

Effect of intravenous infusion of magnesium sulphate on postoperative analgesia in patients undergoing arthroscopic knee surgeries under spinal anaesthesia

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ABSTRACT

Background: Magnesium sulphate is being used for postoperative pain relief intravenously, intrathecally and epidurally. Currently, it is also gaining popularity as an adjuvant in blocks. The objective of the study was aimed at the postoperative analgesic effects of magnesium sulphate when given as intravenous infusion in patients undergoing arthroscopic knee surgeries under spinal anaesthesia and to compare the postoperative analgesic effects of magnesium sulphate infusion in a study cohort who received magnesium sulphate with the control cohort who were not given magnesium sulphate and underwent arthroscopic knee surgeries under spinal anaesthesia.

Methods: After obtaining ethical committee clearance and consent from the patients, 31 patients each were placed in study cohort and control cohort. Spinal anaesthesia was administered in the lateral decubitus position through the L3–4 or L4–5 interspace. Hyperbaric bupivacaine 0.5% solution with fentanyl 20 µg was injected intrathecally. After spinal anaesthesia, patients received magnesium sulphate 50 mg/kg for 15 min and then 15 mg/kg/hr by continuous intravenous infusion until the end of surgery. The other group did not receive magnesium sulphate infusion. Postoperative pain scores and postoperative analgesic consumption were the primary end points.

Results: The results of the study reveal the efficacy of perioperative intravenous infusion of magnesium sulphate in prolonging the spinal block as well as reducing the postoperative pain scores without hemodynamic variability or side effects.

Conclusions: Post-operative pain and analgesic consumption was reduced with the use of intravenous magnesium following spinal anaesthesia.

Keywords: Cohort study, Intravenous infusion, Intravenous infusion, Magnesium sulphate

INTRODUCTION

Spinal anaesthesia is a popular and time-tested regional anaesthetic technique with good safety profile and high success rate but has a limited duration of action. In recent times, the use of intrathecal adjuvants with sub therapeutic doses of local anaesthetic has become popular as they have a synergistic effect, boosts analgesia, extends the period and rises the intensity of block, provides better patient satisfaction with fewer complications.¹ Postoperative pain following arthroscopic knee surgeries is usually moderate to severe in nature. For early rehabilitation and functional recovery, adequate

postoperative pain management and satisfactory analgesia is important.

Magnesium, a physiological calcium antagonist by blocking NMDA receptors in a voltage dependent manner, abolishes hypersensitisation and produces a reduction of NMDA induced currents. Intrathecal magnesium sulphate has shown to prolong analgesic effects of opioids in spinal anaesthesia as a non competitive NMDA antagonist in the first randomized human study.² During general anaesthesia, Magnesium sulphate infusion reduced the anaesthetic requirement and postoperative pain and analgesic consumption as demonstrated by numerous clinical trials.³ Magnesium

sulphate is being used for postoperative pain relief intravenously, intrathecally and epidurally. Currently, it is also gaining popularity as an adjuvant in blocks. The effects of magnesium sulphate infusion during spinal anaesthesia have been investigated only in a limited number of studies.⁴ The effect on postoperative pain and analgesic consumption by systemic magnesium sulphate during spinal anaesthesia has not been fully determined yet.

Thus, it was hypothesized that use of intravenous infusion of magnesium sulphate may have an effect on the duration of action of intrathecal bupivacaine and block characteristics and this study was planned to evaluate the effect of an intravenous infusion of magnesium sulphate on postoperative pain and analgesic consumption in patients undergoing arthroscopic knee surgeries under spinal anaesthesia.

METHODS

A prospective cohort study was designed in department of anaesthesiology, Amala Institute of Medical Sciences, Thrissur from December 2014 to June 2016. This study was approved by Institutional Ethics committee of Amala Institute of Medical Sciences. Sixty two patients belonging to ASA category I and II, undergoing arthroscopic knee surgeries under spinal anaesthesia at Amala Institute of Medical Sciences, Thrissur.

