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Intravenous Magnesium Sulfate can be Infused in Spinal Anesthesia for Postoperative Analgesia

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Abstract

Introduction: Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Spinal anesthesia using local anesthetics like hyperbaric bupivacaine is one of the most popular techniques for both elective and emergency surgical procedures. One disadvantage with spinal anesthesia is relatively short duration of action. Postoperative pain relief provides comfort to the anxious patients and improve their morale and mobility there by contributing to a rapid and complete recovery. *Aims:* Study done on IV. Magnesium Sulfate, in patients given spinal anesthesia, for postoperative analgesia. *Materials and Methods:* This prospective study was conducted on 50 adult patients of ASA physical status 1 & 2 in the 18–60 age group, of either sex, posted for elective lower limb orthopedic surgeries under spinal anesthesia over a period of 12 months. Patients were randomly divided on an alternative basis into groups of 25 each. Group-M-Patients receiving IV $MgSO_4$/infusion, Group -S-Patients receiving isotonic saline. *Results:* The mean height and mean weight in either group were identical. The type of surgeries performed were almost identical. There was no significant difference in hemodynamic variables (mean arterial pressure and heart rate) during the intra-or-postoperative period. Perioperative mean arterial pressure. Time of first pain medication in Group M was 334 min whereas in Group S was 227 min. This was statistically significant ($p < 0.001$). VAS was statistically significant at the end of 3 and 6 hours ($p < 0.001$), but it was insignificant at the end of 12 hours ($p > 0.05$). The cumulative requirement in 24 hrs of both tramadol and diclofenac was statistically significantly less for group M vs. S ($p = <0.05$). Postoperative serum Mg concentrations in Group M were significantly higher than those in Group S ($p < 0.001$ immediately after surgery, and at 1 and 24h after surgery. However, all patients in Group M had a serum Mg concentration in the normal range 24h after surgery. *Conclusion:* IV Magnesium sulfate infusion in spinal anesthesia decreases intra-operative hemodynamic variabilities, prolongs duration of analgesia and improves the quality of analgesia in the early postoperative period with better hemodynamic stability. It also decreases the postoperative analgesic requirements, thus it can be used as a beneficial additive for prolonging spinal anesthesia.

Keywords: Magnesium Sulfate, Spinal Anesthesia, Postoperative analgesia

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Introduction

The International Association for the study of pain had described pain as unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. The aim of an anesthesiologist is to render the patient pain free, during a surgical

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procedure. However the patient problem does not end with the surgical procedure, as pain following surgery is a universal problem. So pain during postoperative period is a cause of concern for both the patient and the physician.[1]

Spinal anesthesia defined as regional anesthesia obtained by blocking nerves in the subarachnoid space was introduced in clinical practice. Spinal anesthesia using local anesthetics like hyperbaric bupivacaine is one of the most popular techniques for both elective and emergency surgical procedures. One disadvantage with spinal anesthesia using hyperbaric bupivacaine alone is relatively short duration of action, which means that early analgesic intervention is needed in the postoperative period. Postoperative pain increases the morbidity and mortality and prolongs the stay in hospital. Effective postoperative analgesia results in decreased respiratory and CVS complications, early returns of GIT motility, early ambulation and discharge from hospital.[2,3]

Postoperative pain relief provides comfort to the anxious patients and improve their morale and mobility thereby contributing to a rapid and complete recovery. However, their use has been hampered by their potential to cause respiratory depression. Thus, other drugs have been tried that have the advantage of opioids, but not their drawbacks. A number of adjuvants have been used to improve postoperative analgesia, along with bupivacaine. These are epinephrine, clonidine, ketamine, neostigmine and midazolam. In this study, we have infused IV. Magnesium Sulfate, in patients given spinal anesthesia, for postoperative analgesia.

Materials and Methods

This prospective clinical study was conducted on 50 adult patients of ASA physical status 1 & 2 in the 18–60 age group, of either sex, posted for elective lower limb orthopedic surgeries under spinal anesthesia after taking informed consent at Osmania General Hospital, Hyderabad over a period of 12 months. After approval from the hospital ethical committee, a comparative study was carried out on 40 adult patients.

Patients were randomly divided on an alternative basis into groups of 25 each.

