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Original Research Article

Effect of Intraoperative Intravenous Infusion of Magnesium Sulphate during Spinal Anaesthesia on Postoperative Analgesia: A Randomized Study

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Conflict of interest: Nil

Abstract:

Background: Intravenous infusion of magnesium sulphate given before noxious stimulation provides good postoperative analgesia.

Aim: To study effect of intravenous infusion of magnesium sulphate during spinal anaesthesia, on duration of analgesia in postoperative period and need for rescue analgesia in postoperative period.

Material and Methods: Study was conducted in June 2018 to august 2019 after approval from ethical committee of hospital. Fifty ASA grade I & II patients were randomly assigned into two groups (Group M and Group S of 25 patients each). Group M patients received inj. magnesium sulphate ($MgSO_4$) as bolus dose of 50mg/kg over 15mins given before incision and maintenance dose of 15 mg/kg/hr IV infusion till end of surgery. Group S patient received saline infusion throughout the surgery. Intra-operative and post-operative hemodynamic parameters, post-operative VAS score and sedation score were recorded. Statistical analysis was carried out using statistical package for social science (SPPS Inc., Chicago, IL, version 11.5 for windows). Parametric data were analyzed using paired and un-paired t-tests. Qualitative or categorical variables were compared using Chi-square test or Fisher's exact test.

Results: No significant difference was found between the two groups in terms of age, weight, height, or gender. Postoperative VAS score was significantly lower in Group M than in Group S at 4hr, 12hrand 24hr ($p=0.0001$). The need for rescue analgesia in Group M as compared to Group S was significantly low ($p<0.05$). There was no significant difference in haemodynamic variables during the intraoperative or postoperative period in both the groups ($p>0.05$). 80% patients of Group M had grade 2 sedation score after 30 min of starting $MgSO_4$ infusion as compared to 32% in Group S. 28% patients in Group M had PONV as compared to 40% in Group S. There was no adverse effect owing to $MgSO_4$.

Conclusion: Intravenous infusion of $MgSO_4$ decreases post-operative pain, need for rescue analgesia and need for intraoperative sedation. In addition there is decrease incidence of PONV and shivering.

Keywords: Analgesia, Intravenous, Magnesium Sulphate, Postoperative.

Introduction

Post-operative pain control is a major concern for doctors and patients. Pain causes tachycardia and high BP which may lead to distress and immobility, causing delayed recovery.

Measures need to be taken before the effect of spinal anaesthesia weans off. Various drugs are used via different routes for analgesia like epidural or intravenous route. Each modality has its advantages and disadvantages. Magnesium is an inorganic ion which has been used in many studies for decreasing total anesthetic and analgesic requirements in different surgeries and post-operative pain control [1,2,3,4,5].It has also been used for decreasing stress response during intubation [4].

Magnesium isN-methyl D-aspartate receptor antagonist, which when administered before generation of noxious stimuli, prevents pain [5] by preventing neuronal plasticity and central sensitization to painful stimulation [5,6]. Few

studies have been done on the effect of intravenous magnesium sulphate during regional anesthesia [7,8]. Agarwal A et. al, in their study used intravenous magnesium sulphate with spinal anesthesia to reduce post-operative pain and analgesic consumption [9]. They added Fentanyl with Bupivacaine for spinal anesthesia. Thus, postoperative analgesia may be prolonged due to Fentanyl. The effect of magnesium infusion during spinal anesthesia on postoperative analgesia while using Bupivacaine for spinal block has not been fully determined.

The aim of this study was to investigate the effect of intravenous infusion of magnesium sulphate during spinal anesthesia with Bupivacaine on quality and duration of postoperative analgesia. The secondary objective was to see the effect of intravenous magnesium sulphate on need of intraoperative sedation.

Material and Methods

This randomized clinical study was carried out at Gujarat Cancer and Research Institute from year 2018 to 2019.Institutional ethics committee's (IRC number: P-54) approval was taken.

Inclusion criteria: Fifty patients of ASA grade I & II of age belonging to 18-70 years of either sex who were posted for lower abdominal and lower leg surgery.

Exclusion criteria: Patients with comorbidities like cardiovascular disease, hepatic & renal dysfunction, peripheral neuropathy, bleeding disorder, anemia & emergency surgeries.

All patients were examined thoroughly pre-operatively. All routine necessary investigations and spine examination were done. A written informed consent was obtained from the patient. Patients were randomly divided into two groups of 25 patients in each group (Group M & Group S), using closed envelops chosen by patients.

