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ORIGINAL ARTICLE

A RANDOMIZED CLINICAL STUDY TO EVALUATE THE EFFECT OF INTRAVENOUS MAGNESIUM SULPHATE FOR POSTOPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING LOWER SEGMENT CAESAREAN SECTION

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ABSTRACT: BACKGROUND: In this randomized, double-blind, prospective study, we have evaluated the effect of i.v. infusion of magnesium sulphate during spinal anaesthesia, for postoperative pain relief in patients undergoing lower segment caesarean section. **AIM**: A comparative evaluation of intravenous magnesium sulphate for prevention of postoperative pain relief in lower segment caesarean section under spinal anaesthesia". **METHODS AND MATERIALS:** 60 female patients of ASA grade I and II of the age group 20-40 yrs., posted for lower segment caesarean section under spinal anaesthesia were selected after pre anaesthetic fitness. Randomly patient were divided into two groups (n=30 patients each) group NS, and group MS to receive 100ml of 0.9% Normal saline and Magnesium sulphate 50mg kg-1 in 100ml of 0.9% Normal saline respectively to be given over 15 min, 60min after performing spinal anaesthesia. After surgery, rescue analgesia in form of inj. tramadol 100 mg i.v was provided for the patients. The Postoperative pain scores, Rescue analgesic consumption, and incidences of sedation, shivering, dysrhythmia, bradycardia, and hypotension evaluated immediately after surgery, and at 30 min, 1, 2, 3, hrs. After surgery. **STATISTICAL ANALYSIS:** Results were expressed as mean and standard deviation. P value of <0.05 was considered statistically significant. **RESULTS:** IV Magnesium sulphate 50 mg kg-1 bolus significantly prolonged duration of analgesia, superior quality of analgesia (Lower VAS) and significant reduction in postoperative analgesic requirement than normal saline under spinal anaesthesia. No significant hemodynamic and respiratory instability occurred with Magnesium Sulphate use. **CONCLUSION:** I.V. magnesium sulphate administration during spinal anaesthesia improves postoperative analgesia without any notable complications.

KEYWORDS: Magnesium Sulphate, Postoperative pain, LSCS, Rescue analgesia.

INTRODUCTION: Spinal anaesthesia is a widely used and easy to perform regional anaesthesia technique which provides rapid onset analgesia with good muscle relaxation but relatively lesser post-operative pain free period. During postoperative period surgical stress response peaks and has major deleterious effects on all body systems. However a good pre-emptive analgesia attenuates neuro-humoral stress responses to a great extent. The goals of pre-emptive analgesia are to decrease post-operative pain and the development of chronic pain. It is important to have a pain free postoperative period as it reduces the morbidity and mortality.[1]

Magnesium (Mg^{++}) is the fourth most abundantcation in the body responsible for many biochemical reactions. It exerts antinociceptive effects via its antagonistic effect on N-methyl-D-aspartate (NMDA) receptor.

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This antagonism reduces the induction and maintenance of central sensitization of nociceptive stimulation by altering pain processing. There are experimental and clinical support that magnesium may play role in the modulation of acute pain, reducing post-surgical pain intensity or the dosage of analgesics.[2-8]

Because of its numerous physiologic activities, magnesium is called "nature's physiologic calcium channel blocker".[9] Magnesium exerts its calcium antagonist activity mainly by competing with calcium for entry through membrane channel in a variety of tissues.

Numerous clinical investigations have demonstrated that Mg^{++} infusion during general anaesthesia reduces anaesthetic requirement and postoperative analgesic consumption,[10] whereas few studies suggested that perioperative Mg^{++} administration had little effect on postoperative pain.[10] relatively very few studies have been conducted to evaluate the effects of magnesium sulphate administration during regional anaesthesia.[11, 12] for improving the postoperative pain relief.

Therefore on the basis of above studies we planned a study to evaluate the intravenous magnesium sulphate for postoperative pain relief after lower segment caesarean section (LSCS) surgeries under spinal anaesthesia.

