Evaluation of intravenous magnesium sulphate on postoperative pain after spinal anesthesia

Subodh S Kamtikar[1]*, Sangamesh B Kunakeri[2]

[1]Associate professor, Department of Anesthesia, BRIMS, Bidar, India
[2]Assistant professor, Department of Anesthesia, BRIMS, Bidar, India

ABSTRACT

The major goal in postoperative pain management is to minimize the dose of medications and lessen side effects, while still providing adequate analgesia. Effective post-operative analgesia may facilitate recovery and decrease morbidity in surgical patients. Magnesium sulphate ($MgSO_4$), a NMDA receptors antagonist, has been tried to control peri-operative pain by modifying the pain mechanism. The present study was conducted to determine efficiency and safety of preventive intravenous $MgSO_4$ to postoperative pain relief and analgesic requirement after spinal anesthesia. This was a open label randomized study conducted in a tertiary care hospital in South India, from March 2013 to September 2013. The study was approved by institutional ethics committee and informed consent was taken from the subjects. The patients were randomized to receive either magnesium sulphate 50 mg/kg in 250 ml of isotonic sodium chloride solution IV (Group MG) or same volume of isotonic sodium chloride solution (Group NS). Pain at rest was evaluated using a 0-10 cm visual analogue scale at emergence from anesthesia and 2, 4, 8, 16 and 24 hrs after surgery. Rescue analgesia was provided in the form of diclofenac 75mg intramuscularly. The dosage and timing of analgesia was recorded immediately after consciousness, 2, 4, 8, 16 and 24 after operation. Results on continuous measurements are presented on Mean ± SD and results on categorical measurements are presented in Number (%). Repeated measures ANOVA were used to compare measurements over time. $P<0.05$ was considered statistically significant. The results of the present study showed that infusion of $MgSO_4$ during operation under spinal anesthesia reduced postoperative pain and analgesic consumption. Hemodynamic parameters of both groups were also comparable and no patient developed hypotension or bradycardia in both groups.

Keywords: Magnesium sulfate, Post-operative pain, Spinal anesthesia, Visual analogue scale

Introduction

Postsurgical pain is one of the most important issues that could have a serious effect on postoperative peace and comfort. The major goal in postoperative pain management is to minimize the dose of medications and lessen side effects, while still providing adequate analgesia [1]. Effective post-operative analgesia may facilitate recovery and decrease morbidity in surgical patients [2]. Surgical pain is due to inflammation from tissue trauma (surgical incision, dissection, burns) or direct nerve injury (nerve transaction, stretching, or compression) [3].Pre-emptive analgesia has been defined as an anti-nociceptive treatment that prevents establishment of altered central processing of afferent input from injuries [4]. Therapies that have been tested in pre-emptive trials include NSAIDS, intravenous (I.V.) opioids, I.V. ketamine, peripheral local anesthetic, caudal and epidural analgesia, dextromethorphan and gabapentin and one I.V. adjuvant medication that has shown potential in pre-emptive analgesia is magnesium [4]. Magnesium sulphate ($MgSO_4$), a NMDA receptors antagonist, has been tried to control peri-operative pain by modifying the pain mechanism [5,6].$MgSO_4$ has been previously investigated as a possible adjuvant for post-operative analgesia[7,8]. These studies suggest that peri-operative $MgSO_4$ improves post-operative analgesia. However, some studies do not these findings [9,10]. The present study was conducted to determine efficiency and safety of preventive intravenous $MgSO_4$ to postoperative pain relief and analgesic requirement after spinal anesthesia.

**Correspondence*
Dr. Subodh S Kamtikar
Associate professor. Department of Anesthesia, BRIMS, Bidar, 585401, India
E Mail: cdkad@rediffmail.com

Material and methods

This was a open label randomized study conducted in a tertiary care hospital in South India, from March 2013 to September 2013. The study was approved by institutional ethics committee and informed consent was taken from the subjects.