Group "M" Receiving $MgSO_4$ (50 mg/kg over 15 min-bolus)

(15 mg/kg/ltr infusion)

Group "S" Receiving isotonic saline (10 ml/kg/hr)

Inclusion criteria

ASA grade 1 and 2 patients, Age group of 18–60, patients scheduled to undergo elective orthopedic lower abdominal, lower extremity, gynecological or urological surgeries under subarachnoid block.

Exclusion criteria

With gross spinal abnormality, localized skin sepsis, hemorrhagic diathesis or neurological involvement/diseases, Head injury, Patients with cardiac, pulmonary, hepatic or renal disorders.

Pre-anesthetic check-up was carried out preoperatively with a detailed history, general physical examination and systemic examination, Airway assessment and spinal column examination were done.

The following laboratory examinations were done in selected cases, i.e., hemoglobin, urine analysis, blood sugar, blood urea, serum creatinine, coagulation profile, blood grouping and Rh typing, ECG-for patients over 40 years of age and Chest X-ray.

Procedure

Patient was shifted to the OT table; IV access was obtained on the forearm with 18 Gauge IV cannula and Lactated Ringer's solution 10 ml/kg was infused intravenously before the block. The monitors connected to the patient included non-invasive B.P., oxygen saturation using pulse oximeter. Baseline PR, BP and RR, SpO_2 was recorded.

Under strict aseptic precautions, lumbar puncture was performed in left lateral position or sitting position by midline approach by using disposable Quincke spinal needle (23G) at L3–L4 intervertebral space. Patients were monitored continuously using Non-invasive blood pressure, pulse oximeter and electrocardiogram. After spinal anesthesia, oxygen (6 L/min) by facemask was given. Fluid therapy was maintained with lactated Ringer's solution infused according to patients hemodynamic and volume status.

After induction of spinal Anesthesia, the magnesium group (Group M), received magnesium sulphate 50 mg/kg for 15 min bolus using a burette set and then 15 mg/kg/hr by continuous IV infusion until the end of surgery. For IV bolus-$MgSO_4$ (50 mg/kg) is mixed in 30 ml NS in burette set and infused over 15 minutes (1 ml/min). Magnesium Sulfate Infusion Calculates volumes required for adult dosage of 1.5g injected into

100 ml NS infusion bottle. Drip rate is 100 drops/minute, Usual diluents—D5w, NS.

Amount of drug	1g	2g	3g	4g
Infusion volume	50 ml	100 ml	100 ml	250 ml
Infusion rate	30 min	60 min	2 hr	3 hr

The rate or I.V. injection should generally not exceed 150 mg/minute (1.5 mL of a 10% concentration or its equivalent). Solutions for iv infusion should be diluted to 20% or less.

The following parameters were observed and recorded as HR, B.P and RR, SqO_2 monitored at 1, 3, 5, 10, 15, 20, 25, 30, 45, 60, 120, 180 minutes.

Assessment of Sensory Blockade

The onset of sensory block was tested by pinprick method using a hypodermic needle. The time of onset was taken from the time of injection of drug into subarachnoid space to loss of pinprick sensation. The highest level of sensory block and time was noted. The time for two-dermatomal segment regression of sensory level was noted. The duration of sensory blockade was taken as time from onset to time of return of pinprick sensation to S1 (heel) dermatomal area.

Assessment of Motor Blockade

This was assessed by Bromage scale. The time interval between injections of drug into subarachnoid space, to the patient's inability to lift the straight extended leg was taken as onset time (Br. 3). The duration of motor block was taken from time of injection to complete regression of motor block (ability to lift the extended leg) (Br 0).

Intensity of motor block (with sensory block to s 5)

I. Complete Block	Unable to move feet or knees
II. Almost Complete	Able to move feet only
III. Partial	Just able to flex move Knees
IV. None	Full flexion of knees or Feet and hip and extend Knee

Bromage scale for assession motor block and degree of paralysis

Modified Bromage Scale

* Grade 0 — Full flexion of knees and feet.

* Grade 1 — Just able to flex knees, full flexion of feet.

* Grade 2 — Unable to flex knees, but some flexion of feet possible

* Grade 3 — Unable to move legs or feet

Assessment of analgesia

Pain was assessed by visual analogue score (VAS)

The patient simply marks the line to indicate the pain intensity and the provider then measures the length of the line to mark a point scale. All the patients were instructed about the VAS and to point out the intensity of pain on the scale 0 – no pain, 10 – worst pain.

