

# Incisional Injection of Magnesium Sulfate for Post-Cesarean Section Pain Management

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**Background:** Effective pain relief is very important for parturient women because they are expected to recover expeditiously and to care for their newborns within a few hours following surgery. Recent studies have identified N-methyl-D aspartate (NMDA) receptors peripherally and their major role in nociceptive transmission. Magnesium has an antagonistic effect on NMDA receptors.

**Objectives:** The aim of the present study was to evaluate the analgesic effect of intra-incisional Mg on women undergoing elective cesarean section.

**Patients and Methods:** In this blinded clinical trial, 192 patients undergoing elective cesarean section were randomly divided into two groups; intervention (n = 96, 20 mL of 750 mg magnesium sulfate diluted in normal saline) and control (n = 96, 20 mL normal saline) groups. Intra-incisional injection was applied before wound closure. Postoperative pain based on visual analogue scale (VAS) score and cumulative rescue analgesia in the first 24 hours was recorded and compared between the groups.

**Results:** The mean age of participants was  $27.91 \pm 5.19$  years old. The mean duration of surgery was  $41.05 \pm 7.87$  minutes. The mean of VAS score in the magnesium sulfate group was significantly lower than the control group in all the evaluations. The means of cumulative diclofenac requirement in the case and control groups were  $146.57 \pm 92.89$  and  $205.7 \pm 108.43$  mg, respectively, which in the case group was significantly less than the control group ( $P = 0.000$ , CI 95% = 64.23-54.04)

**Conclusions:** According to the result of the present study, it seems that incisional injection of magnesium sulfate in post-cesarean section pain management is safe and useful. Further studies are required to evaluate other doses as well as toxicity in longer durations than the first postoperative day.

**Keywords:** Cesarean Section; Magnesium; N-Methylaspartate; Postoperative Pain

## 1. Background

Cesarean section (CS) is one of the most commonly performed surgical procedures. It is estimated for about 30% of births worldwide (1). Post-cesarean pains are unpleasant feelings resulting from tissue damage, signaling the actual injury to the body (2). Post-operative pain management is necessary because women are expected to recover expeditiously and to care for their newborns within a few hours following the surgery. Consequently, using safe, simple and effective analgesic methods is essential. Post-cesarean pain has two components: visceral and somatic pain. Visceral pain is originated from uterine incision and contractions. Somatic pain arises from nociceptors within the surgical wound (2). A variety of systemic and local anesthetic techniques have been introduced and implemented for post-cesarean pain management with regard to somatic pain control. Some of these medications are systemic, epidural and local narcotics, nonsteroidal anti-inflammatory drugs (NSAIDs), ketamine, and tramadol (3). Despite the common use of these drugs, there are some common annoying side ef-

fects such as hypotension, arrhythmia, drowsiness, nausea and vomiting, skin pruritus, and urinary retention in systemic analgesic techniques. Local anesthetic drugs are increasingly administered for wound healing following different surgeries. Recently, some studies have shown N-methyl-D aspartate (NMDA) receptors peripherally in skin, muscles and knee joints in addition to their central location and their major role in sensory transmission of noxious signals in acute pain state (4-6).

Magnesium is the fourth most abundant cation in body and second most abundant intracellular cation which activates many of the metabolic enzymes and acts as a natural calcium antagonist and physiological blocker of NMDA receptors (7). Numerous clinical trials have demonstrated that systemic administration of magnesium sulfate during general and tracheal anesthesia reduces anesthetics requirement and post-operative analgesic consumption (8-10) due to its antagonistic effect on NMDA receptors (11, 12). Moreover, the postoperative analgesic effect of magnesium has been studied by many

authors, most of which showing that systemic use of magnesium minimized the postoperative analgesic requirement and pain (13).

## 2. Objectives

Tauzin-Fin and his colleagues have shown that intra-incisional co-administration of magnesium sulfate and ropivacaine after radical prostatectomy could significantly reduce the need for analgesia (14); so, we were interested to determine the effect of intra-incisional injection of magnesium sulfate on women undergoing elective cesarean section.

## 3. Patients and Methods

In this randomized triple-blinded controlled clinical trial, 192 patients 18-35 years old in functional class, scheduled for elective cesarean section under spinal anesthesia, admitted to educational hospital of Arak University of Medical Sciences, were enrolled in the study. Random allocation was performed; odd numbers were for the intervention group and even numbers for the control group. All the patients underwent spinal anesthesia using 75 mg lidocaine 5%. Patients in the intervention group received intra-incisional magnesium sulfate at the end of the surgery, before wound closure (n = 96, 20 mL of 750 mg magnesium sulfate diluted in normal saline), and patients in the control group received normal saline (n = 96, 20 mL normal saline). The patients and the clinicians who were responsible for intervention and visiting the patients remained blind during the trial. Demographic data, including age and medical history were collected. The primary outcomes were postoperative pain based on visual analogue scale (VAS); cumulative intramuscular rescue analgesia was applied every four hours during the first 24 hours. Patients with history of heart, liver, kidney or mental disorders, chronic hypertension, pre-eclampsia, chronic opioid abuse, or calcium channel blocker

consumption and no satisfactory anesthetic level during the surgery for which general anesthesia was needed, or patients with postoperative hypertension who had to be prescribed with magnesium sulfate generally were excluded from the trial. All the statistical analyses were performed using SPSS software version 21 (using independent t-test) and statistical significance was considered at  $P \leq 0.05$ . This random clinical trial was ethically approved by the Research Ethical Committee of the Arak University of Medical Sciences and was registered in Iranian Registry of Clinical Trials (IRCT201104303247N2). Written informed consents were obtained from all the patients or their relatives before the trial.

