Solanki *et al.*
Ain-Shams Journal of Anesthesiology (2023) 15:91
https://doi.org/10.1186/s42077-023-00389-5

Ain-Shams Journal
of Anesthesiology

ORIGINAL ARTICLE

Open Access

Evaluation of adding magnesium sulphate to intrathecal bupivacaine in lower limb orthopedic surgery

Nilesh M. Solanki[1*], Maulik P. Bhimani[1], Nirmal S. Mistry[1] and Diya Rajan[1]

Abstract

Background A subarachnoid block is the cheaper and widely used regional block for lower limb surgery. Postoperative pain occurs after lower limb orthopedic surgery from moderate to severe. We conducted a prospective, randomized, double-blind controlled trial. All patients were assessed for onset and duration of sensory and motor block, total duration of analgesia, and postoperative pain relief.

This study was conducted to evaluate the efficacy of intrathecal bupivacaine with magnesium undergoing lower limb orthopedic surgery.

Results One hundred patients were randomly divided into two equal groups. Group M: Intrathecal 3 ml (15 mg) of 0.5% bupivacaine + 0.2 ml (50 mg) of preservative-free 25% of magnesium sulphate. Group B: Intrathecal 3 ml (15 mg) of 0.5% bupivacaine + 0.2 ml preservative-free 0.9% normal saline. The mean time that occurred for the sensory blockade at T10 was 2.49 ± 0.49 min in group B, while it was 4.13 ± 0.74 min in group BM (*p* value < 0.0001). The mean of the total duration of the sensory block in group B was 139.5 ± 32.01 min, while it was 366.4 ± 30.12 min in group BM (*p* value < 0.0001). The time taken for the onset of motor block in group B was 5.28 ± 1.31 min, while it was 7.86 ± 1.19 min in group BM (*p* value < 0.0001). The mean total duration of the motor block in group B was 136.3 ± 8.19 min, while it was 336.5 ± 37.08 min in group BM (*p* value < 0.0001). The total duration of analgesia in group B was 141.4 ± 14.85 min, while it was 365.9 ± 44.91 min in group BM (*p* value < 0.0001). The mean dose required for rescue analgesia in group B was 2.2 ± 1.14, while in group BM was 1.28 ± 0.96 (*p* value < 0.0001).

Conclusions The addition of 50 mg magnesium sulphate in intrathecal hyperbaric bupivacaine significantly prolongs the extended duration of sensory, motor blockade, and total duration of analgesia for patients undergoing lower limb orthopedic surgery.

Keywords Analgesia, Bupivacaine, Magnesium sulphate, Subarachnoid block

Background

In clinical practice, spinal anesthesia was first introduced by Karl August Bier in 1898 (Parameshwara 2001). An unpleasant sensory and emotional experience associated with actual or potential tissue damage is known as pain (Ripamonti 2012). Postoperative pain is reported to be moderate to severe after lower limb orthopedic surgery and has major effects on almost all body systems. Several studies have reported the effect of intrathecal magnesium sulphate as an adjuvant to intrathecal bupivacaine

*Correspondence:
Nilesh M. Solanki
nmscbaps@gmail.com
[1] Department of Anesthesia, B. J. Medical College and Civil Hospital, 44-Devshrusti Bungalows-II, B/H Kena Bungalows, Motera Stadium Road, Motera, Sabarmati, Asarwa, Ahmedabad 380005, Gujarat, India

prolongs the analgesic duration of spinal anesthesia, but there is inconsistency with relative data (Alur et al. 2021; Wang et al. 2020). Magnesium sulphate is a noncompetitive antagonist to *N*-methyl D-aspartate (NMDA) receptors at the spinal cord to prevent central sensitization from peripheral nociceptive stimulation. Some other studies have reported that magnesium, due to its antinociceptive property, has been used to relieve chronic pain (Tramer et al. 1996; Xiao and Bennett 1994) as well as to determine the intensity of duration and postoperative pain (Woolf and Thomas 1991; Lysakowaski et al. 2007).