Linear Visual Analog Scale Score

VAS Score	Intensity of pain
0–2	No pain to slight pain
2–5	Mild pain
5–7	Moderate pain
7–9	Severe pain
10	Worst possible pain

Quality of intraoperative analgesia was assessed by VAS score. Analgesics were avoided until demanded by the patient and the time taken for the first pain medication was also noted (i.e., when Vas >6) VAS was also recorded 3, 6, 12 hours postoperatively.

Postoperatively, monitoring of vital signs was continued every 30 minutes until the time of regression of sensory block to L1 dermatome. The incidence of hypotension (arterial blood pressure < 20% of baseline), and was treated with Inj.Mephentermine 6 mg intravenous increments and bradycardia as pulse rate < 60/min was treated by atropine 0.6 mg intravenous stat. Side effect like sedation, nausea, vomiting urinary retention were monitored in the recovery room and then shifted to the ward.

Neurological examination was done to rule out any neurological deficits at discharge.

After surgery, both groups M and S received Inj. diclofenac sodium 75 mg/IM/BD and Inj.Tramadol 100 mg IV/BD depending on the requirement for analgesia.

Postoperative pain score, analgesic consumption, incidence of shivering, postoperative nausea and vomiting were evaluated immediately after surgery, and at 30 min, 1 hr, 2 hr, 4 hr, 6 hr, 12 hr, 24 hr, 36 hr and 48 hr after surgery.

Serum magnesium concentrations were checked before the induction of anesthesia, immediately after surgery and at 1 and 24 hr after surgery.

Statistical Analysis

The demographic data were analyzed using either Student's t-test or chi-square test. Quantitative data were analyzed by student t-test and qualitative data was analyzed by chi-square test. All values were expressed as mean +/- standard deviation. $p < 0.05$ was considered statistically significant.

Results

Patient characteristics and anesthetic time. Values shown are mean (range) for age, mean (SD), or patient numbers (n), Group M, Mg group; Group S, Saline group. No significant differences between the two groups (Table 1).

Table 1: Demographic Data in Present Study

Patient characteristics	Group M (n=25)	Group S (n=25)
Age	36	44
Sex (M/F)	12/13	17/8
Weight (kg)	52	47.8
ASA (I/II)	15/5	16/4
Anesthetic Time (min)	298	200.6

No significant difference was found between the two groups in terms of age, weight, height, gender, or anesthetic time.

Table 2: Characteristics of Spinal Block in Present Study

Characteristics of spinal block	Group M	Group S
Height of spinal block	T5 (T3-6)	T6 (T4-8)
Time of first pain (min)	334	227
Dose of bupivacaine (mg)	13.1	13.4

No technical failure related to spinal anesthesia occurred and all surgery proceeded without difficulty. The two groups were similar in terms of height of spinal block, mean time to first pain, and administered dose of bupivacaine (Table 2).

Postoperative serum Mg concentrations in Group M were significantly higher than those in Group S ($p < 0.001$ immediately after surgery, and at 1 and 24h after surgery. However, all patients in Group M had a serum Mg concentration in the normal range 24h after surgery. Perioperative mean arterial pressure. Group M, Mg group; Group S, saline group. Values are presented as means (SD). Group M patients had a lower mean arterial pressure except immediately after the induction of spinal anesthesia. No significant difference was observed between the two groups during the perioperative period. There was no significant difference in hemodynamic variables (mean arterial pressure and heart rate) during the intraoperative period (Fig. 1)

Time of first pain medication in Group M was 334 min whereas in Group S was 227 min. This was statistically significant ($p < 0.001$) (Table 3).

Table 3: Duration of Analgesia in Present Study

Parameter	Group M		Group S		Mean Difference	*p** value Significance
	Mean	SD	Mean	SD		
Time of first pain medication	334	15.6	227	29.4	100.12	<0.001 HS

