	0.001
B(n = 28)	82.78± 24.33	
Weight ≥ 55 kg		
A (n = 35)	150.47± 28.51	0.001
B(n = 22)	89.72± 20.88	

DISCUSSION

Objective of presents was to compare mean duration of postoperative analgesia between perioperative infusion of magnesium sulfate versus placebo in patients undergoing upper abdominal surgery.Mean age of the patients of study group A and B was 42.77 ± 9.48 years and 39.42± 8.87 years and mean weight of study group A was 59.50 ± 12.35 kg and group B was 53.74 ± 11.07 kg. Mean duration of analgesia was 138.45 ± 32.11 minutes and 84.32 ± 23.84 minutes respectively in study group A and B. Mean duration of analgesia of study group A was significantly higher as compared to study group B with p value 0.001. similar results were reported in some studies.[12-13]

Three main results emerged from the review of the literature. First, in some trials, magnesium had a beneficial effect on postoperative pain intensity and analgesic requirements. Second, magnesium treatment decreased the incidence of postoperative shivering. Third, in most trials, magnesium serum concentrations in control patients decreased. The beneficial effects of magnesium were not unequivocal. In some trials, the benefit seemed to

be obvious; others were unable to show any improvement or even showed some deterioration in patients treated with magnesium.

The quantity and quality of the trials did not allow for the necessary subgroup analyses to evaluate the degree of efficacy with various regimens of magnesium. There was a large variability in doses; some trials tested a single bolus, and in the majority, a subsequent infusion was added. The largest trial tested a single bolus dose of magnesium sulfate 4 g and was unable to find any benefit in favor of magnesium.[14]Zarauzaet al.[15] infused more than 16 g of magnesium sulfate in their patients and were unable to find a beneficial effect. On the other hand, Levauxet al.[16] injected a bolus dose of magnesium sulfate 3.6 g and reported a significant decrease in opioid consumption and pain intensity. As a consequence, we still do not know whether there is dose-responsiveness for the analgesic efficacy with magnesium. Similarly, it remains unknown whether there is a difference between magnesium sulfate, laevulinate, and gluconate. One trial tested a cumulative dose of magnesium laevulinate 1.2 g for 5 h. Cumulative morphine consumption up to 4 h after surgery, and the number of episodes without any pain, did not differ between patients treated with magnesium laevulinate and those receiving placebo. However, those who had received magnesium laevulinate reported significantly more episodes with severe or unbearable pain and they had higher pain scores. In another trial, a cumulative dose of magnesium gluconate that exceeded 25 g for 12 h was given.[17]The number of patients with inadequate pain control before tracheal extubation, average pain intensity at 7 and 8 h after surgery, and remifentanil consumption during the first 12 h after surgery, were all significantly decreased in patients who had received magnesium gluconate.

Thus, it remains unclear whether these differences in efficacy were due to differences in doses and regimens (1.2 g during 5 h vs 25 g during 12 h), or due to differences in the chemical form of magnesium (gluconate versus laevulinate), or due to other factors. Not unexpectedly, magnesium treatment was shown to decrease the risk of postoperative shivering. This was perhaps the clearest beneficial effect of magnesium supplementation. In healthy volunteers, magnesium sulfate (80 mg kg 1 bolus followed by an infusion at 2 g/h was shown to reduce the shivering threshold.[18]

In clinical practice, magnesium's beneficial effect on shivering is of minor importance (NNT about 14) compared with, for instance, the efficacy that was reported with meperidine or clonidine (NNT 3–4).[19] In trials including patients undergoing abdominal hysterectomies and hernioplasties, average magnesium serum concentrations in control patients who did not receive magnesium supplementation decreased by 11%–27%. Serum levels, which are those generally measured, reflect only a small part of the total content of magnesium; the intracellular magnesium content can be low, despite normal serum levels. However, it may be inferred from the data reported in these trials and from observations from others that longer and larger surgical interventions are more likely to lead to hypomagnesemia. It remains unclear what the clinical relevance of low magnesium serum levels in surgical patients is. There is evidence that the response of the NMDA receptor is greatly enhanced by reducing the extracellular magnesium concentration below the physiological level. It may be hypothesized that the reported outcomes in these trials, for instance, decrease in pain intensity or in morphine consumption, were not due to a direct analgesic effect of magnesium but, rather, to the prevention of hypomagnesemia, and thus prevention of subsequent NMDA activation. However, most of the trials were small. Small trials may detect a beneficial treatment effect by random chance.[20] The largest trial included 200 patients;[12] that trial was negative but it tested only a bolus dose of magnesium sulfate. Thus, it is not know whether that trial was negative since it was large, and therefore the risk of random variation was minimal, or because the magnesium regimen in

that trial was inadequate. Second, some trials reported on low pain scores in controls. For instance, in the trial by Ko et al.[21], patients postoperatively received epidural fentanyl and bupivacaine with or without systemic magnesium and pain scores were below 40 mm at all time points in both groups. That trial was part of those that were unable to show any benefit with magnesium. However, if there is not enough baseline pain, an experimental intervention has no scope to show analgesic efficacy.[21]

CONCLUSION

Results of present study showed significantly higher mean duration of analgesia in treatment group as compared to placebo group. Mean duration of analgesia was also significantly higher in treatment group for gender, age, weight and type of surgery.

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