The primary objective was the onset as well as the duration of sensory and motor block. The secondary objectives included were postoperative analgesia, hemodynamic variations, and adverse effects of drugs.

Methods

The study was approved by the institutional ethical committee, ref number 162/2019, dated November 25, 2019. The duration of the study period was from the 1st of December 2019 to the 31st of December 2020.

After written informed consent, this randomized, prospective, and experimental double-blind study included 100 patients of sex, belonging to the American Society of Anesthesiologists (ASA) physical statuses I and II posted for lower limb orthopedic surgeries under spinal anesthesia. Surgery duration was limited from 80 to 190 min. Pre-anesthetic check-ups with all routine investigations were done a day before surgery. All patients were explained about the risks and advantages of the procedure and the visual analog scale (VAS) (Scott and Huskisson 1976) (mark 0 = no pain, 10 = worst pain imaginable).

Randomization was done by using a computer-generated random number table. Both the observer and participants were blinded by the intervention.

Group B ($n = 50$) patients received 3 ml of 0.5% heavy bupivacaine (15 mg) + 0.2 ml of preservative-free 0.9% normal saline.

Group BM ($n = 50$) patients received 3 ml of 0.5% heavy bupivacaine (15 mg) + 0.2 ml of preservative-free 25% magnesium sulphate (50 mg).

Inclusion criteria

- Age 20–60 years
- Either sex
- ASA I or II
- Elective lower limb orthopedic surgeries

Exclusion criteria

- Patient refusal
- Patient with h/o bleeding diathesis
- Significant cardiac, renal, hepatic disease, and neuromuscular disease
- Psychological disorder
- Allergic reaction to local anesthetics

All the patients included in the study were kept nil per oral since midnight. All patients received tab diazepam 10 mg the night before surgery. After shifting the patient to the operating room, basic anesthesia monitors like pulse-oximetry, electrocardiogram (ECG), and non-invasive blood pressure (NIBP) were connected and baseline vital parameters (blood pressure, heart rate, and oxygen saturation (SpO_2)) were recorded. An intravenous line with an 18-G cannula was placed, and adequate infusion was started. All patients were premedicated with inj. glycopyrrolate 0.2 mg and inj. ondensetron 4 mg intravenously. No sedative agent was administered.

With proper antiseptic precaution, lumbar puncture was done with a 25-G Quincke (BD, USA) spinal needle at the level of L3–L4 vertebra in a sitting position, and after confirming the free flow of cerebrospinal fluid, 3.2 ml of the study drug solution was administered by an anesthesiologist not aware of the drug solution. The sensory level was assessed by pinprick method using a blunt 23-gauze needle along the midclavicular line, after placing the patient in a supine position. No tilt of the table was allowed till 20 min after the administration of the drug. The time between the end of the injection of the intrathecal anesthetic drug and the absence of pain at the T10 dermatome is considered as the onset of sensory block. The time for regression of two segments from the maximum block height evaluated by pinprick is known as the duration of the sensory block. The Modified Bromage Score ((0) no motor loss, (1) inability to flex the hip, (2) inability to flex the knee, and (3) inability to flex the ankle) (Breen et al. 1993) was used for assessment of motor block. The time from intrathecal injection to Bromage score 1 is defined as the onset of motor block, whereas when the Bromage Score 0, it was defined as the duration of motor block. The period from spinal injection to the time when the patient complained of pain for the first time in the postoperative period was considered as the duration of analgesia.