Patients aged between 18 to 65 years belonging to ASA category I and II were included. From the patients selected for the study following patients were excluded.

- a) Patients having coexisting systemic disorders like neuromuscular diseases, neuronal degenerative disorders, cardiovascular, hepatic or renal dysfunction, bleeding and haematological disorders.
- b) Patients with past history of allergies to the study drugs, on analgesics or calcium channel blockers or with a history of opioid and analgesic abuse.
- c) Patients having contraindications to central neuraxial blockade.
- d) Patient refusal.

Sample size was calculated following the study by Hwang et al based on intravenous infusion of magnesium sulphate improving postoperative analgesia in patients undergoing total hip arthroplasty with slight modifications.⁴

$$n = \frac{(S_1^2 + S_2^2) \times (Z_{1-\frac{\alpha}{2}} + Z_1 - \beta)}{(X_1 - X_2)^2}$$

Where n is the sample size.

X_1 is the mean for the time to first pain in mins in patients who received intravenous magnesium sulphate.

S_1 is the standard deviation for the time to first pain in patients who received intravenous magnesium sulphate.

X_2 is the mean time to first pain in mins in patients who did not receive magnesium sulphate infusion.

S_2 is the standard deviation for the time to first pain in patients who did not receive magnesium sulphate infusion.

$$Z_{1-\alpha/2} = 1.64 \text{ at } \alpha = 5\%.$$

The sample size calculated for each group was 31.

All patients who were posted for arthroscopic knee surgeries under spinal anaesthesia were consecutively placed in the study cohort and comparative cohort till the sample size was obtained. All patients who received intravenous magnesium sulphate formed the study cohort (Mg group) and all patients who were not given intravenous magnesium sulphate formed the comparative cohort (Non Mg group). Study protocol was explained in detail to all patients and written informed consent obtained prior to the study. 31 patients each were placed in study cohort and comparative cohort. Patients were shifted to the operating theatre after premedication with intravenous midazolam 0.03 mg/kg. Normal saline 500 ml was given over 15 min, mandatory monitors including ECG, non-invasive blood pressure and pulse oximeter were connected and initial vitals recorded. Spinal anaesthesia was administered in the lateral decubitus position through the L3–L4 or L4–L5 interspace. A 25 G Quincke needle was used to puncture the dura, following which hyperbaric bupivacaine 0.5% solution (bupivacaine dose was decided based on height; height <155 cm=12 mg; 155–170 cm=13 mg; 170–180 cm=14 mg; ≥180 cm=15 mg) with Fentanyl 20 µg was injected intrathecally.

Pinprick testing was performed to assess the height and regression of spinal sensory block using a sterile needle compared to a non-anaesthetised part of the body so the patient can perceive the difference. Motor block onset and duration was decided as the time to achieve modified Bromage scale grade 2 i.e., able to move feet but inability to rise extended leg and move knee. Pre and intraoperative administration of magnesium sulphate (50 mg/kg bolus and maintenance of 15 mg/kg/hr) in gynaecology patients receiving TIVA (Total Intravenous Anaesthesia) reduced rocuronium requirement and improved the quality of postoperative analgesia without any significant side-effects.

Accordingly, in the present study, after spinal anaesthesia, magnesium sulphate was administered to the patients in the Magnesium group (Mg group) or study cohort (n = 31) as 50 mg/kg for 15 min and then 15 mg/kg/hr by continuous intravenous infusion until the end of surgery. Patients in the Non Magnesium group (Non Mg group) or control group (n = 31) did not receive

Magnesium Sulphate infusion. Postoperative pain scores and postoperative analgesic consumption were the primary end points.

If the systolic blood pressure dropped to below 90 mm Hg or if mean arterial pressure decreased more than 20% from baseline, ephedrine 3 to 6 mg was given intravenously and if the heart rate decreased to less than 45 beats/min, intravenous atropine 0.6 mg was administered.

