Original Research Paper

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Anesthesiology

EFFECT OF INTRAVENOUS MAGNESIUM SULPHATE IN SPINAL ANAESTHESIA WITH BUPIVACAINE FOR POSTOPERATIVE PAIN MANAGEMENT

Anisha Choksi	Associate Professor
Sonal	Tutor
Deepika Reddy Cheruku	M.D Anaesthesia Resident

ABSTRACT **Objective:-** To improve analgesia without or with minimal side effects by non-invasive technique is the utmost necessity for the patients undergoing surgery under spinal anaesthesia. Effect of continuous infusion of magnesium sulphate during subarachnoid anaesthesia for post-operative pain relief has been studied.

Methodology:- A total of 50 patients undergoing lower limb surgeries under spinal anaesthesia were randomly divided into two groups; each group included 25 patients

Study Group: Group M, patients received MgSo4 8 mg/kg/hour infusion till the end of surgery.

Control Group: Group S, patients received isotonic saline infusion till end of the surgery

Results:-Postoperative VAS score was significantly lower in Group M than in Group S at **4H**[1(0)]vs[1.52(0.51)], **8H**[1.28(0.46)]vs[4(0)], **12H**[2(1.42)]vs[2.8(0.41)],**16H**[3(1.5)]vs[4(0)],**20H** [1.2(0.41)] vs [2.92(0.28)] and **24H**1.6(1.23)] vs [4(0)] (p=0.0001).

Conclusion:-We conclude that IV infusion of MgSO4 reduces postoperative pain, need for rescue analgesia and incidence of PONV and shivering without complications.

KEYWORDS : Magnesium sulphate,postop pain relief,lowerlimb surgeries.

1.Introduction

"Pain is perfect misery, the worst of all evils and if excessive, overturns all patients" - John Milton. Pain in post operative period leads to adverse effects like hypertension, tachycardia, psychological distress, immobility, respiratory discomfort and delayed recovery. Magnesium sulphate (MgSO4) has been assessed in a number of studies in the field of anesthesiology and for the treatment of eclampsia and pre-eclampsia, hypokalemia, premature labor, myocardial protection after ischemia, asthma crisis, post-operative acute pain control and hemodynamic stability during intubation.As the effect of spinal anaesthesia weans off, pain control becomes the major concern in postoperative period.NMDA is an inotropic receptor (ligand-gated ion channel),involved in pain processing, neuronal plasticity and generation of central sensitization.NMDA receptor antagonists, like Mg^{2+} and Ketamine, can prevent induction of central sensitization attributed to peripheral nociceptive stimulation and can abolish hypersensitivity, once it is established.

Mode of action:-1. Magnesium is a Ca^{2+} antagonist.2. It competes with calcium to inhibit vasoconstriction.3. It blocks the NMDA receptor thus decreasing intracellular calcium.4.Magnesium inhibits Ryanodine receptors decreasing muscle contraction.5. Also directly inhibits catecholamine release from the adrenal medulla.

2.Materials and Methods:

INCLUSION CRITERIA: Patients with

- ASA grade I and II of either sex
- Belonging to 18 to 70 years age group
- Fit for surgery under spinal anaesthesia

EXCLUSION CRITERIA: Patients with

- ASA grade III and IV
- Cardiovascular, Hepatic and Renal dysfunction
- Neuromuscular disease
- Opioid abuse
- Allergy
- Peripheral neuropathy
- Bleeding disorders and anemia
- Taking calcium channel blockers
- Unfit for spinal anaesthesia

Patients were randomly divided into two groups; each group included 25 patients

- **Study Group:GroupM,** received MgSo4 8 mg/kg/hour infusion till the end of surgery.
- **Control Group: Group S,** patients received isotonic saline infusion till end of surgery.