Heart rate, systolic, diastolic, mean blood pressure, oxygen saturation, and respiratory rate were monitored every 5 min for the first 30 min and then every 15 min until the end of surgery in the operating room. Hypotension (decrease in blood pressure of more than 20% from baseline) was immediately treated with intravenous fluids or ephedrine, and bradycardia (heart rate < 60 beats/minute) was managed with atropine. The postoperative analgesia was defined as the time to first analgesic request

Table 1 Demographic data

Variables		Group B ($n = 50$)	Group BM ($n = 50$)	*P* value
ASA grade	I	25 (50%)	24 (48%)	0.84
	II	25 (50%)	26 (52%)	
Gender	Male	33 (66%)	40 (80%)	0.11
	Female	17 (34%)	10 (20%)	
Age (years)		40.19 ± 12.4	42.17 ± 12.0	0.81
Weight (kg)		57.80 ± 4.4	58.20 ± 6.5	0.71
Height (cm)		155.7 ± 2.6	156.1 ± 4.0	0.55
Surgery duration (minutes)		127.5 ± 29.42	133.9 ± 52.89	0.45

Data presented as mean ± SD or number, percentage: $P > 0.05$ not significant

(when VAS reached ≥ 4) from the time of injection of the study drug. The quality of postoperative analgesia was assessed using VAS scores at 2, 3, 4, 8, 12, 18, and 24 h postoperatively. Any patient showing VAS ≥ 4 was administered a supplemental dose of injection Tramadol 1 mg/kg intravenously slowly. The primary outcome measure in this study was the onset and duration of sensory and motor block. The secondary outcome measures included postoperative analgesia, hemodynamic stability, and side effects.

Statistical analysis

In this study, the sample size was calculated on the basis of the pilot study. To get the clinically relevant difference of 20% in the duration of sensory and motor blockade with 0.05 significant levels and 80% power, we needed 41 patients in each group. To compensate for the attrition rate, we included 50 patients in each group. Collected data were presented as mean ± SD, numbers, and percentages as appropriate. Statistical analysis was carried out using MS Excel 2010 (Microsoft Corporation, USA) and Graph Pad Prism 9.0 software (Graph Pad Software Inc., La Jolla CA, USA). Appropriate univariate and bivariate analyses were done by using the Students' *t* test for continuous variables and the chi-square test for categorical variables. $P < 0.05$ is considered as significant level, and $p < 0.0001$ was taken as highly significant.

Results

Demographic data (Tables 1 and 2) revealed that there was no statistically significant difference between the two groups with regard to age, gender, weight, height, or duration of surgery and ASA grades.

As regards block characteristics (Table 3), there was a statistically significant delay in the onset of sensory and motor block in group BM when compared to group B.

The duration of sensory blockade in group BM was prolonged than in group B which was statistically highly significant ($p < 0.0001$). The duration of motor blockade in group BM was prolonged than in group B which was also statistically highly significant ($p < 0.0001$).

A statistically significant difference was observed for the prolonged duration of analgesia in group BM compared to group B ($P < 0.001$). The group B patient's

Table 2 Type of surgery

Surgical procedure	Group–B ($n = 50$)	Group-BM ($n = 50$)	*P* value
Plating of the lower end of the femur	16 (32%)	18 (36%)	1
PFN	13 (26%)	11 (22%)	
TKR	16 (32%)	17 (34%)	
Plating of the upper end of the tibia	05 (10%)	04 (8%)	

Data presented as number or percentage

Table 3 Characteristics of spinal block

Variables	Group B ($n = 50$)	Group BM ($n = 50$)	*P* value
Onset of sensory block (min)	2.49 ± 0.49	4.13 ± 0.74	< 0.0001
Duration of sensory block (min)	139.5 ± 32.01	366.4 ± 30.12	< 0.0001
Onset of motor block (min)	5.28 ± 1.31	7.86 ± 1.19	< 0.0001
Duration of motor block (min)	136.3 ± 8.19	336.5 ± 37.08	< 0.0001
Total duration of analgesia (min)	141.4 ± 14.85	365.9 ± 44.91	< 0.0001
Analgesic dose request (number)	2.2 ± 1.14	1.28 ± 0.96	< 0.0001
Requirement of analgesia (min)	142.5 ± 32.01	369.8 ± 26.48	< 0.0001

Data presented as mean ± SD or number: $P < 0.0001$ highly significant requirement of the dose of inj tramadol was earlier as compared to group BM patients ($P < 0.0001$) (Table 3).