Group Patients received $MgSO_4$, Bolus dose: 50mg/Kg over 15 min given before incision and Maintenance dose: 15mg/Kg/hr IV infusion till end of surgery. Group S, patients received isotonic saline infusion till end of the surgery.

CONSORT 2010 Flow Diagram

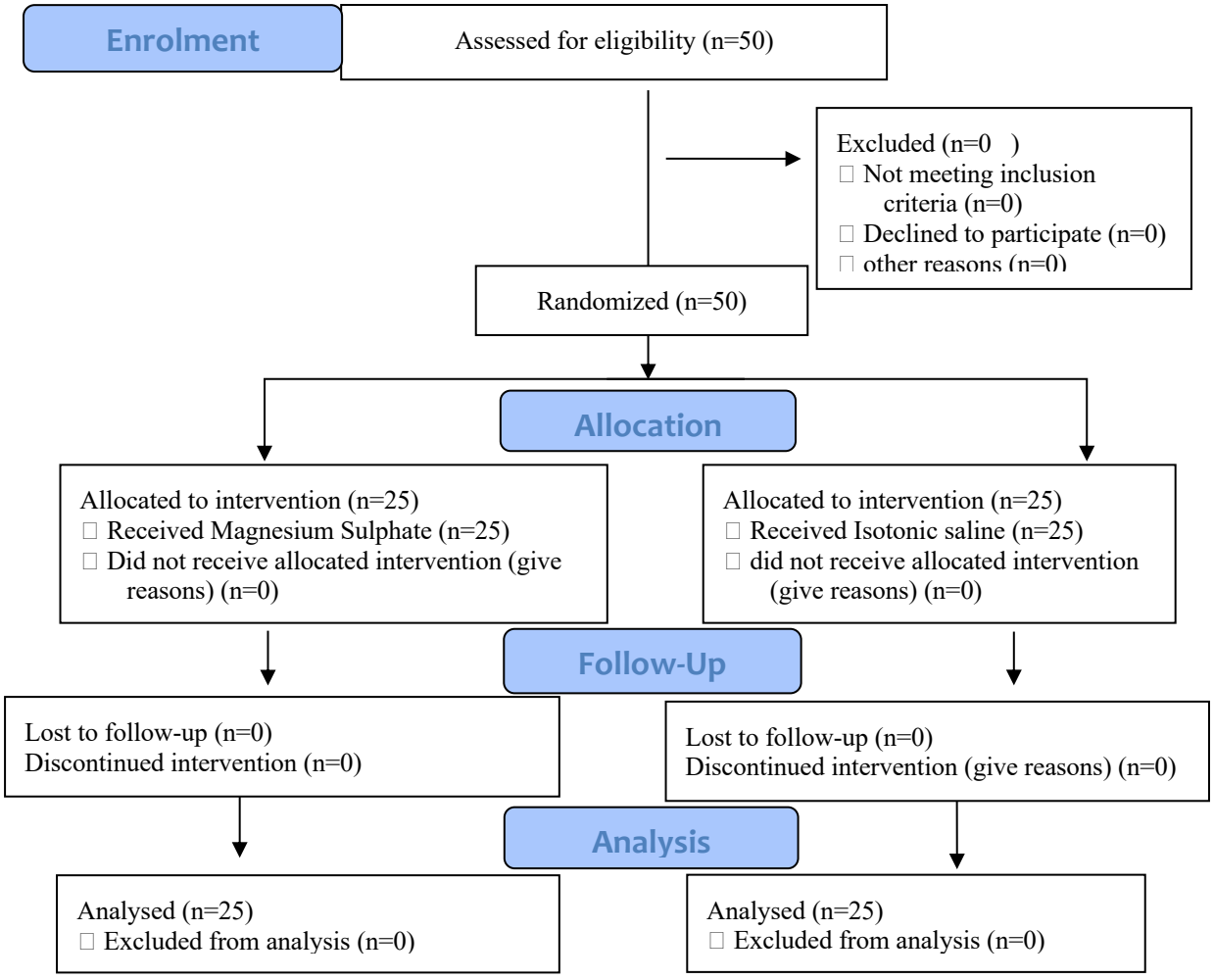

Figure 1: CONSORT 2010 Flow Diagram

Baseline HR, and BP were measured. In operating room 18 G intravenous cannula was inserted and 1 liter Ringer lactate's solution was given as preload. Patient was positioned left lateral and under all aseptic and antiseptic precautions, 25 G Quincke spinal needle was inserted in L3-L4 space. Inj Bupivacaine 0.5% (hyperbaric) 4 ml injected in subarachnoid space after checking free flow of CSF. Patient was made supine. After 20 min of spinal anaesthesia, Dermatomal level of block was checked by pinprick method.