TECHNIQUE OF ANAESTHESIA

Patients were transported to operating room where 18 G intravenous cannula was inserted and 500 ml Ringer lactate's solution was given as preload. Baseline HR, and BP were measured. With all aseptic and antiseptic precautions, patient was positioned left lateral and lumber puncture was done using 23 G spinal needle in L3-4 space. After free flow of CSF, Inj Bupivacaine (hyperbaric) 3.4 ml of 0.5% injected in subarachnoid space and spinal needle was removed. Patient was made supine with 10^0 trendelenberg position with small pillow placed under shoulder.

Onset of sensory block was determined by pinprick method. Dermatomal level of block was noted 20 min after giving the spinal anaesthesia and it is considered to be final level.

$MgSO_4$ [2 ampoules (2gm) in 50 ml normal saline prepared in 50cc syringe (40mg/ml)] or saline infusion was prepared and started. Patients in the magnesium group (Group M) received magnesium sulphate 8 mg/kg/hr by continuous IV infusion till the end of surgery. Patients in the saline group (Group S) received isotonic saline infusion till end of the surgery.

Intraoperative monitoring included HR, BP, SpO_2% and ECG. If the mean arterial pressure decreased >20% from baseline, Mephentermine was given IV. when heart rate decreased to 50 beats/min, IV atropine 0.6 mg was administered.After surgery, patients were transferred to the postoperative ward. HR, BP, and pain scores were recorded immediately after surgery and at 1,2,3, 4,8,12,16,20 and 24 hr after surgery. Pain scores were evaluated using a 0–10 mm VAS (0 - no pain, to 10 - worst pain imaginable). Diclofenac sodium (2 mg/kg i.v.) was used as rescue analgesia when VAS score>3.

3.Observation and results:

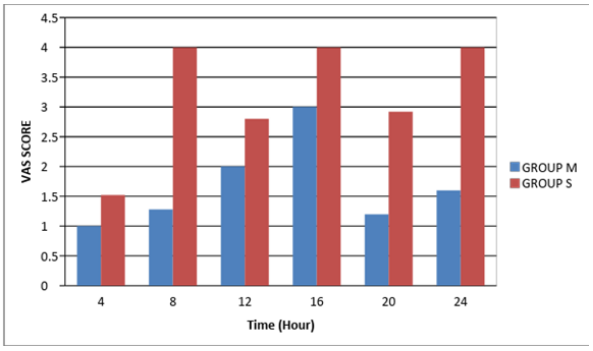
Group M patients had a lower mean heart rate. No significant difference was observed between the two groups during the intraoperative period (p value >0.05) No significant difference in SBPor DBP was observed between the two groups during the postoperative period

Table 1 and Figure 1 show postoperative VAS pain score. The postoperative VAS score was significantly less in Group M (P=0.0001) at 4, 8, 12, 16, 20 and 24 hours after surgery.

TABLE 1: POSTOPERATIVE VAS SCORE

TIME (HR)	Group Mean(SD)	Group S Mean(SD)	P Value
0	0(0)	0(0)	-
1	0(0)	0(0)	-
2	0(0)	1(0)	0.0001
3	1(0)	1.16(0.374166)	0.0001
4	1(0)	1.52(0.51)	0.0005
8	1.28(0.458258)	4(0)	0.0001
12	2(1.414214)	2.8(0.408248)	0.0091
16	3(1.5)	4(0)	0.0017
20	1.2(0.408248)	2.92(0.28)	0.0001
24	1.6(1.224745)	4(0)	0.0001

FIGURE 1: POSTOPERATIVE VAS SCORE



AVERAGE NO. OF RESCUE ANALGESIC (I.V. DICLOFENAC)

	Group M Mean(SD)	Group S Mean(SD)	P Value
NO. of rescue analgesic	1.2(0.408248)	3(0)	0.0001

Table 2. Shows average no. of rescue analgesic which was less in Group M than in Group S (P value < 0.0001).