In the immediate postoperative period, no patient had a VAS score ≥ 4. The mean VAS score was higher at the end of 4 h in group B as compared to group BM at the same time. The difference was statistically highly significant ($P < 0.0001$) (Fig. 1).

There was no significant difference in the heart rate, SBP, and DBP found between the two groups.

As regards side effects, only 4 cases reported nausea, 2 cases reported vomiting, and 2 cases reported shivering in group B, while in group BM, 2 cases reported nausea and 2 cases reported headache; the difference between both groups was statistically insignificant.

Discussion

Subarachnoid block with hyperbaric bupivacaine is a safe, inexpensive technique and popular mode of anesthesia for lower limb orthopedic surgery. One of the major drawbacks of spinal anesthesia using local anesthetics alone is an early postoperative need for analgesia.

For postoperative pain relief, there are multimodal analgesic methods including systemic opioids or NSAIDS or NMDA receptor antagonist (magnesium) and regional techniques in the form of spinal, epidural, or peripheral nerve blocks, etc. It diminishes autonomic, somatic, and endocrine reflexes that finally result in a remarkable reduction in perioperative morbidity (Shukla et al. 2011).

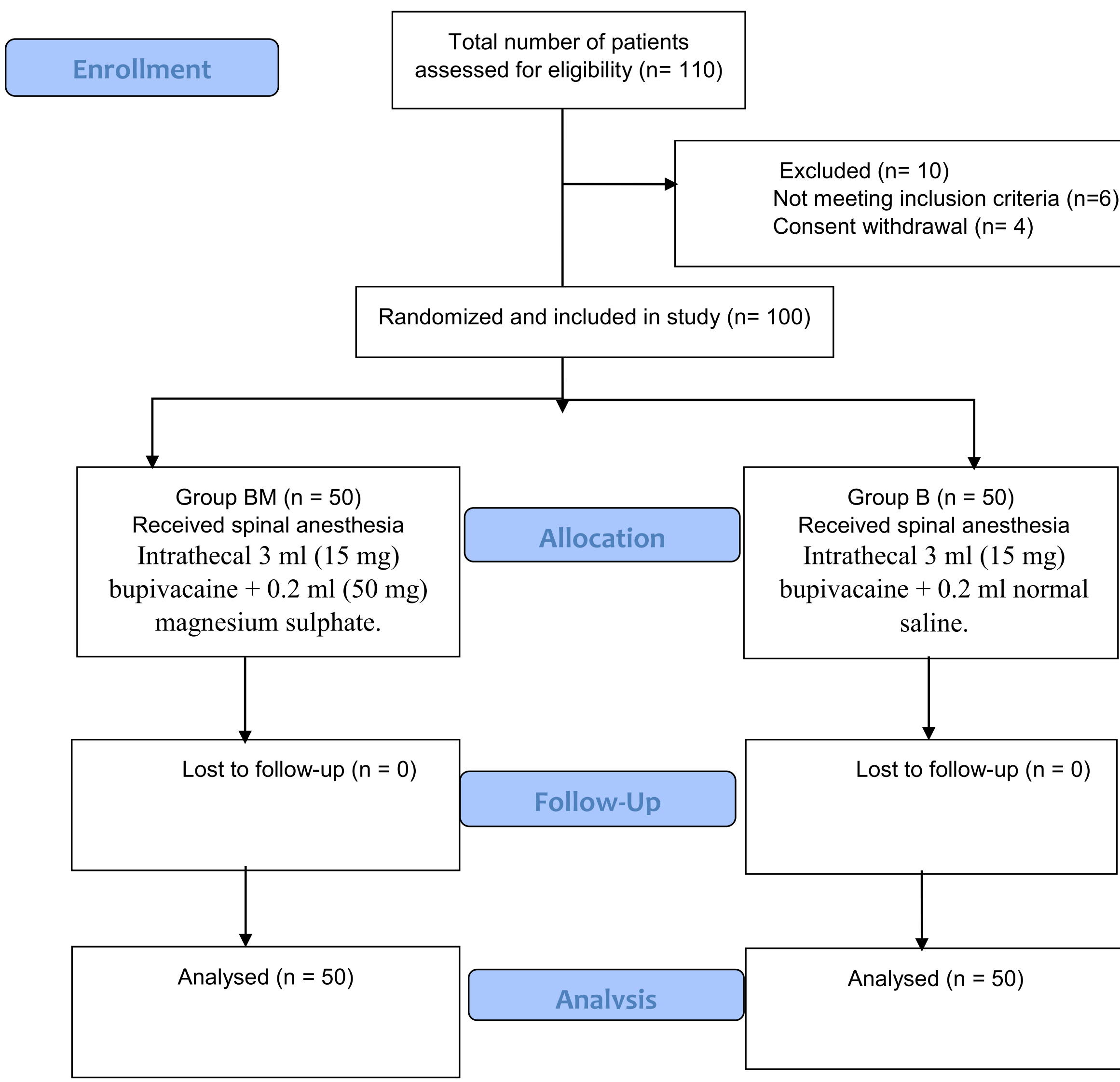

Fig. 1 Consort flow diagram

NMDA receptor antagonist has an important role in the prevention of central sensitization of pain. Magnesium sulphate being a non-competitive NMDA receptor antagonist stimulates peripheral nociceptive and helps in the prevention of central sensitization (Tramer and Glynn 2007; Woolf and Thompson 1991; Woolf and Chong 1993).

The present study was designed to examine the onset and duration of sensory and motor block and the analgesic effects of intrathecal magnesium sulphate (50 mg) as an adjuvant to bupivacaine (15 mg) in spinal anesthesia for lower limb orthopedic surgery.