$MgSO_4$ was prepared in 50ml normal saline in 50cc syringe infusion (40mg/ml) or saline infusion was prepared and started after 30 mins of subarachnoid block. Patients in group M received $MgSO_4$ 50 mg/kg over 15 min before incision followed by 15 mg/kg/hr by continuous IV infusion until end of surgery. Patients in Group S received saline infusion till end of the surgery.

Intraoperative monitoring included heart rate, mean blood pressure, SPO_2, ECG and Sedation score. IV atropine 0.6mg was administered if heart rate decreased to 50 beats/min. IV Mephentermine was given If mean arterial pressure decreased >20% from baseline. After surgery; HR, BP, and pain scores were recorded immediately and at 30 min, 4hr, 12hr and 24 hr postoperatively.

Pain score were evaluated using 0-10 mm VAS. Diclofenac sodium was used as rescue analgesia when VAS score >3.

Statistical analysis

The primary outcome of this study was postoperative PCA drug consumption. On the basis of the unpublished pilot data showing a mean (SD) 24 h consumption of PCA solution of 20 [7] ml a sample size of 25 patients per group was calculated based on a minimum clinically significant difference between the groups in postoperative 24 h PCA consumption of 5 ml and taking alpha=0.05 and beta=0.2 [10].Data entry and analysis were performed using SPSS software (version 11.5). For data analysis, Student's t-test and Chi-squared test were used. To present the results, mean ± SD were used and a P value<0.05 was considered significant.

Results

Duration of surgery (mins) and subarachnoid block (mins) was 148(28.75) and 179.2(18.3) in Group S and 147(22.17) and 176.8(16.5) in Group M, respectively which was comparable in both groups. As shown in table 1 there was no statistically significant difference between the two groups in terms of age, weight, height, or gender.

Table 1: Demographic Data

Group	Group S Mean(SD)	Group M Mean(SD)
Sex(male/female)	9/16	8/17
Age	41.64(14.47)	41.08(13.63)
Weight	51.68(4.8)	50.96(4.47)
Height	156.96(2.86)	155.88(3.45)
Duration of surgery (mins)[Mean(SD)]	148(28.75)	147(22.17)
ASA I/II	21/4	20/5

Table 1 shows patient's sex as m/f ratio and age, weight and height as Mean (SD). Between two groups there was no significant difference (p> 0.05). At different time intervals (4, 12 and 24 hr), patients in group M had significantly less pain score than group S except at emergence of anaesthesia (table2).

Table 2: Postoperative VAS Pain Score

Time	Group S Mean (SD)	Group M Mean (SD)	p value
Immediate postoperatively	0.2(0.5)	0.16(0.47)	0.77
30 min	0.32(0.63)	0.2(0.5)	0.45
4hr	4.36(0.7)	2.8(0.5)	0.0001
12hr	4.52(0.65)	3(0.29)	0.0001
24hr	4.36(0.7)	3.12(0.33)	0.0001

Table 2 shows postoperative VAS pain score. The postoperative VAS score was significantly less in Group M (P=0.0001) at 4, 12 and 24 after surgery. Patients in Group M were significantly more sedated(80% patients with grade 2 sedation) as compared to Group S patients(32% with grade 2 sedation) (P<0.05) after 30mins of starting $MgSO_4$ infusion (table 3).

Table 3: Sedation Score during Surgery

Time	Group S Mean(SD)	Group M Mean(SD)	P Value
Pre-operative	1.4(0.5)	1.32(0.47)	0.56
Intraoperative			
0 min	1.36(0.49)	1.32(0.47)	0.77
5 min	1.32(0.48)	1.28(0.46)	0.76
10 min	1.28(0.46)	1.36(0.49)	0.55
15 min	1.32(0.48)	1.4(0.5)	0.56

30 min	1.32(0.47)	1.8(0.41)	0.0004
1 hr	1.32(0.47)	1.8(0.41)	0.0004
End of surgery	1.32(0.47)	1.8(0.41)	0.0004

Table 3 shows sedation score during surgery. Patients in Group M were more sedated as compared to Group S patients ($p<0.05$). There was no significant difference in mean arterial pressure and heart rate during intraoperative or postoperative period (Table-4, 5, 6, 7). No one developed hypotension or bradycardia during surgery or in the postoperative period.