Inclusion criteria

1) Patients of either sex aged between 25 to 50 years undergoing below umbilical surgery under spinal anesthesia
2) American Society of anaesthesiologists grade-I & II patients and the ability to understand the Visual Analogue Scale.

Exclusion criteria

1) Patient with history to magnesium sulfate, NSAIDS or narcotic analgesics.
2) Patients having compromised renal, hepatic, cardiac functions, bleeding disorder, skeletal muscles disorder or any other neurological deficit.
3) Pregnant and lactating woman.
4) Patients with drug or alcohol abuse, obese patients and patients on calcium channel blockers.

Spinal anesthesia was performed for all patients through the L3-L4 interspaced in the sitting position. After dural puncture with a needle size 25 G, 12.5 mg Bupivacaine 0.5% solution was injected intrathecally. The patients were randomized to receive either magnesium sulphate 50 mg/kg in 250 ml of isotonic sodium chloride solution IV (Group MG) or same volume of isotonic sodium chloride solution (Group NS). Pain at rest was evaluated using a 0-10 cm VAS (0 – No pain at all to 10 – Worst pain imaginable) at emergence from anesthesia and 2, 4, 8, 16 and 24 hrs after surgery. During first 4 hrs the patients were kept in recovery room and rescue analgesia was provided in the form of diclofenac 75mg intramuscularly.. The dosage and timing of analgesia was recorded immediately after consciousness, 2, 4, 8, 16 and 24 after operation. Thereafter, the patients were sent to ward and diclofenac sodium 75mg intramuscularly was given on demand. The timing and dosage of rescue analgesic and total consumption of diclofenac sodium during first 24 hrs after operation was noted. Post operative hemodynamic parameters such as hypotension, heart rate, respiratory rate and saturation levels were noted.

Statistical analysis

Power analysis (α= 0.01 and β= 0.05) suggested that a sample size of 35 patients per group was needed to detect a 20% reduction in post-operative pain score and also post-operative analgesic requirement. The data was recorded and analyzed using SPSS software (version 16). Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD and results on categorical measurements are presented in Number (%). Repeated measures ANOVA was used to compare measurements over time. $P<0.05$ was considered statistically significant.

Results

A total of 35 patients in each group were included in the study. The demographic characteristics of the participants is shown in table 1.

Table 1: Demographic characteristics of the participants

Parameter	Group MG	Group NS
Age	**36.29±4.25**	**34.91±3.96**
Male	**19**	**21**
Female	**16**	**14**
Weight(kg)	**74.24±6.74**	**71.56±714**
Height (cms)	**174.56±5.96**	**172.45±6.12**
Duration of surgery (Minutes)	**87.45±7.76**	**85.43±6.18**
Time of recovery (Minutes)	**30.45±3.76**	**28.12±3.23**

There was no statistically significant difference in the demographic characteristics between the groups.
The assessment of pain in postoperative period by Visual analogue scale is shown in table 2.

Table 2: Assessment of pain in postoperative period by Visual analogue scale (1-10)

Timing	Group MG	Group NS
Immediately after consciousness	**3.67±1.24**	**4.76±1.59**
2 hr after operation	**4.32±1.14**	**5.89±0.65***
4 hr after operation	**4.34±1.78**	**6.12±2.13***
8 hr after operation	**3.65±1.43**	**4.27±2.01***
16 hr after operation	**2.56±1.12**	**3.65±1.92***
24 hr after operation	**1.54±0.24**	**1.84±0.54***

***** P<0.05 = Highly significant

The post-operative analgesic consumption is shown in table 3.