In our study, we observed prolonged onset and duration of sensory and motor blockade in the BM group with better postoperative analgesia without any untoward effects in comparison to the B group. Haubold and Meltzer (1906) utilized intrathecal magnesium sulphate (1000–2000 mg) in human-produced spinal anesthesia, including motor and sensory blocks for 3.27 h without neurological damage.

Faiz et al. (2012) found that intrathecal $MgSO_4$ when combined with local anesthetic agents is known to potentiate the analgesic effect.

In a meta-analysis published by Ramirez et al. (2013), intrathecal magnesium sulphate doses range from 50 to 100 mg. The most commonly used dose is 50 mg.

Paul et al. (2009) showed that adding 50 mg $MgSO_4$ intrathecally in patients undergoing lower limb surgeries delayed the onset of the sensory block as well as the time to reach peak sensory block in the magnesium group (6.65 ± 1.08 min, 19.26 ± 4.41 min) than the control group (5.2 ± 1.21 min, 14.83 ± 3.46 min) significantly, $p < 0.001$.

Shukla et al. (2011) concluded that the addition of 50 mg intrathecal $MgSO_4$ prolonged the onset of sensory block and motor block in the magnesium group (6.46 ± 1.33 and 7.18 ± 1.38 min) as compared to the control group 4.14 ± 1.06 and 4.81 ± 1.03 min) in lower abdominal surgeries.

The authors of these studies suggested that delayed onset may be due to differences in the pH and baricity of the solution containing $MgSO_4$ (Shukla et al. 2011; Paul et al. 2009). Another study has provided the reason for delayed onset due to the activation of cytochrome P450 (CYP) by magnesium which increases the metabolism of bupivacaine (Morrison et al. 2013). In some studies, it is observed that sensory and motor blockade onset was directly dependent on the dose of magnesium sulphate used (Chaudhary et al. 2016; Prabhavathi et al. 2017).