METHODS: This double blind randomized controlled study was carried out in the Department of Anaesthesiology, G. R. Medical College and J. A. Group of Hospitals, Gwalior (M. P.), after approval of ethics committee. 60 female patients of ASA grade I and II of the age group 20-40 yrs., posted for lower segment caesarean section under spinal anaesthesia were selected after pre anaesthetic fitness. Exclusion criteria were contraindication to spinal anaesthesia, known history of allergy or sensitivity or any other reaction to local anaesthetic of amide type, patients with impaired renal or hepatic function, patients with varying degree of heart blocks, Hypertension, Diabetes mellitus and drug or alcohol abuse, patients with neurological disorders, myopathy, obese patients (body mass index more than $30kg/m^2$), patients on treatment with calcium channel blockers or magnesium and poor compliance with the study procedure. Details of procedure were explained to all the patients during pre-anaesthetic check-up and an informed consent was obtained.

Pre-op., intra-op. and post-op. patient characteristics, hemodynamic parameters and side effects related to drugs was observed and recorded. All patients were uniformly premeditated with inj. glycopyrrolate 0.2mg IM 30min before operation as per institution protocol. Preloading of 500ml Ringer's lactate solution was started with 18 G Cannula, 1/2 hour before start of anaesthesia, and routine non-invasive arterial blood pressure, ECG and pulse oximeter were placed.

Spinal anaesthesia performed at L3/4 or L4/5 intervertebral space with the patient in the lateral decubitus position using a 25-gauge Quinckes spinal needle. After free flow of CSF Lignocaine heavy 5% (Hyperbaric) 1.4ml was injected at a rate of about 1ml in 4–5 seconds. Thereafter, the patients were placed in the supine position for surgery. During surgery crystalloids, colloids and blood were administered according to intraoperative requirement to maintain hemodynamic stability.

After 60min of spinal anaesthesia, Group NS received 100ml of 0.9% Normal saline, and Group MS received Magnesium Sulphate 50mg/kg in 100ml of 0.9% Normal saline over 15min. As soon as the patient started feeling pain sensation IV Tramadol 100 mg was prescribed. Vital parameters were monitored throughout the procedure intraoperatively and postoperatively till the patient demanded for rescue analgesia.

After the study drug was injected following parameters were recorded-Pulse rate, electrocardiogram, systolic and diastolic BP, respiratory rate and peripheral arterial hemoglobin

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oxygen saturation were monitored intraoperatively. Data monitoring performed continuously but for statistical analysis data were recorded at 0,5,10,15,30,60 minutes after intrathecal injection and thereafter every hour until patient complaints of pain and requesting for analgesia.

Bradycardia: A pulse rate of 60/min or less was treated by injection atropine I/V. Hypotension: a fall in systolic BP 20% or greater from the base line value was treated by injection mephentermine I/V, intravenous fluids (Cystalloid, Colloid and Blood) as per requirement and oxygen by face mask. Respiratory depression: a respiratory rate of less than 10 breaths per min or peripheral arterial hemoglobin oxygen saturation less than 85% was treated by oxygen supple-mentation through face mask.

Onset time of sensory blockade, highest level of sensory blockade, time of onset of pain, VAS score at onset of pain, duration of analgesia (Pain relief),time for rescue analgesia were also recorded. Assessment of pain was done by visual analogue scale (VAS). It is a 0-10 numeric pain distress scale. Patients were closely observed in the intraoperative and postoperative period for complications like nausea, vomiting dyspnoea, respiratory depression, chest pain, sedation, shivering, dysrrhythmia, bradycardia, hypotension and any other. Sedation is assessed by Ramsay sedation score.

STATISTICS: Results were expressed as mean and standard deviation. The data were compared by applying student's "t" test for inter group comparison. P value of <0.05 was considered statistically significant.

RESULT: No significant difference was found between the two groups in terms of demographic data like age, weight (Table 1).

No technical failure related to spinal anaesthesia occurred and all surgery proceeded without difficulty like inadequate relaxation or pain. The two groups were similar in terms of onset time of sensory block, time taken to reach highest level, highest level of sensory blockade and mean time of first pain in the form of inj. tramadol 100mg. (Table 2)

Time of rescue analgesia I (TRA I) was statistically comparable in both the groups. (Table 3).