Statistical analysis

Data were analyzed using the statistical software - Statistical Package for Social Sciences (SPSS) and presented in mean ± standard deviation. Baseline characteristics of study subjects were explained in terms of frequency, percentage, mean and standard deviation. The vital signs (heart rate, respiratory rate and non invasive blood pressure), need for first analgesic requirement, total tramadol consumption and the postoperative pain scores in both the groups were compared using Student ‘t’ test. The incidence and severity of nausea, vomiting and shivering in both the groups were compared with the help of Chi square test. The level of significance was estimated with 95% confidence intervals and P value <0.05.

RESULTS

Sixty two patients belonging to ASA physical status I and II, aged between 18 to 65 years, scheduled for arthroscopic knee surgeries under spinal anaesthesia were included in the study. Data of each patient were statistically analysed.

Demographic profiles of the patients are presented in Table 1. No significant difference was found between the two groups in terms of age, gender, height, weight, ASA grade or duration of surgery and the demographic profile was similar in both the groups.

Table 1: Demographic profile.

Patients characteristics	Mg Group (n=31)	Non Mg Group (n=31)
Age (years)	35.29±10.885	34.61±9.684
Sex (M:F)	28:3	23:8
Weight (Kg)	58.00±5.848	57.16±6.383
Height (cm)	168.03±7.468	168.77±7.003
ASA grade I / II	28/3	27/4
Duration of surgery (min)	103±9.03	103.55±9.50

No technical or procedural failure related to spinal anaesthesia occurred and all cases were completed as planned. Mean block height was T8 in two groups, administered dose of bupivacaine was similar between the two groups (13.52±0.50 mg in Mg group and

13.55±0.56 in Non Mg group). Time for regression of sensory block to T12/L1 was 193.55±6.08 min (Mg group) and 155.81±5.016 min (Non Mg Group) (P = 0.001). Mean duration of motor block was longer in Mg group (155.94±5.176 min) compared with Non Mg Group (122.45±6.191 min) (P = 0.001).

Table 2: Characteristics of block.

Characteristic	Mg group (n=31)	Non Mg Group (n=31)
Height of spinal block (level)	T8	T8
Mean dose of bupivacaine (mg)	13.52±0.50	13.55±0.56
Onset of sensory blockade (min)	7.45±0.506	7.68±0.475
Sensory block duration (min) (Regression to T12/L1)	193.55±6.08	155.81±5.016
Onset of motor blockade (min)	9.52±1.06	9.0± 0.87
Motor block duration (min)	155.94±5.176	122.45±6.191

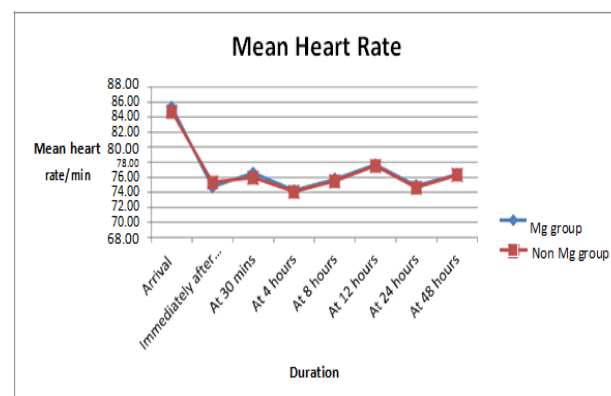


Figure 1: Hemodynamic parameters.

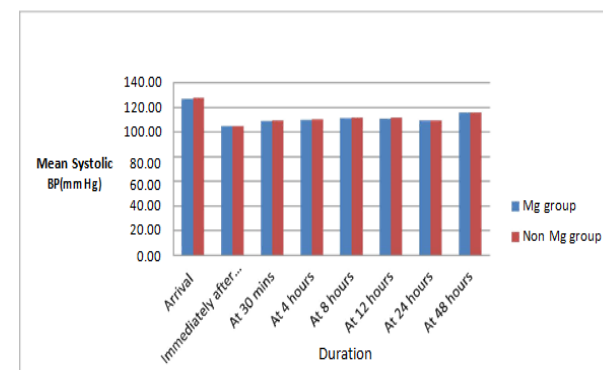


Figure 2: Mean systolic BP.