4.Discussion:

Pain is generated through multiple mechanisms.Therefore it requires multimodal approach.Understanding the mechanism of pain has resulted in the administration of analgesics before exposure to pain stimuli as pre-emptive analgesia to prevent the central sensitization and the amplification of postoperative pain.

Magnesium is the second most abundant intracellular cation and is involved in the regulation of many ion channels and enzymatic reactions. Magnesium has applications in anaesthesia as an adjuvant for perioperative analgesia is based on the properties of NMDA receptor antagonist and calciumchannel blocker. NMDA receptor antagonists are best administered before the generation of noxious stimuli in order to prevent pain processing, neuronal plasticity and central sensitization to painful stimulation..Many clinical studies have demonstrated that i.v. magnesium infusion during general anesthesia reduced anesthetic requirement and postoperative analgesic consumption. Relatively few studies have been investigated on the effects of magnesium sulphate infusion during spinal anesthesia.We therefore decided to conduct this randomized control study to check the effect of intravenous magnesium sulphate in spinal anaesthesia with bupivacaine for postoperative pain management in patients undergoing lower limb orthopedic surgery.50 Patients were randomly divided into two groups; each group included 25 patients. Demographic parameters like age, weight male/female ratio and ASA physical status were comparable in both groups.Our study has demonstrated that intravenous infusion of magnesium sulphate in dose of 8mg/Kg/hr IV till end of surgery, during spinal anaesthesia, reduced postoperative pain and analgesic consumption.

There was no significant difference in level and duration of sensory block and duration of surgery in both groups.

Duration of surgery (mins) and subarachnoid block (mins) was 120.2(3.22) and 179.64(3.37) in Group M and 119.92(3.35) and 179.8(2.74) in Group S, respectively which was comparable in both groups**.** There was no significant difference in haemodynamic variables (Blood pressure and heart rate) during the intra- or postoperative period. Mean HR and mean SBP were lower in Group M as compared to Group S during intraoperative period. Hemodynamic variables were statistically not significant (p value > 0.05).

Postoperative VAS score in our study was significantly lower in Group M than in Group S at4, 8, 12, 16, 20 and 24 hr postoperatively which was statistically significant (p=0.0001). PONV occurred in significantly fewer patients in Group M (6 patients, 24%) than in Group S (10 patients, 40%). Postoperative shivering occurred in significantly fewer patients in Group M (2 patients, 8%) as compared to group S (5 patients, 20%). Average no. of rescue analgesics (i.v. diclofenac 2 mg/kg) was 1.2 in Group M compared to 3 in Group S (P value <0.0001) in ostoperatively 24 hours. None of our patients developed hypotension or bradycardia or Side-effects of MgSO4 (nausea, flushing, headache) during surgery or in the postoperative period.

These findings were comparable with study done by **A. Dabbagh, H. Elyasi, S.S. Razavi et al in 2009** who studied and observed effect of IV $MgSO_4$ for post-operative pain in 60 patients undergoing lower limb orthopedic surgery under subarachnoid block. Patients in Magnesium group received 8mg/kg IV $MgSO_4$, started before the incision and continued up to the end of the surgical procedure. They found that pain reported by the first group that received magnesium sulfate was significantly less at the first, third, sixth and 12th hours ($p<0.0001$) after the operation in comparison with the group that received placebo and the IV morphine requirements in the first 24 h after the surgery were also less in the magnesium group (4.2 ±1.6mg) than in the control group (9.8 ± 2.1mg)[4].