Furthermore, the time of rescue analgesia II and total duration of analgesia were significantly prolonged in Group MS as compared to Group NS. (Table 4) Postoperative intensity of pain was assessed by VAS score at the time of onset of pain; MS group showed a superior quality of analgesia as assessed by lower VAS compared with NS group. (Table 5).

Magnesium and control groups were similar with respect to haemodynamic parameters such as heart rate, systolic and diastolic blood pressure, respiratory rate and Spo_2. There was no case of postoperative haemodynamic or respiratory instability during the study periods. Although no serious side effects or complications were observed in this study but three incidence of nausea and vomiting (10%) and shivering (10%) in group NS, and one incidence of nausea and vomiting (3.33%) and shivering (3.33%) in group MS were observed and all these were comparable. All the patients were complaining of pain at the site of infusion in magnesium group which was highly significant as compared to group NS.

DISCUSSION: Regional anaesthesia is a safe, inexpensive technique with an advantage of prolonged postoperative pain relief. Effective treatment of postoperative pain blunts autonomic, somatic, and endocrine responses.

It has become common practice to use a multimodal approach for the treatment of postoperative pain, as no single drug has yet been identified which inhibits nociception without

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associated side-effects.[13] Research still continues to find out different techniques and drugs that could prolong the duration of regional anaesthesia and postoperative pain relief.

The concept of preemptive analgesia was introduced by Woolf.[14] Who demonstrated through experimental studies that post injury pain hypersensitivity results via central mechanism. Pre-emptive analgesia has been defined as an anti-nociceptive treatment that prevents establishment of altered central processing of afferent input from injuries. Therapies that have been tested in preemptive trials include NSAIDS, intravenous opioids, intravenous ketamine, peripheral local anaesthetic, caudal and epidural analgesia, dextromethorphan and gabapentin.[15]

Magnesium sulphate has been used in obstetric and cardiac patients. Magnesium (Mg^{++}) the fourth most common cation in the body responsible for many biochemical reactions has shown potential for preemptive analgesia in various studies.[16,17]

Lower segment caesarean section is accompanied by moderate to severe pain after surgery and adequate postoperative pain management is important for early rehabilitation and functional recovery. Magnesium sulphate infusion during surgery under spinal anaesthesia reduced postoperative pain and analgesic consumption without any notable complications.

This study was done only in the pregnant female patients so it is comparable in both the groups as regard to age, weight and sex distribution. In our study onset of sensory block, highest level of sensory block, and time taken to reach highest level were comparable because the study drug were infused after 60 mins of spinal anaesthesia hence both the groups were similar till this stage.

Time of rescue analgesia I (TRA I) was comparable and statistically insignificant ($p>0.05$) in both the groups. Lignocaine have short duration of action (60 – 90 min).[18] in addition peak effect of $MgSO_4$ is obtained in 60 mins. Therefore at this stage (TRA I) timing for first rescue analgesia is similar in both the groups because effect of lignocaine has started to wear off and the peak effect of $MgSO_4$ is yet to be achieved. On intergroup comparison total duration of analgesia (TRA II–TRA I) was statistically significantly prolong in group MS as compared to other group. ($p<0.01$).

These finding were in accordance to Elgebaly et al.[11] Who studied the effect of intravenous magnesium sulphate (6gm i.v. as a loading dose over 20-30mins, followed by infusion of magnesium sulphate 2gm h^{-1} for 24 h) versus intrathecal fentanyl (25mcg) in severe pre-eclampsia patients undergoing caesarean section under spinal anaesthesia. They found that magnesium sulphate statistically significantly ($p<0.01$) increases the duration of postoperative analgesia as compared to intrathecal fentanyl (7.05±1.95 and 6.85±1.7 hours respectively).

Hwang et al.[10] compared magnesium sulphate 50mgkg^{-1} for 15min then 15mgkg^{-1} h^{-1} by until the end of surgery with control group undergoing total hip arthroplasty under spinal anaesthesia and found that the time to first pain was 249±41 mins in magnesium group and 224±38 mins in control group but cumulative postoperative VAS score and PCA consumption were significantly lower in magnesium sulphate group at 4, 24 and 48 hrs. After surgery ($p<0.05$).

