

Effect of Magnesium Sulphate on Postoperative Analgesia Requirements in Caesarean Section - A Retrospective Study in a Tertiary Care Rural Hospital in Midnapore, West Bengal

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ABSTRACT

BACKGROUND

Post caesarean section pain requires effective analgesia. Effective analgesia is integral to improvement of quality and patient care among lower segment caesarean section (LSCS) patients. Magnesium, an N-methyl-D-aspartate receptor antagonist along with calcium-channel blocker, has previously been investigated for its analgesic properties. But there is scanty previous literature available for intramuscular magnesium sulphate in the analgesic role in post caesarean mothers. The purpose of this study was to evaluate the effect of existing MgSO₄ regimens (among severe pregnancy induced hypertension patients, excluding eclampsia) during early 1st 24 hours' postoperative analgesic requirements in caesarean section patients comparing to only analgesic group.

METHODS

It is a retrospective observational study, conducted from January 2019 to June 2020. Patients were randomly selected, normal patients as control = 50 who got post-operative inj. diclofenac 75 mg IM twice a day and rescue analgesia inj. diclofenac 75 mg IM. Test sample comprised of 50 randomly selected severe pregnancy induced hypertension (PIH) patients who got prophylactic inj. magnesium sulphate by Pritchard regimen for 24 hrs. post delivery with 4 gm 20 % inj. magnesium sulphate intravenous with 10 gm 50 % intramuscular in both buttocks as loading dose followed by 5 gm 50 % inj. magnesium sulphate intramuscular 4th hourly for 24 hrs. along with inj. diclofenac 75 mg IM twice a day. Visual analogue scale for pain was noted among both the groups, and were compared for the effect of analgesics in the study groups.

RESULTS

There was a decrease in analgesic consumption and immediate post-operative pain in the group receiving MgSO₄ with analgesic (inj. diclofenac 75 mg), in comparison to control group of inj. diclofenac 75 mg. ($P < 0.0001$).

CONCLUSIONS

There was a decrease in analgesic consumption in the group receiving MgSO₄ plus analgesic, in comparison to control group (analgesic group). Pain severity assessment 2, 6, 12 and 24 hours post operatively showed that there was a statistically significant decrease in pain scores between the study and the control groups ($P < 0.0001$). It established the role of magnesium sulphate as an adjuvant analgesic along with diclofenac or other traditionally used pain medications among the post caesarean mothers in early post-operative period.

KEYWORDS

Analgesia, Pregnancy, Post-Operative Analgesia, Magnesium Sulphate, Lower Segment Caesarean Section (LSCS), Pain Relief, Obstetrics

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BACKGROUND

Postoperative pain control (post op analgesia as a whole) has always been an important issue amongst surgeons and obstetricians in particular in modern era. The incidence of postoperative pain and tenderness described by postoperative patients differ in various articles. In one of these studies, approximately 75 % of patients undergoing surgery suffered from acute postoperative pain and tenderness.¹ Proper analgesia can reduce morbidity and complications in surgical patients by blunting autonomic, somatic and endocrine reflexes.² Caesarean section is increasing among patients and post-operative pain control is one of the main problems in patients undergoing these operations.³

Magnesium is an intracellular cation that contributes to modification of enzyme reactions and adjustment of ionic channels along nerve endings and intracellular reactions. It is also being used for anaesthetic purposes due to its blocking effect on calcium channels.^{4,5} Although Magnesium sulphate's mechanism of action is not clearly understood, interference in N-methyl-D-Aspartate (NMDA) receptor regulations is assumed to play an important role.⁶ Several studies have evaluated the role of magnesium sulphate (MgSO₄) as an agent for pain control and reduction of analgesic requirement pre op, intra op and post-operatively which might be due to antagonism at the NMDA receptor is thought to alter the mechanism of centrally acting hypersensitivity, and to ultimately decrease analgesic requirements including opioids / pain killer consumption. In some of these studies (articles), scientists concluded that MgSO₄ may reduce the need for opioid analgesic agents.^{7,8,9,10} Narcotics such as pethidine, diclofenac, paracetamol are the mostly used and cost-effective agents in postoperative pain control. However, side effects associated with their usage is a worrisome case.¹¹ Finding a safe and cost-effective method for reducing pain has always been a debate and issue in surgical and obstetric field. Magnesium sulphate has its established role in severe preeclampsia and eclampsia as a neuro protective agent (saving millions of lives) but its role in analgesics is a new side of its versatile actions. On the other hand, magnesium sulphate also has side effects like respiratory depression, oliguria, delayed deep tendon reflexes, etc. but generally on higher therapeutic doses. So magnesium sulphate can be a double edged sword which if used wisely can be a wonder drug in case of modern obstetrics and post-operative care for the mothers who are undergoing LSCS.