Table 4: Changes in Intraoperative HR

Time	Group S	Group M	p value
	Mean(SD)	Mean(SD)	
Baseline	90.4(7.6)	88.68(7.17)	0.415
After spinal			
0min	91.68(6.62)	89.64(6.12)	0.263
5min	89.36(6.61)	88.04(7.44)	0.51
10min	88.48(6.93)	86.88(5.68)	0.37
15min	82.96(5.2)	81.08(5.09)	0.2
30min	78.52(5.59)	77.48(5.58)	0.51
1 hr	78.36(5.75)	77.36(5.76)	0.51
End of surgery	80(5.39)	78.32(4.44)	0.23

Table 4 shows intraoperative heart rate. Group M had a lower mean heart rate than Group S. There was no significant difference between the two groups during perioperative period (p value>0.05).

Table 5: Changes in Postoperative HR

Time	Group S	Group M	p value
	Mean(SD)	Mean(SD)	
0min	81.36(5.8)	79.76(5.25)	0.31
30min	81.04(4.58)	80.24(4.78)	0.55
4hrs	82.28(4.26)	81.2(5.12)	0.42
12hrs	83.6(4.83)	80.92(5.18)	0.065
24hrs	84.56(5.68)	82.52(4.99)	0.184

Table 5 shows postoperative heart rate. Group M had a lower mean heart rate than Group S. There was no significant difference between the two groups during the perioperative period (p value >0.05).

Table 6: Changes in Intraoperative MAP

Time	Group S	Group M	p value
	Mean(SD)	Mean(SD)	
Baseline	78.28(6.69)	75.2(6.49)	0.1
After spinal			
0min	71.32(6.22)	70(6.83)	0.47
5min	68.76(5.06)	66.08(6.28)	0.1
10min	68.12(5.25)	65.44(6.18)	0.1
15min	68.64(5.43)	66.04(6.02)	0.1
30min	68.36(4.08)	65.84(6.13)	0.09
1 hr	68.48(3.86)	66.56(5.71)	0.09
End of surgery	68.92(4.89)	66.32(5.91)	0.096

Table 6 shows intraoperative mean arterial pressure. There was no significant difference in MAP during the intraoperative period in both the groups (p value >0.05).

Table 7: Changes in Postoperative MAP

Time	Group S	Group M	P value
	Mean(SD)	Mean(SD)	
0min	68.84(4.4)	66.68(4.37)	0.088
30min	69.52(5.16)	66.88(4.97)	0.076
4hrs	70.28(4.84)	67.80(3.95)	0.053
12hrs	71.2(5.4)	68.48(4.60)	0.061
24hrs	73.44(5.64)	70.52(5.46)	0.069

Table 7 postoperative mean arterial pressure. There was no significant difference in MAP during the postoperative period in both the groups (p value >0.05). Pre infusion serum magnesium level in both groups was same. S. Mg concentration in Group M was significantly higher than those in Group S ($P<0.001$) at 2 hrs

after stopping the infusion. However, all patients in Group M had a serum Mg concentration in the normal range.

Table 8: Serum Magnesium Levels

	Group S Mean(SD)	Group M Mean(SD)	p value
Pre infusion	0.834 (0.071)	0.85 (0.072)	0.43
2hr post infusion	0.833 (0.070)	1.09 (0.101)	0.0001

Table 8 shows serum magnesium concentrations (mmol/litre), pre and post infusion. Postinfusion, the S.Mg levels were significantly higher in the magnesium group than in the control group ($p<0.05$).
Incidences of PONV and shivering were less in group M.

Table 9: Incidence of PONV and Shivering

	Group S	Group M	P value
PONV	10(40%)	7(28%)	<0.01
Shivering	6(24%)	3(12%)	<0.005

Table 9 shows incidence of PONV and shivering.

Discussion

This study showed that intravenous administration of magnesium sulfate in patients undergoing surgery under spinal anesthesia with bupivacaine reduces postoperative pain and requirement of rescue analgesia. Regional anaesthesia is preferred to general anaesthesia for surgery due to avoidance of intubation, earlier return of gastrointestinal function, and lower incidence of postoperative thromboembolic events. Studies have proved analgesic efficacy of $MgSO_4$ in preventing postoperative pain [7,8,9,10,11,12].

In a previous study, administration of $MgSO_4$ in gynaecological procedures under total IV anaesthesia showed significant reductions in intraoperative propofol, atracurium and postoperative morphine consumption [13].