Hemodynamic parameters were similar in two groups and statistically not significant. 3 patients in Mg group

and 4 patients in Non Mg Group developed hypotension, 1 patient in Mg Group developed bradycardia during surgery. According to the study protocol, ephedrine 6 mg and atropine 0.6 mg were administered and arterial pressure and heart rate normalized.

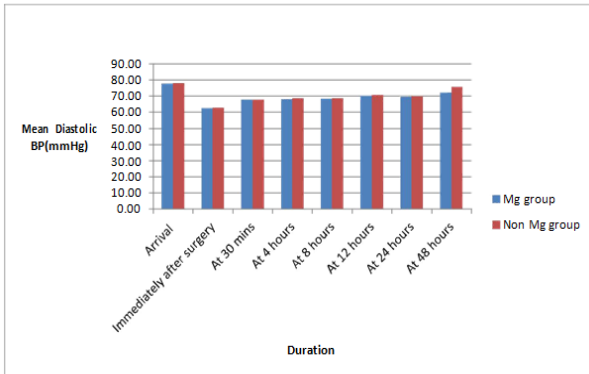


Figure 3: Mean diastolic BP.

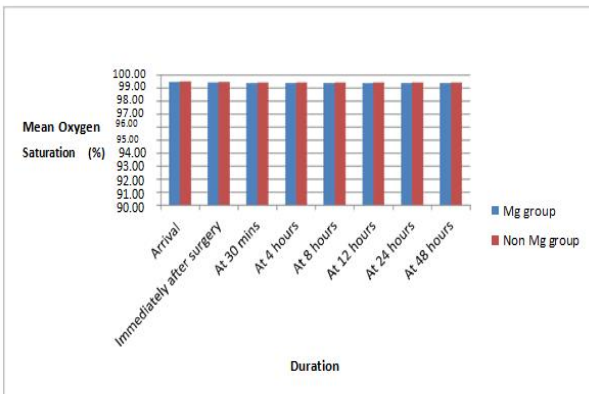


Figure 4: Mean oxygen saturation.

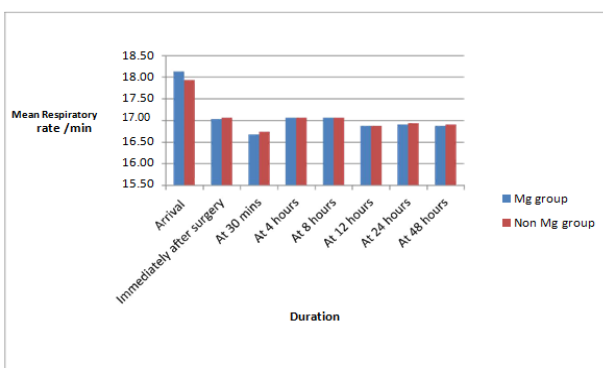


Figure 5: Mean respiratory rate.

Significant hemodynamic depression was not seen in our study and hemodynamic variability did not differ from the control group. Prehydration with 500 ml of Normal saline solution was given considering the negative inotropic effect of magnesium sulphate and then the magnesium sulphate bolus dose was infused over 15 min, which is why no significant hypotension developed after

administering the bolus dose (even though magnesium sulphate has vasodilatory effects).

Table 3: Need for first analgesic requirement.

	Mg group	Non Mg group	p value
Need for first analgesic requirement/ Time to first pain (min)	289.67±8.36	231.19±2.53	0.001

Need for first analgesic requirement was after 289.67±8.36 min in Mg group and 231.19±2.53 min in the Non Mg group (P=0.001) which is presented in Table 3.

Table 4: Postoperative pain scores.