However, Limbu et al. (2017) concluded that the addition of 75 mg $MgSO_4$ had no effect onset of sensory or motor block which is contradictory to our study results.

In addition, intrathecal magnesium sulphate (50–100 mg) along with bupivacaine provided the extended duration of the sensory and motor blockade to a significant level (Prabhavathi et al. 2017; Hemalatha et al. 2017; Kathuria et al. 2014).

Shah et al. (2016) and Kahraman et al. (2014) found that intravenous infusion of magnesium sulphate under spinal anesthesia prolongs sensory block duration.

However, Khezri et al. (2012) and Limbu et al. (2017) concluded that the addition of 50 mg $MgSO_4$ intrathecally was no difference in sensory and motor block duration which is not in accordance with our study.

In some studies, it is found that the addition of 50 mg magnesium to hyperbaric bupivacaine (12.5 mg) with fentanyl (25 μg) for spinal anesthesia for infraumbilical surgeries results in a significantly delay of the onset of the sensory and motor block with prolonged analgesia, less score of VAS, without significant hemodynamic changes and side effects (Sen et al. 2020; Singh and Sen 2019).

Our results were partially comparable with Rashad and El-Hefnawy (2015) found that the use of magnesium sulphate as an adjunct in spinal anesthesia was associated with increased duration of postoperative analgesia and decreased amounts of postoperative opioid use (6.95 ± 1.19, 6.25 ± 2.22 vs. 5.60 ± 0.94, 9.50 ± 2.76, respectively).

In our study, the addition of intrathecal magnesium to bupivacaine decreased the VAS scores of the group in which magnesium was not used.

Hemalatha et al. (2017) found that higher doses of intrathecal magnesium reported bradycardia and Morrison et al. (2013) found the risk of respiratory depression.

However, Kathuria et al. (2014) showed that 75 mg of intrathecal magnesium was used, without any hemodynamic variability and any adverse effects.

There is a study of the use of intrathecal magnesium sulphate in rats observing neurodegeneration based on electron microscopic examination (Ozdogan et al. 2013).

In our study, we used 50 mg of intrathecal magnesium for better perioperative hemodynamic stability and no adverse effects.

Limitations

Our findings are limited to bupivacaine only, and future studies are needed for some other local anesthetic drugs.

Conclusions

Intrathecal magnesium sulphate (50 mg) as an adjuvant to bupivacaine (15 mg), in a subarachnoid block for lower limb orthopedic surgeries, significantly prolongs the onset and duration of sensory as well as motor block and decreases the mean VAS score with longer duration of postoperative analgesia than bupivacaine alone without significant hemodynamic variations and adverse effects.

Abbreviations

ASA	American Society of Anesthesiology
IV	Intravenous
NS	Normal saline
G	Gauge
VAS	Visual analog score
RCT	Randomized control trial
$MgSO_4$	Magnesium sulphate
TKR	Total knee replacement
PFN	Proximal femoral nailing
NMDA	*N*-Methyl D-aspartate
NSAIDS	Non-steroid anti-inflammatory drugs

Acknowledgements
We would like to thank the Department of Orthopaedic Surgery for their kind support.

Authors' contributions
NS conceived of the study, wrote and drafted the manuscript, revised the final manuscript, and provided tables. MB contributed to the manuscript, collected the clinical data, and contributed the tables. NM and DR contributed to the manuscript. All authors have read and approved the manuscript.

Funding
None.

Availability of data and materials
The data used/analyzed during this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
After obtaining local ethical committee approval (B.J. Medical College & Civil Hospital, Ahmedabad, dated November 25, 2019, Ref No. 162/2019), written and informed consent was obtained from patients/relative, and all surgical procedure was done under spinal anesthesia.

Consent for publication
Written informed consent was taken from all the patients.

Competing interests
The authors declare that they have no competing interests.