Hwang et al [7] evaluated the effect of IV infusion of $MgSO_4$ in dose of 50mg/kg for 15 min and then 15 mg/kg/h by continuous IV infusion until the end of surgery, during spinal anaesthesia for postoperative analgesia. Postoperative pain score and consumption of rescue analgesia were significantly lower in patients receiving $MgSO_4$. They did not encounter any complications. They found significantly lower pain score in Mg Group at 4, 24, and 48 h after surgery.

Similarly in the present study, $MgSO_4$ in bolus dose of 50mg/Kg IV over 15 min was given before incision then maintenance dose of 15mg/Kg/hr IV infusion till end of surgery for postoperative analgesia. The postoperative VAS score was significantly lower in Group M than in Group S at 4hr, 12hr and 24hr. There was no significant difference of postoperative pain score immediately and 30 min after surgery, which can be attributed to the residual effect of spinal anaesthesia.

Agrawal et.al studied effect of perioperative infusion of Mg during spinal anaesthesia, on the block characteristics and duration of action of intrathecal bupivacaine [9].They added fentanyl 10 mcg to bupivacaine, unlike our study, which may have been the reason for increased duration of analgesia in their study. They did not measure the serum Mg level.

In the present study, 2hr post infusion serum Mg concentrations of patients in the magnesium group were significantly higher than in the saline group. There are studies where cases of magnesium toxicity leading to cardiac arrest and death have been reported [14,15]. Magnesium toxicity begins at serum concentration of 2.5–5 mmol/litre and cardiac arrest occurs at 12.5 mmol/litre [14,15], which is much higher than the highest level (1.22 mmol/litre) found in Group M in our study. Magnesium causes a dose-dependent negative inotropic effect causing peripheral vasodilation [16]. Also spinal anaesthesia causes peripheral vasodilation. In present study, patients were preloaded with 1 liter Ringer lactate's solution. Therefore none of the patients had any significant hypotension after administering the Magnesium. None of the patients had any significant bradycardia that required treatment.

Various studies have been carried out to see the effect of $MgSO_4$ on postoperative analgesia and PONV. Sedative effect of $MgSO_4$ have not been measured in many of them [11,17, 18]. Kiran et.al [8] found that patients who received IV $MgSO_4$, 50 mg/kg in 250 ml of isotonic sodium chloride solution were more sedated as compared to control group although they were easily arousable. In the present study, 80% patients of Group M had grade 2 sedation score after 30 mins of starting $MgSO_4$ infusion as compared to control group (32% patients), but they were easily arousable which reduced the need for intraoperative sedation. This effect is due to CNS depressant action of magnesium. In post-operative period, patients were calm and easily arousable.

Shivering aggravates postoperative pain [19,20] and discomfort. It also increases oxygen requirement. Prevention of shivering may attenuate postoperative pain and discomfort. Ryu et al [11]

studied effects of MgSO4 in 50 gynaecological patients receiving total intravenous anaeshesia (50 mg/kg IV bolus and then 15 mg/kg/h IV by continuous infusion). PONV and postoperative shivering occurred in significantly fewer patients who received $MgSO_4$. Similar to this, in present study, PONV and shivering occurred in significantly fewer patients in Group M. Wadhwa and colleagues [19] concluded that magnesium sulphate infusion slightly reduces the shivering threshold. Kizilirmak S et al also concluded that IV $MgSO_4$ suppresses post-anesthetic shivering [20]. $MgSO_4$ inhibit the presynaptic release of acetylcholine and desensitizing the postsynaptic membrane. Thus administration of $MgSO_4$ may potentiate neuromuscular block during general anaesthesia [21]. Thismay lead to respiratory depression. In the present study, there was no such complication. Thus, intravenous infusion of mgso4 Intraoperatively provides good postoperative analgesia along with decrease in need of intraoperative sedation without any complication.

Limitations of the study were in our study we determined serum magnesium concentrations before and immediately after surgery. The relationship between postoperative pain and serum magnesium could not be evaluated. Also we did not determine the CSF magnesium concentration as this was invasive.

Conclusion:

Intravenous infusion of magnesium sulphate (bolus dose 50mg/Kg IV over 15 min before incision and maintenance dose 15mg/Kg/hr IV till end of surgery), given during spinal anaesthesia, provides good postoperative analgesia and reduces postoperative discomfort. Also there is decreased need for intraoperative sedation and decreased incidence of PONV and shivering in intraoperative and postoperative period.

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