Severe preeclampsia (severe pregnancy induced hypertension) is defined as increase in systolic blood pressure (SBP) to ≥ 160 mmHg and / or diastolic blood pressure (DBP) to ≥ 110 mmHg for at least 6 h in association with abnormal proteinuria or if there is hypertension in association with severe proteinuria (at least 5 g / 24-hour urine collection sample). Preeclampsia is also considered severe in the presence of multi-organ involvement such as pulmonary oedema, oliguria (< 500 ml / 24-hour time period), thrombocytopenia (blood platelet count $< 100,000$ / mm³), abnormal liver enzymes (> 2 times of normal values) in association with persistent epigastric or right

upper quadrant pain, or persistent severe CNS symptoms (altered mental status, headaches, blurred vision, or blindness) even if all criteria of definitions are not fulfilled. Prophylactic Inj. Magnesium sulphate by Pritchard regimen in severe preeclampsia for 24 hrs post-delivery (inj. MgSO₄ 4gm 20 % slow intravenous with 10 gm 50 % deep intramuscular as loading dose and inj. MgSO₄ 5gm 50 % deep intramuscular every 4 hourly for 24 hours as maintenance dose) as a part of neuroprotective regimen in pregnancy induced hypertension.

Objectives

- To evaluate the effect of existing MgSO₄ regimens (among severe pregnancy induced hypertension patients, excluding eclampsia) during early 1st 24 hours' postoperative analgesic requirements in caesarean section patients comparing to only analgesic group.
- To summarize the evidence for use of intramuscular magnesium sulphate for analgesic effect in caesarean section patients in initial post-operative 24 hours.

METHODS

Retrospective observational study done in Midnapore medical college and hospital from January 2019 to June 2020. Patients were randomly selected, normal patients as control (N = 50) who got post-operative inj. diclofenac 75 mg intramuscular (IM) twice a day and rescue analgesia inj. diclofenac 75 mg IM. Test sample comprised of 50 (N = 50) randomly selected severe PIH (pregnancy induced hypertension) patients who got prophylactic Inj. Magnesium sulphate by Pritchard regimen for 24 hour post-delivery (inj. MgSO₄ 4 gm 20 % slow intravenous with 10 gm 50 % deep intramuscular as loading dose and followed by inj. MgSO₄ 5 gm 50 % Deep intramuscular every 4 hourly for 24 hours as maintenance dose) along with inj. diclofenac 75 mg intramuscular twice a day. Here patients who had either pre-delivery magnesium sulphate regimen or post-delivery magnesium sulphate regimen, were included irrespective of the pre-delivery magnesium sulphate regimen status. All the test patients included in our study were those who neither had any active eclampsia nor any history of neurological disorder.

Both the study groups were compared with post-operative visual analogue scale (VAS) for pain (in 100 scoring) post-operatively for 2 hours, 6 hours, 12 hours and 24 hours. Immediate post-operative pain management for initial 24 hours was important for mothers and was also an area of concern for modern obstetricians with rising caesarean section rates, which was also our study time window (post-delivery 24 hours).

Pain Scale

Patients were followed up for the 1st 24 hours post-delivery with amount of analgesic requirement and pain scores by visual analogue scales and added analgesics required.

Study Materials

Patient bed head tickets, operative log books for the said study period.

