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A Comparative Evaluation of Intravenous Magnesium Sulphate in Two Different Doses For Prevention of Postoperative Pain After Infraumbilical Surgeries Under Spinal Anaesthesia

KEYWORDS: Subarachnoid block, Postoperative analgesia, Magnesium sulphate, Infraumbilical surgeries.

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ABSTRACT *BACKGROUND: In a randomized, double-blind, prospective study, we have evaluated the effect of i.v. infusion of magnesium sulphate in two different doses during spinal anaesthesia, postoperative analgesia and postoperative analgesic requirements in patients undergoing infra umbilical surgeries. AIM: A comparative evaluation of intravenous magnesium sulphate in two different doses for prevention of postoperative pain after infraumbilical surgeries under spinal anaesthesia. METHODS AND MATERIAL: 90 female patients of ASA grade I and II of the age group 20-40 yrs, posted for infra umbilical surgeries (lower segment caesarean section) under spinal anaesthesia were selected after pre anaesthetic fitness. Randomly patient were divided into 3 groups (n = 30 patients each) group MS, group MS-30 and group MS-50 to receive 100 ml of 0.9% Normal saline, Magnesium sulphate 30 mg kg-1 in 100 ml of 0.9% Normal saline and Magnesium sulphate 50 mg kg-1 in 100 ml of 0.9% Normal saline respectively to be given over 15 min,60 min 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 nausea, vomiting, dyspnoea, respiratory depression, chest pain, sedation, shivering, dysrrhythmia, bradycardia, and hypotension evaluated immediately after surgery, at 30 min, 1, 2, 3, hr 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 30 mg kg-1 under spinal anaesthesia. No significant hemodynamic and respiratory instability occurred with two doses of Magnesium sulphate used. CONCLUSION: I.V. magnesium sulphate administration during spinal anaesthesia improves postoperative analgesia without any notable complications.*

INTRODUCTION:

Spinal anaesthesia with lignocaine heavy provides rapid onset analgesia with good muscle relaxation for short surgical procedures as it has predictable onset and dense sensory and motor blockade but relatively lesser post operative pain free period.[1] During postoperative period surgical stress response peaks and has major deleterious effects on all body systems.[2] However a good pre-emptive analgesia attenuates neuro-humoral stress responses to surgery 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^{++}) has antinociceptive effects due to its antagonistic effect of N-methyl-D-aspartate (NMDA) receptor. 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 in two different doses for prevention of postoperative pain after infraumbilical surgeries under spinal anaesthesia.

MATERIALS & METHODS:

This double blind randomized controlled study was carried on 90 female patients of ASA grade I and II of the age group 20-40 yrs, posted for infra umbilical surgeries under spinal anaesthesia after approval from institutional ethics committee. 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 30 kg/m^2), patients on treatment with calcium channel blockers or magnesium, 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 premedicated with i.v.glycopyrrolate 0.2 mg IM 30 min before operation. Patients were randomly divided into three groups by sealed envelope technique. Preloading of

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500ml Ringer's lactate solution was started with 18 G Cannula, 1/2 hour before start of anaesthesia, and routine non invasive arterial pressure, ECG and pulse oximeter were placed.

Spinal anaesthesia induced with 1.4 ml Lignocaine heavy 5% (hyperbaric) at L3-L4 intervertebral space with the patient in the lateral decubitus position using a 25-gauge Quinckes spinal needle. Thereafter, the patients were placed in the supine position for surgery. During surgery crystalloids, colloids and blood were administered according to requirement perioperatively to maintain hemodynamic stability.

After 60 min of performing spinal anaesthesia, Group NS received 100 ml of 0.9% Normal saline, Group MS-30 received 30 mg kg^{-1} in 100 ml of 0.9% Normal saline and Group MS-50 received 50 mg/kg in 100 ml 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 postoperatively. A blind observer was assigned to collect the data after the study drug was injected and following parameters were monitored and recorded - Pulse rate, electrocardiogram, systolic and diastolic BP, respiratory rate and peripheral arterial hemoglobin oxygen saturation. Data monitoring performed continuously but for statistical analysis datas 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 (crystalloid, 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 supplementation 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 various tests of statistical analysis as applicable. P value of <0.05 was considered statistically significant.