*Student's unpaired test

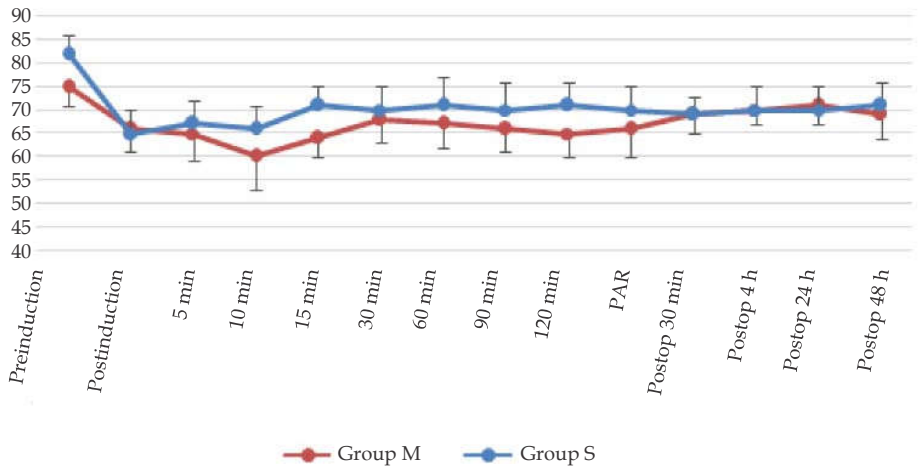

Fig. 1: Mean arterial pressure in both groups

VAS at the end of 3 hours was 0.7 in Group M whereas in Group S it was 2.4 at the end of 6 hours VAS in Group M was 1.6 whereas in Group S it was 3.4. VAS at the end of 12 hours in Group M was 4.18 whereas in Group S it was 4.2 (Fig. 2).

VAS was statistically significant at the end of 3 and 6 hours ($p < 0.001$), but it was insignificant at the end of 12 hours ($p > 0.05$) (Table 4).

The cumulative requirement in 24 hrs of both tramadol and Diclofenac was statistically significantly less for group M vs. Group S (p=<0.05) ranging from 64.42 ± 36 mg in Group M vs

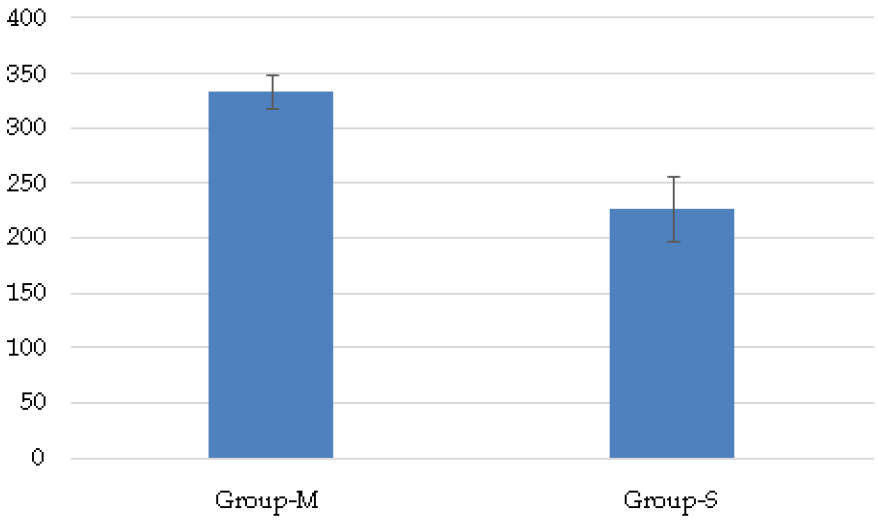

Fig. 2: Mean time of first pain in group M and group S

Table 4: Quality of Postoperative Analgesia

Quality of post of Analgesia	Group M		Group S		Mean Difference	P* value Significance
	Mean	SD	Mean	SD		
3	0.0	0.7	1.0	0.9	1.80	<0.001 HS
6	0.0	1.6	2.0	1.1	1.62	<0.001 HS
12	1.0	1.2	2.0	1.5	0.060	0.8 NS