Exclusion Criteria

1. Eclampsia,
2. The American Society of Anaesthesiology (ASA) class III and more.
3. Body mass index (BMI) ≥ 35 kg m² and < 18.5 ,
4. Reported adverse reactions to any of the drugs included in the study,
5. Patients with history of ischemic heart disease, renal, hepatic and pulmonary diseases, those on antipsychotics, anticoagulants, epileptics, diabetics, or on any other drug affecting the metabolism of anaesthetics used, any chronic pain syndrome, thrombocytopenia, history of seizures, allergy to Non steroidal anti-inflammatory drugs (NSAIDS).

Inclusion Criteria

1. Severe pregnancy induced hypertension patients who were already in Pritchard regimen as prophylaxis magnesium sulphate regimen as case.
2. Spinal anaesthesia at T10-L1, severe pre-eclampsia with prophylaxis Pritchard regimen magnesium sulphate dose given.
3. American Society of Anaesthesiology (ASA) class I - II criteria for elective lower segment caesarean section patients.
4. LSCS patients were included.

Statistical Analysis

Data were registered in MS EXCEL (windows) including demographic details, patient's complaints, VAS score, and amount of analgesic used. Quantitative values were reported as mean \pm standard deviation (SD). We used an independent-t test and chi-square test to compare data. A P value ≤ 0.05 was taken as statistically significant. All analysis was performed using SPSS 23 for Windows and MS EXCEL.

RESULTS

There was a decrease in analgesic consumption and post-operative tenderness and pain in the group receiving MgSO₄, in comparison to control group of inj. diclofenac 75 mg (P < 0.0001) (Table 1) Mean age group in MgSO₄ group was 22.48 ± 4.87 years compared to analgesic group of 22.84 ± 4.65 years (P > 0.05). Gestational age of MgSO₄ group was 37.68 ± 2.004 weeks similar to 37.92 ± 1.919 weeks of only analgesic group (P > 0.05). Our study had mean Gravida of 1.78 ± 1.200 in magnesium sulphate group compared to 1.82 ± 0.928 of analgesic group, which was almost similar in both the groups (P > 0.05).

Duration of stay among the group receiving MgSO₄ was 6.8 ± 0.78 days compared to 7.04 ± 0.72 days in only analgesic group, which was comparable (P > 0.05). None of the above parameters were statistically significant.

	MgSO ₄ + Analgesic Group	Analgesic Group	P Value (T Test)
Age (mean \pm SD) years	22.48 ± 4.87	22.84 ± 4.65	> 0.05
Gravida (mean \pm SD)	1.78 ± 1.20	1.82 ± 0.928	> 0.05
Duration of Stay (mean \pm SD)	6.8 ± 0.78	7.04 ± 0.72	> 0.05
Gestational Age (mean \pm SD) weeks	37.68 ± 2.004	37.92 ± 1.919	> 0.05

Table 1.Characteristics of Patient Profile

VAS (visual analogue scale for pain) was compared in both the (Table 2) groups and VAS in 2-hour post-operative among caesarean patients was 51.3 in magnesium sulphate group compared to the analgesic group of 59.6, which was significant (P < 0.0001). Similarly, VAS in 6-hour post-operative among caesarean patients was 39.88 in magnesium sulphate group compared to the analgesic group of 55.58, which was significant statistically (P < 0.0001). And in VAS in 12-hour post-operative among caesarean patients was 26.08 in magnesium sulphate group compared to the analgesic group of 36.06, which was statistically significant (P < 0.0001). In the end, VAS in 24-hour post-operative among caesarean patients was 22.88 in magnesium sulphate group compared to the analgesic group of 25.48, which was significant (P < 0.0001).

	MgSO ₄ + Analgesic Group	Analgesic Group	P Value (T Test)
VAS 2 Hour (Mean)	51.3	59.6	< 0.0001
VAS 6 Hour (Mean)	39.88	55.58	< 0.0001
VAS 12 Hour (Mean)	26.08	36.06	< 0.0001
VAS 24 Hour (Mean)	22.88	25.48	< 0.0001

**Table 2. Post-Operative Pain Score in
Analgesic Group and MgSO₄ + Analgesic Group**

In our study none of the patients demonstrated bradycardia, hypotensive episodes, hypoxia, or hypoventilation in the postoperative period in the recovery room or immediate post-operative 24 hours. There was no significant respiratory depression in the magnesium sulphate group. Hemodynamic variables (BP, pulse urine output, respiratory rate) and the incidences of shivering, nausea, and vomiting were similar in the two groups. This can be attributed to the safety of the Pritchard Regimen in severe preeclampsia used for years with very less toxicity incidences. Magnesium sulphate may induce hypotension (decreased blood pressure) directly by vasodilatation as well as indirectly by sympathetic nerve end root blockade and inhibition of catecholamine neurotransmitters release.