Duration	Mean postoperative pain score (VAS)		P value
	Mg group (n=31)	Non Mg group (n=31)	
At 4 hours	0.87±0.34	3.35±0.66	0.001
At 8 hours	0.58±0.50	2.61±1.08	0.001
At 12 hours	1.58±0.50	3.42±0.95	0.001
At 24 hours	0.84±0.30	3.03±1.04	0.001
At 48 hours	2.81±0.40	2.94±0.25	>0.05

Postoperative pain scores assessed by visual analogue scale was less in Mg group till 24 hours (Table 4). The values were significantly different. The pain scores were similar in both the groups between 24 to 48 hours.

Table 5: Mean dosage of tramadol consumption.

	Mg group	Non Mg group	p value
<24 hours	251.61±50.80	393.55±24.97	0.001
>24 hours - 48 hours	300	300	

Table 6: Rescue analgesia required in patients.

	Rescue analgesia		Relative Risk (95% CI)	P value
	Given	Not given		
Mg Group (n=31)	1 (3.2%)	30 (96.8%)	0.25	<0.05
Non Mg Group (n=31)	4 (12.9%)	27 (87.1%)	(0.03-2.11)	

Mean dosage of Tramadol needed in first 24 hrs was less in Mg group compared to the Non Mg group (251.61±50.80 mg versus 393.55±24.97 mg, P=0.001) (Table 5). There was no change in Tramadol dosing required between 24 to 48 hours. One patient in Mg

group and 4 patients in Non Mg group required rescue analgesia which is shown in Table 6 and morphine 4.5 mg intramuscularly ($P < 0.05$).

The incidences of postoperative nausea, vomiting and

shivering are given in Table 7. The incidence of postoperative nausea and vomiting after surgery were similar in the two groups. There was no statistically significant difference in the incidence of shivering between the two groups.

Table 7: Postoperative nausea, vomiting and shivering.

	Postoperative nausea and vomiting		P value	Postoperative shivering		P value
	Study Group (n=31)	Control Group (n=31)		Study Group (n=31)	Control Group (n=31)	
Immediately after surgery	0	0		0	0	
At 30 mins	0	0		0	0	
At 4 hours	2	2		1	2	
At 8 hours	0	0	>0.05	0	0	>0.05
At 12 hours	1	2		0	0	
At 24 hours	0	0		0	0	
At 48 hours	0	0		0	0	

DISCUSSION

Patients who fulfilled selection criteria were selected for the study. A total of sixty two patients who belonged to ASA physical status I and II, with age between 18 to 65 years and scheduled for arthroscopic knee surgeries under spinal anaesthesia.

There was no difference in the onset of sensory and motor block between the two groups were shown from the results of Table 2. Malleswaran et al have postulated that delayed onset of block might be because of the changes in pH and baricity of local anaesthetic solution with the addition of intrathecal magnesium sulphate.⁵ With intravenous administration of magnesium sulphate, the same mechanism does not work and further research is needed to evaluate this aspect.

Time for regression of sensory block to T12/L1 found in this study was similar to the study done by Agarwal and coworkers, where time for regression of sensory block to T12/L1 was 206.88 ± 20.96 min (Group Mg) and 163.88 ± 15.46 min (Group Non Mg) ($P = 0.000$).⁶ Mean duration of motor block was longer in Mg group (160.63 ± 17.76 min) compared with Non Mg Group (130.12 ± 20.70 min) ($P = 0.000$). Kahraman F and Eroglu A also found that in Group Mg, sensorial block regression was longer than that in Group Non Mg (175 ± 39 versus 136 ± 32 min) ($P < 0.01$).⁷

Sensory block has been found to be increased with the use of magnesium sulphate. Anti-nociception property is by decreasing calcium mediated release of neurotransmitters which are implicated in nociception and inflammation. The reason for a decrease in post nociception central sensitization of pain is said to be blocking of NMDA receptors.⁸ Direct depression of

excitability of muscle fiber membrane and reduction of acetylcholine release from motor nerve terminals produces motor blockade.⁴

The results of hemodynamic depression were not significantly different in this study and hemodynamic variability did not differ from the control group (Figure 1). No significant hemodynamic differences were observed during the surgery and in the postoperative period between the two groups. Similar results were found in the studies of Hwang et al, Agarwal et al, and Kahraman F, Eroglu A.^{4,6,7}