*Mann Whitney U test

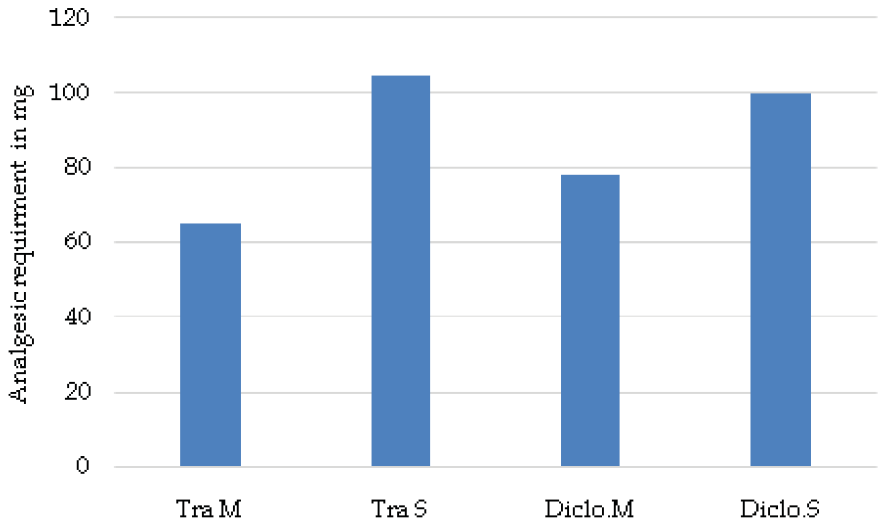

Fig. 3: Postoperative 24 hrs cumulative analgesic requirement

Tra – Tramadol; Diclo - Diclofenac; M-Magnesium Sulphate group; S-Normal Saline group

104 ± 45 mg in Group S for Tramadol and from 72 ± 35.82 mg to 100 ± 50.03 mg in Group M and Group S respectively for Diclofenac. In Group M, less patients required a single dose of Tramadol, during the first 24 hrs postoperatively, whereas in Group S, more patients required 2 or more than 2 doses of Tramadol. Similarly, fewer patients required only one dose of Diclofenac sodium during first 24 hrs postoperatively in Group M and in control group S more patients required a second dose of Diclofenac sodium to alleviate postoperative pain. No incidence of bradycardia, hypotension, hypoxia or hypoventilation was recorded during intra as well as postoperative period (Fig. 3).

Discussion

In our study majority of patients were middle aged in both groups. In group M there were 12 males and 13 females, whereas in group S there were 17 males and 8 females.

The mean height and mean weight in either group were identical. The types of surgeries performed were almost identical. These parameters were kept identical to avoid variations in intra- and post-operative outcome of patients.

Hemodynamic stability intraoperatively and postoperatively

In our study there was no significant difference in hemodynamic variables (mean arterial pressure and heart rate) during the intra- or postoperative period. Perioperative mean arterial pressure. Group M, Mg group; Group S, saline group. Values are presented as means (SD). Group M patients had a lower mean arterial pressure except immediately after the induction of spinal anesthesia. In 2004, effect of IntraOperative magnesium Sulfate infusion on perioperative analgesia in open cholecystectomy study conducted by Bhatia, Kashyap, Pawar, Trikha[4] concluded that administration of intraoperative $MgSO_4$ as an adjuvant analgesic in patients undergoing open cholecystectomy, resulted in better pain relief and comfort in first postoperative hour and remitted in better sleep quality during the postoperative period without any significant side effects difference was observed between the two groups during the perioperative period.

Thus we can compare our study to above study and conclude that Group M patients were more hemodynamically stable.

Assessment of analgesia—time of first pain medication, quality of analgesia

Time of first pain medication in Group M as 334 min whereas in Group S was 227 min. This was statistically significant ($p < 0.001$). In 2009 IV $MgSO_4$ for postoperative pain in patients undergoing lower limb orthopedic surgeries, a study concluded that IV $MgSO_4$ can serve as a supplementary analgesic therapy to suppress the acute postoperative pain, leading to less morphine requirements in first 24 hrs. The study was conducted by A. Dabbagh, H. Elyasi, S. Razavi, M. Fathi.[5] VAS at the end of 3 hours was 0.7 in Group M whereas in Group S it was 2.4 at the end of 6 hours VAS in Group M was 1.6 whereas in Group S it was 3.4. VAS at the end of 12 hours in Group M was 4.18 whereas in Group S it was 4.2. VAS was statistically significant at the end of 3 and 6 hours ($p < 0.001$), but it was insignificant at the end of 12 hours ($p > 0.05$).

In 2010 Hwang JY, Jean YT, Kincs[6] study done on IV infusion of $MgSO_4$ during spinal anesthesia improves postoperative analgesia, concluded IV $MgSO_4$ administration during spinal anesthesia improves postoperative pain.

In 2011, Shashi Kiran, Rachna Gupta and Deepak Verma[7] conducted a study Evaluation of Single dose of IV $MgSO_4$ for prevention of postoperative pain after inguinal surgery, concluded administration of IV $MgSO_4$ perioperatively significantly reduces, postoperative pain in patients undergoing inguinal surgery. Thus our study concluded time of first pain management was longer in Group M and also the quality of analgesia was better in Group M when compared with group S with reference to above studies.