DISCUSSION

Magnesium sulphate (MgSO₄), an NMDA receptor antagonist and a calcium channel blocker, in the past has also been utilized intravenously as an adjunct pain medication in various surgical procedures with varying results and outcomes. However, evidence for its analgesic role post caesarean section has not been published well in past literatures. This study concretizes the evidence for post caesarean analgesia and pain relief outcomes following intravenous and intramuscular magnesium (with existing Pritchard regimen) which revealed encouraging results. The trend amongst available evidence from previous literatures suggest that analgesic requirements in the immediate 24 -

hour postoperative period may be reduced with IV magnesium. Beyond this, there is currently insufficient evidence for the role of post-operative intravenous followed by intramuscular magnesium for post caesarean analgesia, which is supported by our retrospective study.

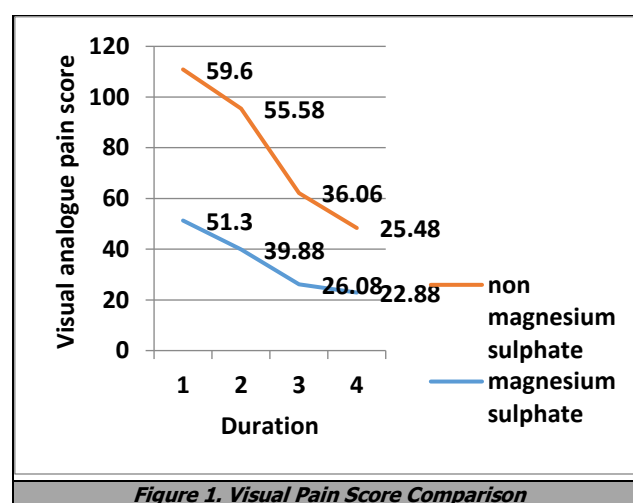
Based on our results pain severity scores were significantly lower in the study group (analgesic + MgSO₄) at 30 minutes, 2 hours, 6 hours, 12 hours and 24 hours, postoperatively ($P < 0.0001$). Previous articles have also reported that magnesium administration significantly reduced opioids / analgesic drug requirements.¹²⁻¹⁵ In their study, Choi and colleagues showed that the use of propofol reduced from 167 to 81 mg / kg / min after administering bolus dose of MgSO₄ (50 mg / kg) followed by continuous MgSO₄ infusion (8 mg / kg / min) in gynaecological surgery.¹⁴ Anaesthetic and analgesic effect of magnesium was believed to be due to magnesium and calcium ions competition in pre-synaptic calcium channels.¹⁵ KO et al. concluded that CSF magnesium concentration affects postoperative pain, but perioperative IV magnesium administration had no analgesic effects.¹⁶ It had been proposed that MgSO₄ could prevent central sensitization after peripheral nociceptive stimulation and suppress hypersensitivity, and this analgesic pain relieving property was all due to its action on NMDA receptors and calcium channels. Previous articles have also proved this finding that one of the main target sites for general anaesthesia was release of glutamate by pre-synaptic calcium channels.¹⁷⁻¹⁹ NSAIDs are seen as an analgesic option for postoperative pain and tenderness. However, many concerns about adverse effects of these NSAIDs, such as gastrointestinal bleeding (Without proton pump inhibitors), acute renal failure (ARF) and allergic reactions have limited their usage.²⁰ The analgesic / pain relieving adjuvant effect of magnesium after surgery has been described in several reports.^{21,22,23} Our study shows less post-operative pain among analgesic + MgSO₄ group than control group. These findings are same with old reports on the analgesia - potentiating effect of magnesium sulphate²⁴ but our study includes subjects with existing Pritchard regimen for prophylactic magnesium sulphate among severe preeclampsia with intravenous magnesium sulphate loading dose followed by intramuscular dose for next 24 hours' post-partum.