In our study we have used 8 mg/kg/hr $MgSO_4$ infusion in patients undergoing lower limb orthopedic surgery in spinal anaesthesia. We found that there were significant reduction in postoperative pain and total analgesic requirement without any clinically evident side effects. Similarly Apan A, Buyukkocak U et al in 2004 assessed 50 ASA I-II patients undergoing surgery under spinal anaesthesia with 12.5 mg 0.5% heavy bupivacaine, using a 25 G Quincke needle. Patients received a 5 mg kg/1 bolus of magnesium sulphate followed by a 500 mg/h IV infusion or saline in the same volumes for 24 h. Total analgesic consumption was reduced in the magnesium group (meperidine consumption 60.0 +/- 73.1 mg control group, 31.8 +/- 30.7 mg magnesium group, p= 0.02).They concluded that magnesium sulphate infusion reduces analgesic requirements and may be used for reducing analgesic consumption after spinal anaesthesia. In contrast J.-Y. Hwang et al in 2010 evaluated the effect of IV infusion of MgSO4 in 40 patients undergoing total hip replacement arthroplasty under spinal anaesthesia and divided into 2 groups. Group M received MgSO4 50 mg/kg for 15 min and then 15 mg/kg/h by continuous IV infusion until the end of surgery. They found that postoperative pain scores and cumulative postoperative PCA consumptions were significantly lower in Group M at 4, 24, and 48 h after surgery ($p<0.05$), but in group M 6 patients developed hypotension and 2 patients developed bradycardia compared to group S in which 3 developed hypotension and 1 bradycardia requiring treatment. On the other hand, In a comparison of the effects of three different dose regimens of Mg on postoperative morphine consumption done by T. O. Seyhan, M. Tugrul et al in 2006 a single bolus injection at 40mg/kg was found to reduce postoperative morphine consumption, and when this was followed by a maintenance infusion of 10 mg/kg/h, the effect was enhanced. One patient in Mg+10 group and 3 patients in Mg+20 group demonstrated bradycardia which was successfully treated with atropine injection. Moreover, increasing the maintenance infusion to 20mg/kg/h provided no additional advantage and induced unwarranted haemodynamic effects Titration of adequate bolus and infusion doses of magnesium sulphate are important for effective analgesia and avoiding complications

HEART RATE AND BLOOD PRESSURE CHANGES

There was no significant difference in haemodynamic variables (Blood pressure and heart rate) during the intra- or postoperative period.None of our patients developed hypotension or bradycardia during surgery or in the postoperative period. Mean HR and mean SBP were lower in Group M as compared to Group S during intraoperative period. Similarly **J.-Y. Hwang et al in 2010** evaluated the effect of IV infusion of $MgSO_4$ in 40 patients undergoing total hip replacement arthroplasty under spinal anaesthesia and found that there was no significant difference in hemodynamic variables during intra or post op period. Group M patients had a lower mean arterial pressure except

immediately after induction of SA and lower mean HR except before induction of SA

POST OPERATIVE VAS SCORE

Our study was undertaken to determine the safety and efficacy of $MgSO_4$ in dose of 8mg/Kg/Hr IV infusion till end of surgery for postoperative analgesia in patients undergoing lower limb orthopedic surgery under spinal anaesthesia.Postoperative VAS score [mean(SD)] in our study was significantly lower in Group M than in Group S at **4 H**[1(0)] vs [1.52(0.51)], **8 H** [1.28(0.46)] vs [4(0)], **12 H** [2(1.42)] vs [2.8(0.41)], **16 H** [3(1.5)]vs [4(0)], **20 H** [1.2(0.41)] vs [2.92(0.28)], and **24 H** [1.6(1.23)] vs [4(0)] (p=0.0001). Similarly **J.-Y. Hwang et al in 2010** evaluated the effect of IV infusion of $MgSO_4$ in 40 patients undergoing total hip replacement arthroplasty under spinal anaesthesia and found significantly lower pain score in Mg Group at 4, 24, and 48 h after surgery (p<0.05)Similarly **A. Dabbagh, H. Elyasi, S.S. Razavi et al in 2009** who studied and observed effect of IV $MgSO_4$ for post-operative pain in 60 patients undergoing lower limb orthopedic surgery under subarachnoid block found that pain reported by the Magnesium group was significantly less at the 1st, 3rd, 6th and 12th hours (p<0.0001) after the operation in comparison with the group that received placebo. There was no significant difference of postoperative pain score immediately and 1 hour after surgery which we attribute to the residual effect of spinal anaesthesia.