Postoperative analgesic requirements

The cumulative requirement in 24 hrs of both tramadol and Diclofenac was statistically significantly less for group M vs. Group S ($p = < 0.05$), ranging from 64 ± 42.36 mg in Group M vs 104 ± 45 mg in group S for Tramadol and from 72 ± 35.82 mg to 100 ± 50.03 mg in Group M and Group S respectively for Diclofenac. In Group M, less patients required a single dose of tramadol, during the first 24 hrs postoperatively, whereas in Group S, more patients required 2 or more than 2 doses of tramadol. Similarly, fewer patients required only one dose of Diclofenac sodium during first 24 hrs postoperatively in Group M and in control Group S more patients required a second dose of Diclofenac sodium to alleviate postoperative pain. No incidence of bradycardia, hypotension, hypoxia

or hypoventilation was recorded during intra as well as postoperative period.

In 2004 McCartney, Avinash Sinha, Joel katz[8] conducted "A Qualitative systematic Review of the role of N-Methyl D-Asparate Receptor antagonist in Preventive Analgesia study conducted $MgSO_4$ as NMDA antagonist and thus reduces pain, analgesic consumption or both.

In 2006 Tauzin Fin P, Sesay M, Delort Laval S, P. Maurette[9] on IV $MgSO_4$ decreases postoperative tramadol requirement after radical prostateclary", which concluded IV $MgSO_4$ reduces tramadol consumption when used as postoperative analgesic protocol in radical prostertomy. Woolf *et al.* studied the dependence of the central sensitization on NMDA receptor activation in rats and found that NMDA receptor activation is involved in the induction and maintenance of central sensitization processes that characterize post-injury pain states.[10] Therefore, NMDA receptor antagonist may play a role in prevention and treatment of perioperative pain. Thompson *et al.* found that IV magnesium sulfate produced a dose-dependent reduction in halothane minimum alveolar anesthetic concentration (MAC), as measured by the tail-clamp technique, which could be considered as an anesthetic effect in an acute pain model.[11] Thus our result correlates with above study. We conclude that in Group M postoperative analgesic requirements were decreased.

Conclusion

On basis of our clinical study, we conclude that IV Magnesium sulfate infusion in spinal anesthesia decreases intraoperative hemodynamic variabilities, prolongs duration of analgesia and improves the quality of analgesia in the early postoperative period with better hemodynamic stability. It also decreases the postoperative analgesic requirements, thus it can be used as a beneficial additive for prolonging spinal anesthesia. Thus, the study concluded that Magnesium sulfate can be infused in spinal anesthesia for postoperative analgesia.

Summary

This study titled "Intravenous Magnesium sulfate can be infused in spinal anesthesia for postoperative analgesia" was done to evaluate the effect of Magnesium sulfate infusion for postoperative analgesia, decrease the postoperative analgesic requirements and negligible side effects.

50 patients aged 18–60 years belonging to ASA I and II undergoing elective lower limb orthopedic surgeries were randomly allocated for the study into two groups.

Group "M" – Receiving $MgSO_4$ (50 ml/kg over 15 min-bolus)

(15 mg/kg/ltr infusion)

Group "S" – Receiving isotonic saline

The mean height and mean weight in either group were identical. The types of surgeries performed were almost identical. These parameters were kept identical to avoid variations in intra- and postoperative outcome of patients. There was no significant difference in hemodynamic variables (mean arterial pressure and heart rate) during the intra-or postoperative period. Perioperative mean arterial pressure. Group M, Mg group; Group S, saline group. Values are presented as means (SD). Group M patients had a lower mean arterial pressure except immediately after the induction of spinal anesthesia.

Time of first pain medication in Group M was 334 min whereas in Group S was 227 min. This was statistically significant ($p < 0.001$). VAS was statistically significant at the end of 3 and 6 hours ($p < 0.001$), but it was insignificant at the end of 12 hours ($p > 0.05$). The cumulative requirement in 24 hrs of both tramadol and Diclofenac was statistically significantly less for Group M vs. S ($p \leq 0.05$).

Postoperative serum Mg concentrations in Group M were significantly higher than those in Group S ($p < 0.001$ immediately after surgery, and at 1 and 24 h after surgery. However, all patients in Group M had a serum Mg concentration in the normal range 24 h after surgery.

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