Received: 5 March 2023 Accepted: 28 October 2023
Published online: 09 November 2023

References

Alur J, Korikantimath VV, Jyoti B, Sushma KS, Mallayyagol NV (2021) A comparative study of analgesic efficacy of intrathecal bupivacaine with ketamine versus bupivacaine with magnesium sulphate in parturients undergoing elective caesarian sections. Anesth Essays Res 15:379–388. https://doi.org/10.4103/aer.aer_125_21

Breen TW, Shapiro T, Glass B, Foster-Payne D, Oriol NE (1993) Epidural anaesthesia for labor in an ambulatory patient. Anesth Analg 77:919–924

Chaudhary S, Verma R, Rana S, Singh J, Danesh A (2016) Magnesium sulfate at two different doses as an adjuvant to bupivacaine in infraumbilical (below knee) orthopedic surgeries under spinal anaesthesia. Ain-Shams J Anesth 9:416–421. https://doi.org/10.4103/1687-7934.189098

Faiz SHR, Rahimzadeh P, Sakhaei M, Imani F, Derakhshan P (2012) Anesthetic effects of adding intrathecal neostigmine or magnesium sulphate to bupivacaine in patients under lower extremities surgeries. J Res Med Sci 17:918–922 PMid:23825989 PMCid: PMC3698648

Haubold HA, Meltzer SJ (1906) Spinal anaesthesia by magnesium sulphate. J Am Me Assoc 46:647–650

Hemalatha P, Banu N, Rao MH, Samantaray A, Venkatraman A, Hemanth N (2017) Comparison of two different doses of magnesium sulphate for spinal anaesthesia: a prospective, randomized double-blind study. J Clin Sci Res 6:18–24. https://doi.org/10.15380/2277-5706

Kahraman F, Eroglu A (2014) The effect of intravenous magnesium sulfate infusion on sensory spinal block and postoperative pain score in abdominal hysterectomy. BioMed Res Int 236024:5. https://doi.org/10.1155/2014/236024

Kathuria B, Luthra N, Gupta A, Grewal A, Sood D (2014) Comparative efficacy of two different dosages of intrathecal magnesium sulphate supplementation in subarachnoid block. J Clin Diagn Rese 8:1–5. https://doi.org/10.7860/JCDR/2014/8295.4510

Khezri MB, Yaghobi S, Hajikhani M, Asefzadeh S (2012) Comparison of postoperative analgesic effect of intrathecal magnesium and fentanyl added to bupivacaine in patients undergoing lower limb orthopedic surgery. Acta Anaesthesiol Taiwan 50(1):19–24. https://doi.org/10.1016/j.aat.2012.03.001

Limbu PM, Sindhu K, Singh SN, Pokharel K, Maharjan R (2017) Intrathecal magnesium sulfate as analgesic and anaesthetic adjunct to bupivacaine in patients undergoing lower extremity orthopaedic surgery. J Soc Anesth Nepal 4:74–80

Lysakowaski C, Dumont L, Czarnetzki C, Tramer MR. Magnesium as an adjuvant to post-operative analgesia: a systemic review of randomized trials. Anaesthesia analog 2007:104–1532–9. https://doi.org/10.1213/01.ane.0000261250.59984.cd

Morrison AP, Hunter J, Halpern SH, Banerjee A (2013) Effect of intrathecal magnesium in the presence or absence of local anaesthetic with and without lipophilic opioids: a systematic review and meta-analysis. Br J Anaesth 110:702–712. https://doi.org/10.1093/bja/aet064

Ozdogan L, Sastim H, Ornek D, Postaci A, Ayerden T, Dikmen B (2013) Neurotoxic effects of intrathecal magnesium sulphate. Rev Bras Anestesiol 63:139–148

Parameshwara G (2001) Spinal, epidural to combined spinal epidural analgesia, the history of central neuraxial block. Indian J Anaesth 45:406–412

Paul S, Bhattactarjee DP, Ghosh S, Chatterjee N (2009) Efficacy and safety of intrathecal magnesium sulphate as an adjuvant to bupivacaine for lower limb orthopedic surgery. Pharmacologyonline 2:570–574