VAS score at the time of onset of pain and rescue analgesia I (TRA I) was comparable & statistically insignificant ($p>0.05$) between both the study groups as the effect of magnesium sulphate is yet to be achieved at this stage. At TRA II stage MS group showed a superior quality of analgesia as assessed by lower VAS 7.16±0.83. These were statistically significant when compared with NS group ($p<0.01$).

These finding are well in accordance with study of Hwang et al.[10] and Kiran et al.[19] Studied the efficacy of single dose of intravenous magnesium sulphate 50mg kg^{-1} in 250ml isotonic sodium chloride solution i.v. with equal volume of normal saline over 30 minutes before the induction of GA.

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They concluded that preoperative administration of 50mgkg^{-1} of magnesium sulphate infusion decreases postoperative pain and rescue analgesia.

Magnesium acts by antagonism of the NMDA receptor. The second theory includes the action of magnesium as a calcium channel antagonist. The analgesic effect of calcium channel antagonist could be mediated by a rise in the nociceptive threshold because of the calcium influx into the cell. This calcium influx is responsible for the release of neurotransmitter connected with nociception and inflammatory response.[20]

Another mechanism could involve the reduction of catecholamine release through sympathetic stimulation by which magnesium might decreases peripheral nociceptive sensitization or the stress response to surgery.[21]

MS group showed superior quality of sedation as compared to NS group ($p<0.01$). These finding are well in accordance with study of Tramer et al.[2] Kiran et al.[19] and Lee and Kwon.[22] who showed better quality of sleep in the postoperative period with the perioperative administration of magnesium sulphate with no adverse effect. This could be explained because magnesium is regarded as a central nervous system (CNS) depressant.

Hemodynamic variables like pulse rate, systolic and diastolic blood pressure, respiratory rate and Spo_2 at different intervals, from the pre- induction to till the end of the study even after infusion of study drug, was comparable and statistically insignificant. ($p>0.05$).

Tramer et al,[2] Hwang et al,[10] Koinig et al,[3] Telci et al,[21] Bilir et al,[13] Turan et al.[23] and Kogler J.[20] also found that magnesium and control groups were similar with respect to haemodynamic parameters such as pulse rate, systolic and diastolic blood pressure, respiratory rate and Spo_2 ($p>0.05$) and there was no case of postoperative haemodynamic or respiratory instability during the study periods.

All the patients were complaining of pain at the site of infusion in magnesium group which was highly significant as compared to group NS. Turan et a.l[23] and Memis et a.l[24] showed mild to moderate pain on injection of magnesium sulphate**.** Mild acidic pH (5.5-7.0) of magnesium sulphate has been blamed for pain on injection.

CONCLUSION: IV Magnesium sulphate 50mgkg^{-1} significantly prolonged duration of analgesia, and provide superior quality of analgesia along with significant reduction in postoperative analgesic consumption under spinal anaesthesia. No significant hemodynamic and respiratory instability and no untoward effect and complications were noticed.

Demographic Characteristic	Group NS	Group MS
Age (yrs.) Mean±SD	25±3.67	25.93±3.18
Weight (kg) Mean±SD	51.83±3.70	51.36±4.29

Table 1: Demographic Data

Analgesia Time	Group NS	Group MS
Time of rescue analgesia I(min)	84.33±11.19	81.33±9.64

Table 2: Spinal Characteristic

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Spinal Characteristics	Group NS	Group MS
Onset time of sensory block (min)	1.56±0.56	1.33±0.48
Time taken to reach highest level(min)	3.94±1.14	3.83±1.05
Highest level of sensory block		
T_4 (no)	16	17
T_6(no)	14	13

Table 3: Analgesia

Analgesic Time	Group NS	Group MS
Time of rescue analgesia II(min)	367±59.31	922.83±217.23
Total duration of analgesia(II-I)(min)	282.33±59.31	841.83±217.10

Table 4: Duration of Analgesia

Parameters	Group NS	Group MS
VAS score at TRA I	2.36±0.49	2.33±0.47
VAS score at TRA II	8.26±0.78	7.16±0.83

Table 5: Vas Score

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