Need for first analgesic requirement per time to first pain (min) is presented in Table 3. The time to first analgesic request was significantly longer in the magnesium sulphate infusion group in the study by Agarwal et al where need for first analgesic requirement was at 262.88 ± 21.11 min in Mg group and 193.25 ± 17.74 min in Non Mg ($P = 0.04$).⁶ Kumar et al also demonstrated that the duration of analgesia and the requirement of first rescue analgesia was longer in Mg group (333.91 ± 202.41) min versus (232.68 ± 140.62) min in the control group with P value of < 0.05 .⁹

Postoperative pain scores assessed by visual analogue scale and the results are depicted in Table 4. The pain scores were similar in both the groups between 24 to 48 hours. Similar results were also found in the study by Hwang et al and Vandana et al where in the Mg group at 4, 24, and 48 hrs after surgery, postoperative VAS scores were markedly and significantly lower ($P < 0.001$).^{4,10} Kahraman et al reported that the VAS scores were lower in Mg group than those in Non Mg group at 2 hrs and 4 hrs after the surgery.⁷ Kumar et al also found that postoperative pain scoring by VAS was much lower in the Mg group than Non Mg group.⁹ Meta analysis done

by Albrecht et al and stated that postoperative pain scores for 24 hours postoperatively was reduced by intravenous magnesium sulphate.¹¹

The results of mean dosage of Tramadol consumption are presented in Table 5. It shows that mean dosage of Tramadol needed in first 24 hrs was less in Mg group compared to the Non Mg group. In a study by Hwang et al, in Group M total postoperative consumptions of PCA were markedly lower at 4, 24 and 48 hrs after surgery and during the postoperative period ($P < 0.001$), more patients in the control group required additional rescue analgesia (2 vs 6 patients), but this was not statistically significant ($P = 0.079$).⁴ Agarwal and associates found that in Mg group, mean dosage of Tramadol needed in first 24 hrs was less compared with Non Mg group (190 ± 30.38 mg versus 265 ± 48.30 mg, $P = 0.000$).⁶ The results of rescue analgesia required in patients are tabulated in Table 6. The results showed that one patient in Mg group and 4 patients in Non Mg group required rescue analgesia, morphine 4.5 mg intramuscularly. Kumar and co-workers reported as decreased mean postoperative rescue analgesia requirement (morphine) in 24 hrs in Mg group (3.99 ± 1.25 mg) as compared to NS group (7.13 ± 2.68 mg) (P value < 0.006).⁹ Meta analysis by Albrecht et al reported that intravenous magnesium sulphate can reduce total postoperative opioid consumption.¹¹

The incidences of postoperative nausea, vomiting and shivering after surgery are shown in Table 7 and were similar in both the groups. Hwang et al and Vandana et al also found that the incidence of postoperative nausea, vomiting and the incidence of shivering were similar in the two groups.^{4,10}

Limitations

The inability to measure the serum magnesium level as well as the inability of use of patient control analgesia (PCA) for control of pain was the major drawback of this study. Minor side effects of parenteral magnesium such as nausea, headache and flushing are seen at serum magnesium levels above 2 mmol/litre and life-threatening adverse events involving the neuromuscular and cardiovascular systems occur at serum magnesium levels above 5 mmol/litre.¹² In this study, no features of magnesium toxicity like depressed patellar reflex, decrease in respiratory rate, decrease in urine output or ECG changes like prolonged PR interval or wide QRS were noted in either groups.

CONCLUSION

This study reveals the effectiveness of perioperative intravenous infusion of magnesium sulphate in prolonging the spinal block as well as reducing the postoperative pain scores and postoperative analgesic requirements without significant hemodynamic variability or side effects. The observations of the study suggest that intravenous bolus (50 mg/kg) and infusion

(15 mg/kg/hr) of magnesium sulphate is safe to use, it improves postoperative analgesia and reduces postoperative analgesic requirement after spinal anaesthesia without having any adverse effects.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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