Prabhavathi R, Anand G, Reddy PN, Umanageshwarah P (2017) A study to observe the effects of addition of magnesium sulphate as an adjuvant to 0.5% bupivacaine for intrathecal anaesthesia in surgeries of lower limbs. India J Clin Anaesth 4:338–344. https://doi.org/10.18231/2394-4994.2017.0070

Ramirez JP, Trujillo SG, Alcantarilla C (2013) Intrathecal magnesium as analgesic adjuvant for spinal anaesthesia: a meta-analysis of randomized trials. Minerva Anesthesiol 79:667–678

Rashad AE, El-Hefnawy E (2015) Magnesium sulphate as an adjunct to bupivacaine in spinal anesthesia for lower limb orthopedic surgery. Aamj 13:145–151

Ripamonti CI (2012) Pain management. Ann Oncol 23(suppl 10):x294–x330. https://doi.org/10.1093/annonc/mds360

Scott J, Huskisson EC (1976) Graphic representation of pain. Pain 2:175–184. https://doi.org/10.1016/0304-3959(76)90113-5

Sen J, Singh S, Sen B (2020) The effect of intrathecal magnesium sulphate on bupivacaine-fentanyl subarachnoid block for infraumbilical surgeries. J Evolution Med Dent Sci 9(10):780–785. https://doi.org/10.14260/jemds/2020/170

Shah PN, Dhengle Y (2016) Magnesium sulfate for postoperative analgesia after surgery under spinal anesthesia. Acta Anaesthesiol Taiwan 54:62e64. https://doi.org/10.1016/j.aat.2016.06.003

Shukla D, Verma A, Agarwal A, Pandey HD, Tyagi C (2011) Comparative study of dexmedetomidine with intrathecal magnesium sulphate used as adjuvant to bupivacaine. J Anaesthesiol Clin Pharmacol 27:495–499. https://doi.org/10.4103/0970-9185.86594

Singh S, Sen J (2019) The effect of intrathecal magnesium sulfate to bupivacaine-fentanyl subarchanoid block for infraumbilical surgeries. J Datta Meghe Inst Med Sci Univ 14:196–201. https://doi.org/10.4103/jdmimsu.jdmimsu_83_19

Tramer MR, Glynn CJ (2007) An evaluation of a single dose of magnesium to supplement analgesia after ambulatory surgery: randomized controlled trial. Int Anaesth Res Soc 104:1374–1379. https://doi.org/10.1213/01.ane.0000263416.14948.dc

Tramer MR, Schneider J, Marti RA, Rifat K (1996) Role of magnesium sulphate in postoperative analgesia. Anesthesiology 84:340–347

Wang J, Wang Z, Shi B, Wang N (2020) The effect of adding intrathecal magnesium sulphate to bupivacaine-fentanyl spinal anesthesia: a meta-analysis of randomized controlled trials. Medicine 99(40):e22524. https://doi.org/10.1097/MD.0000000000022524
Woolf CJ, Thomas WN (1991) The induction and maintenance of central sensitization is dependent on N-methyl d-aspartate acid receptor activation: implications for the treatment of post injury pain hypersensitivity state pain. Pain 44:293-9
Woolf CJ, Chong MS (1993) Preemptive analgesia--treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg 77(2):362–379. https://doi.org/10.1213/00000539-199377020-00026
Woolf CJ, Thompson SW (1991) The induction and maintenance of central sensitization is dependent on N-methyl-D-aspartic acid receptor activation: implications for the treatment of post-injury pain and hypersensitivity states. Pain 44:293–299. https://doi.org/10.1016/0304-3959(91)90100-C
Xiao WH, Bennett GJ (1994) Magnesium suppresses neuropathic pain response in rats via a spinal site of action. Brain Res 666:168–172. https://doi.org/10.1016/0006-8993(94)90768-4

Publisher's Note