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

Table 1:Demographic data

Demographic characteristic	Group NS	Group MS-30	Group ,MS-50
Age-Mean ±SD(yrs)	25 ± 3.67	26.16 ± 3.88	25.93 ± 3.18
Weight(kg)	51.83 ± 3.70	50.5 ± 4.56	51.36 ± 4.29

Table 2: Spinal characteristic

Spinal characteristics	Group NS	Group MS-30	Group MS-50
Onset time of sensory block (min)	1.56 ± 0.56	1.33 ± 0.54	1.33 ± 0.48
Time taken to reach highest level(min)	3.94 ± 1.14	4.1 ±1.06	3.83 ± 1.05
Highest level of sensory block			
T_4 (no)	16	18	17
T_6(no)	14	12	13

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

Table 3:Analgesia

Analgesia time	Group NS	Group MS-30	Group MS-50
Time of rescue analgesia I(min)	84.33 ± 11.19	82.83 ± 10.93	81.33 ± 9.64

Time of rescue analgesia I (TRA I) are statistically comparable in all three groups.

Table 4:
Furthermore, The time of rescue analgesia II and total duration of analgesia were significantly prolonged in Group MS-50 compared to Group MS-30 and Group NS.

Analgesic time	Group NS	Group MS-30	Group MS-50
Time of rescue analgesia II(min)	367 ± 59.31	783 ± 147.04	922.83 ± 217.23
Total duration of analgesia(II-I)(min)	282.33 ± 59.31	700.16 ± 147.41	841.83 ± 217.10

Table 5: VAS SCORE
Postoperative intensity of pain was assessed by VAS score at the time of onset of pain,MS -50 group showed a superior quality of analgesia as assessed by lower VAS compared with MS-30 and NS group.

parameters	Group NS	Group MS-30	Group MS-50
VAS score at TRA I	2.36 ± 0.49	2.53 ± 0.50	2.33 ± 0.47
VAS score at TRA II	8.26 ± 0.78	7.73 ± 0.73	7.16 ± 0.83

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

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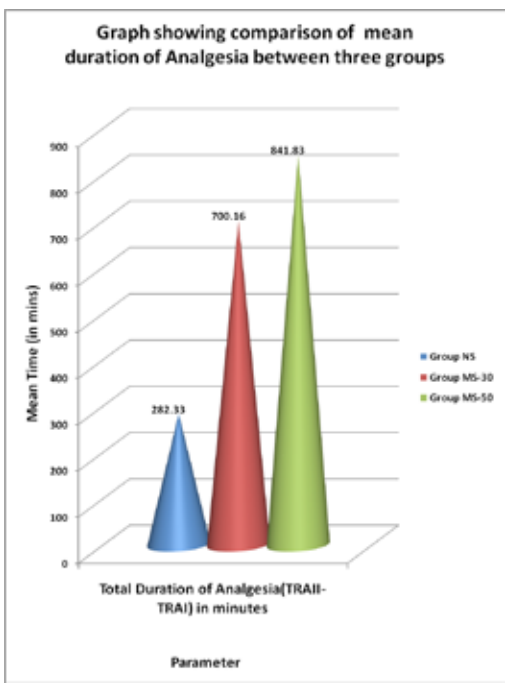
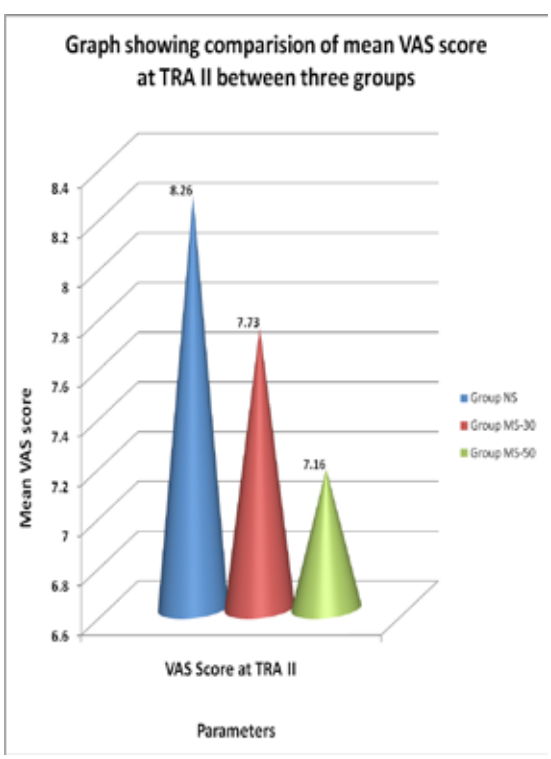
respiratory instability during the study periods. Although no serious side effects or complications were observed in this study but three incidence of nausea and vomiting (10%) and shivering (10%) in group NS, two incidence of nausea and vomiting (6.6%) and one incidence of shivering (3.33%) in group MS-30 and one incidence of nausea and vomiting (3.33%) and shivering (3.33%) in group MS-50 were observed and all these were comparable. All the patients were complaining of pain at the site of infusion in both magnesium groups 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 associated side-effects.[14] 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 [15] 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.[16]