Table 3: Mean of post-operative analgesic consumption (mg)

Timing	Group MG	Group NS
Immediately after consciousness	**39.64±11.24**	**45.92±15.95***
2 hr after operation	**43.95±17.56**	**57.12±21.45***
4 hr after operation	**34.34±10.78**	**38.91±12.87***
8 hr after operation	**29.65±9.43**	**34.27±11.01***
16 hr after operation	**22.56±6.12**	**33.65±10.92***
24 hr after operation	**11.43±3.12**	**18.78±7.63***

***** P<0.05 = Highly significant

The post-operative hemodynamic parameters of both the groups is shown in table 4.

Table 4: Post-operative hemodynamic parameters

Parameter	Group MG	Group NS
Mean BP	**106.7±6.24**	**109.5±5.96**
Mean RR	**16.7±1.4**	**16.1±1.3**
Mean HR	**77.2±5.4**	**80.2±6.2**
SpO2	**99.2±0.4**	**99.3±0.5**

BP-Blood pressure
RR-Respiratory rate
HR-Heart rate
SpO2-Blood oxygen saturation rate

No statistically significant difference was observed between the groups

Discussion

Post operative pain is associated with physical and psychological trauma, it is treated with various drugs and techniques to make a patient pain free [11, 12]. MgSO4 is a noncompetitive NMDA receptor antagonist having antinociceptive effects by two mechanisms: i) it prevents central sensitization which occurs due to peripheral nociceptive stimulation ii) it also acts as physiological calcium antagonist by inhibiting calcium entry inside the cells at different voltage gated calcium channels by blocking NMDA receptors [5, 6, 13].The results of the present study showed that infusion of MgSO4 during operation under spinal anesthesia reduced postoperative pain and analgesic consumption. For comparison, only few studies have used MgSO4 following regional anesthesia as compared to general anesthesia. In these

studies it was observed that administration of MgSO4 as bolus followed by IV infusion under spinal anesthesia was associated with postoperative increased time to analgesic requirement, significantly lower pain score and lower cumulative patient controlled analgesia drug consumption [14, 15].There are some studies which have found no use of MgSO4 in relieving the postoperative pain [9, 16, 17]. These studies are not done under spinal anesthesia and in one study [17] patients study received only diclofenac suppository immediate preoperatively. In this study we used MgSO4 in dosage of 50mg/kg IV infused over 30 min before induction of anesthesia without any subsequent infusion. Other studies have also use MgSO4 bolus does and they found that it was were effective for postoperative pain relief after orthopaedic and gynaecological surgery, but in addition they used continuous infusion or repeat bolus in addition to initial bolus [2, 18, 19].The above dosage has been reported to be safe without any adverse effects. It has been suggested that NMDA blocking drugs should be given before beginning of nociceptive stimulus to inhibit process of central sensitization [20]. As compared to those who received normal saline, patients who received MgSO4 had a longer duration of post-operative analgesia and required lower doses of diclofenac. Hemodynamic parameters of both groups were also comparable and no patient developed hypotension or bradycardia in both the groups. MgSO4 may induce hypotension by vasodilatation, sympathetic blockade and inhibition of catecholamine release. Some others have reported bradycardia [17, 20] while other have not commented on bradycardia [18, 21].Magnesium has been reported enhance the activity of local anesthetic and neuromuscular blocking agents. Magnesium competitively blocks calcium entry at the motor nerve terminal. There may also be a milder postsynaptic affect [22, 23]. In our study, we did not monitor neuromuscular block by train of four method; but no clinical prolongation of neuromuscular block was observed with MgSO4. One of the reason might be that we used MgSO4 only as single bolus dose whereas most of the studies have used MgSO4 as subsequent infusion also in addition to initial single bolus.

Limitations of the study

The sample size in this study was small and we did not measure serum magnesium and cerebrospinal fluid magnesium concentration. Future studies should be double-blind randomized trials with large sample size and measure magnesium in serum and cerebro spinal fluid.

Conclusion

Administration of intravenous magnesium sulphate 50 mg/kg pre-operatively significantly reduced postoperative pain score and analgesic requirement in patients undergoing spinal anesthesia. In the present study we did not find significant adverse effects in both the groups.

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