SHIVERING AND PONV:

In our study, PONV occurred in significantly fewer patients in Group M (6 patients, 24%) than in Group S (10 patients, 40%).Postoperative shivering occurred in significantly fewer patients in Group M (2 patients, 8%) as compared to group S (5 patients, 20%). Shivering causes discomfort, increase in oxygen requirement and aggravates postoperative pain and the prevention of shivering may attenuate postoperative pain and enhance patients' satisfaction. **Wadhwa and colleagues** suggested that magnesium sulphate infusion slightly reduces the shivering threshold in humans, and contrast to this **Kizilirmak S et** al reported IV $MgSO_4$ to suppress post-anesthetic shivering.Similarly, **J.-H. Ryu et al in 2008** studied effects of $MgSO_4$ (50 mg/kg IV bolus then 15 mg/kg/h IV by continuous infusion in 50 patients who underwent gynaecological surgery under TIVA (propofol+ Remifentanil+Rocuronium). PONV occurred in significantly fewer patients in Mg Group (10 patients, 40%) than in control Group (19 patients, 76%, p<0.01) and postoperative shivering also occurred in significantly fewer patients in Group M (1 patient, 4% vs 9 patients, 36%; p<0.005.

AVERAGE NO. OF RESCUE ANALGESICS:

In our study we found that the average no. of rescue analgesics (i.v. diclofenac 2 mg/kg) was less in Group M compared to Group S [1.2 (0.41) vs 3 (0)] (P value <0.0001) in postoperatively 24 hours. Similarly **A. Dabbagh, H. Elyasi, S.S. Razavi et al in 2009** who studied and observed effect of IV $MgSO_4$ for post-operative pain in 60 patients undergoing lower limb orthopedic surgery under subarachnoid block and found that magnesium group patients needed less cumulative dose of i.v. morphine sulfate (4.2 ±1.6 mg) in first 24 hours post operatively than control group (9.8 ±2.1mg).Similarly **J.-Y. Hwang et al in 2010** evaluated the effect of IV infusion of $MgSO_4$ in 40 patients undergoing total hip replacement arthroplasty under spinal anaesthesia and found that cumulative postoperative PCA (morphine + ketorolac) consumptions were significantly low in Group M at 4, 24 and 48 hours postoperatively(P value <0.0001).

COMPLICATIONS AND TOXICITY

Magnesium causes a dose-dependent negative inotropic effect. Haemodynamic studies have shown that it has a peripheral (predominantly arteriolar) vasodilatory effect. Considering the effect of spinal anaesthesia and negative inotropic effect of Mg, we preloaded patients with 500 ml Ringer lactate's solution and then Mg infusion started Which is probably why we did not encounter significant hypotension after administering the Mg infusion and no significant inter-group haemodynamic difference was observed during the surgery(p >0.05). None of our patients had any significant bradycardia that required treatment. Similarly **A. Dabbagh et al** did not find any major side effect during his study.

Magnesium sulphate administration may potentiate neuromuscular block during general anaesthesia which may cause respiratory depression. It has been shown that the basic mechanisms involve a reduction of the amount of acetylcholine released from motor nerve terminals and a decrease in the depolarizing action of acetylcholine at the endplate, or a depression of muscle fibre membrane excitability. In our study we did not encounter any such complication. Accordingly, IV Mg administration during spinal anaesthesia may facilitate muscle relaxation and surgical procedures. However, further study is required to validate this hypothesis.

5.CONCLUSION:

We have concluded from our study that intravenous infusion of magnesium sulphate in dose of 8mg/Kg/hr IV till end of surgery, during spinal anaesthesia, reduced postoperative pain and analgesic consumption. In addition to that there is decrease incidence of PONV and shivering in intraoperative and postoperative period.

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