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.[17,18]

Lower segment ceasarean 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 all the three groups as regard to age,weight and sex distribution.

In our study onset of sensory block, highest levvel 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 all the three groups were similar till this stage.

Time of rescue analgesia I (TRA I) was comparable and statistically insignificant ($p>0.05$) in all the three groups. Lignocaine have short duration of action (60 – 90 min).[19] 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 all the three groups because effect of lignocaine has started to wear off and the peak effect of $MgSO_4$ is yet to be achieved. These parameters were also comparable because the study drug were infused after 60 mins.

On intergroup comparison total duration of analgesia (TRA I –TRA II) was statistically significantly prolong in group MS-50 as compared to other group. [group NS vs MS-30 ($p<0.01$), group NS vs MS-50 ($p<0.01$), group MS-30 vs MS-50 ($p<0.01$)].

These finding were in accordance to **Elgebaly et al**[12] who studied the effect of intravenous magnesium sulphate (6 gm i.v. as a loading dose over 20-30 mins, followed by infusion of magnesium sulphate 2 gm h^{-1} for 24 h) versus intrathecal fentanyl (25 mcg) in severe pre-eclampsia patients undergoing caesarean section under spinal anaesthesia. They found that magnesium sulphate statistically sig-

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nificantly (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[11] compared magnesium sulphate 50 mg kg^{-1} for 15 min then 15 mg kg^{-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 three study groups as the effect of magnesium sulphate is yet to be achieved at this stage. At TRA II stage MS-50 group showed a superior quality of analgesia as assessed by lower VAS 7.16 ± 0.83. These were statistically significant when compared with MS-30 and NS group [group NS vs MS-30 (p<0.01), group NS vs MS-50 (p<0.01), group MS-30 vs MS-50 (p<0.01)].

These finding are well in accordance with study of **Hwang et al**[11], **Kiran et al**[20] and **Lee DH et al**[23] studied the efficacy of single dose of intravenous magnesium sulphate 50 mg kg^{-1} in 250 ml isotonic sodium chloride solution i.v. with equal volume of normal saline over 30 minutes before the induction of GA. They concluded that preoperative administration of 50 mg kg^{-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 anatagonist 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.[21]

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.[22]

MS-50 group showed superior quality of sedation as compared to NS group (p<0.01). [group NS vs MS-30 (p<0.01) and group NS vs MS-50 (p <0.01)]. Whereas between MS-30 and MS-50 the sedation score was statistically insignificant (p >0.05).

These finding are well in accordance with study of **Tramer et al**[3] **Kiran et al**[20] and **Lee and Kwon**[23] 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,[3] **Hwang et al,**[11] **Koinig et al,**[4] **Telci et al,**[22] **Bilir et al,**[14] **Turan et al**[24] **and Kogler J.**[21] 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 were 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 both magnesium groups which was highly significant as compared to group NS. **Turan et al**[24] **and Memis et al**[25] showed mild to moderate pain on injection of magnesium sulphate**.** Mild acidic pH (5.5 – 7.0) of magnesium sulphate has been blaimed for pain on injection.

CONCLUSION:

IV Magnesium sulphate 50 mg kg^{-1} significantly prolonged duration of analgesia, provide superior quality of analgesia and significant reduction in postoperative analgesic consumption than 30 mg kg^{-1} under spinal anaesthesia. No significant hemodynamic and respiratory instability and no untoward effect and complications occurred with two doses of Magnesium sulphate used.

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