Similarly, in other studies like Hwang et al. in 2010²⁴ conducted a study on 40 patients undergoing total hip replacement arthroplasty (THA) under spinal anaesthesia (SA). After the induction of spinal anaesthesia, the magnesium group (Group M) received magnesium sulphate by continuous IV infusion until the end of surgery. The saline group (Group S) received the same volume of isotonic saline. Cumulative postoperative Patient controlled analgesia (PCA) consumptions were also significantly lower in Group M at 4, 24, and 48 h after surgery.

Lee et al. in 2012²⁵ enrolled 66 patients undergoing arthroscopic rotator cuff repair with Inter scalene nerve block was performed with 0.5 % bupivacaine 20 mL with epinephrine (1: 200,000) plus either 10 % magnesium sulphate 2 mL (magnesium group) or normal saline 2 mL

(saline group). The duration of analgesia was longer in the magnesium sulphate group than in the saline group.

A study was undertaken by Kiran et al. in 2011²⁶ to study efficacy of a single dose of IV magnesium sulphate to reduce postoperative pain in patients undergoing inguinal surgery. Pain in the postoperative period was significantly lower in magnesium sulphate group in relation to control group at 2, 4, 6, 12 and 24 h postoperatively. Magnesium sulphate decreases pain and tenderness, with decreased analgesic requirement in post-operative period just as in our study. Figure 1 shows a graphical representation of the post-operative pain scores among both groups showing decreased visual analogue score for pain among the magnesium sulphate + analgesic (inj. diclofenac 75 mg intramuscular) group compared to only analgesic (inj. diclofenac 75 mg intramuscular) group in 2 hours (1), 6 hour (2), 12 hour (3), 24 hour (4) post-operative.



Our study (comparing the analgesic role of both groups, magnesium sulphate + analgesic and analgesic) firmly asserts the role of magnesium sulphate in adjuvant analgesic for immediate post-operative pain management (P value < 0.0001) in caesarean section patients (Table 2) along with traditional analgesic (inj. diclofenac 75 mg used in our retrospective study).

CONCLUSIONS

There was a decrease in analgesic requirement and post-operative pain in the group receiving MgSO₄, in comparison to control group. Pain severity assessment 2, 6, 12 and 24 hours post operatively showed that there was a statistically significant decrease pain scores between study and control groups ($P < 0.0001$).

Magnesium sulphate within existing Pritchard regimen for severe preeclampsia^{33,34} can decrease the requirement of analgesics among the post-operative patients. This study establishes firmly the decreased analgesic requirement post-operative pain management in cases who are already in magnesium sulphate regimens, especially in severe preeclampsia with prophylactic magnesium sulphate. Thus magnesium sulphate can be placed as a safe add on or

alternative to other analgesics or pain medications among caesarean section patients, keeping the safety range of magnesium sulphate in view (being a traditionally used drug for a long time in both obstetrics and modern medicine).^{35,36}

In view of today's increase in caesarean section rates and requirement of post op analgesia for better maternal and foetal outcome in both breast feeding and non-lactating mothers, it is imperative to give options to better analgesics, in which magnesium sulphate can be a viable alternative to the traditional analgesics, especially in cases where magnesium sulphate is already given to the patient for other medical / obstetric causes.

Limitation

Our study also had a few limitations. First, the study population consisted mostly of reproductive age group females. Guo and colleagues²⁴ reported that age played no significant role in postoperative analgesia in adults achieved with magnesium. On the other hand, recent research demonstrates sex differences with respect to pain and tenderness perception.^{27,28} Although the exact mechanism was still unclear and remained controversial, females (as all our study subjects) have shown lower pain thresholds and tolerance to pain stimuli in experimental studies than males^{29,30} with different response and effectiveness to analgesic treatment.²⁸

The safety of IV magnesium for use as an analgesic adjunct can be translated from use elsewhere in obstetrics, or for analgesia in other surgical procedures, with reviews concluding no serious side effects at doses as high as 28 grams over 24 hours with no difference in morbidity or mortality compared with placebo.³¹ A Cochrane review of magnesium use in severe preeclampsia puerperal mothers supported its safety at doses up to 1 g / hr.³²

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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