## 4. Results

The mean age of participants was  $27.91 \pm 5.19$  years old. The mean duration of surgery was  $41.05 \pm 7.87$  minutes. There was no significant difference between the two groups with regard to age, the number of gravity, and parity ( $P > 0.05$ ) (Table 1). The mean scores of VAS, 4, 8, 12 and 24 hours after the surgery, were recorded and compared between the groups (Table 2). The mean of VAS score in the magnesium sulfate group was significantly lower than that of the control group in all the evaluations. Suppository of diclofenac (100 mg) was used as the rescue analgesia and for VAS scores more than 5, we used 1 mg/kg intramuscular meperidin for patients. The means of cumulative diclofenac requirement in case and control groups were  $146.57 \pm 92.89$  and  $205.7 \pm 108.43$  mg, respectively, which in the case group was significantly lower than the control group ( $P = 0.000$ , CI 95% = -64.23 to -54.04). The means of injected meperidin were  $31.33 \pm 26.11$  and  $29.98 \pm 28.75$  mg in intervention and control groups respectively, in which there was no significant difference between the two groups ( $P = 0.6$ ). There was no report of known adverse effects of magnesium sulfate such as hypotension, diplopia, dysarthria, arrhythmias, skin irritation or muscle pain in patients receiving the medications.

**Table 1.** Basic Characteristics of Patients in Both Groups

	Intervention Group (n = 96)	Control Group (n = 96)	P Value
Age	4.85 ± 28.27	5.43 ± 27.65	0.459
Gravity	0.99 ± 2.13	0.98 ± 2.0	0.399
Parity	0.89 ± 0.98	0.85 ± 0.87	0.411
C-Section number	0.82 ± 1.07	0.79 ± 0.76	0.016
Duration of C-Section	6.87 ± 34.77	7.03 ± 42.89	0.000

**Table 2.** The Mean of Visual Analogue Scale Score in 4, 8, 12 and 24 Hours After Surgery in Both Groups

	Intervention Group (n = 96)	Control Group (n = 96)	P Value	Confidence Interval 95%
4 h after	2.27 ± 5.45	1.40 ± 8.17	0.000 <sup>a</sup>	(2.51-2.76) -
8 h after	2.06 ± 2.91	1.38 ± 6.0	0.000 <sup>a</sup>	(2.89-3.08) -
12 h after	1.73 ± 2.17	1.67 ± 4.72	0.000 <sup>a</sup>	(2.64-2.63) -
24 h after	1.24 ± 1.09	1.83 ± 3.63	0.000 <sup>a</sup>	(2.342-2.49) -

<sup>a</sup> Values are statistically significant.

## 5. Discussion

In this randomized controlled trial, local administration of magnesium sulfate showed significant reduction in pain scores as well as in cumulative rescue analgesic requirement in the case group without any side effects. An important part of post-cesarean pain is because of incision in the anterior abdominal wall. A variety of local anesthetic techniques have been introduced and implemented for post-cesarean pain management with regard to somatic pain control. Considering the importance of postoperative pain control and fast rehabilitation and recovery after the surgery, several studies have examined the efficacy of various drugs. A number of our clinical trials have demonstrated that systemic administration of magnesium sulfate during general anesthesia reduced anesthetic requirement and post-operative analgesic consumption (8-10). Intrathecal and systemic administration of magnesium sulfate can improve postoperative analgesia due to its antagonistic effect on NMDA receptors (11, 12). Ghrab et al. in their study concluded that in patients undergoing caesarean section under spinal anesthesia, addition of intrathecal magnesium sulfate to morphine can improve the quality and duration of postoperative analgesia without increasing the incidence of adverse effects (15). Schulz-Stubner et al. have recommended the use of magnesium sulphate as a safe and cost-effective supplement, as a general anesthetic regimen with propofol, remifentanyl and mivacurium, although they did not distinguish between a mechanism of magnesium action as a(n) (co) analgesic agent at the NMDA-receptor site or its properties as a sympatholytic (16). Seyhan et al. showed that magnesium sulfate infusion led to significant reduction in intraoperative propofol, atracurium and postoperative morphine consumption, but increasing the magnesium dosage did not offer any advantages and can induce hemodynamic consequences (17). In all the mentioned studies, magnesium was an adjuvant; but in our study, we use it as a main medication for local anesthesia. In literature review, we found no clinical trial that evaluated the effects of local administration of magnesium sulfate on post-cesarean pain management. Vahabi et al. investigated the effects of local administration of magnesium sulfate on pain relief in pediatric adenotonsillectomy and the results showed that pain score in the first two hours after the surgery in the case group was significantly lower than that of the control group (18). A new study showed that admixture of magnesium sulfate to local anesthetic bupivacaine during femoral nerve block can provide a profound prolongation of the duration of both sensory and motor blocks, in addition to a significant decrease in postoperative pain scores and the total dose of rescue analgesia (7). Contrary to the result of the mentioned and the present study, Hung et al. in their study concluded that magnesium shortened the duration of sciatic nerve block with amide local anesthetics; thus, it did not seem to be a useful adjuvant for local

anesthetics in peripheral nerve blockage (19). However, Bondok et al. studied the effects of intra-articular magnesium on knee arthroscopy and showed a significant decrease in postoperative pain score as well as in the dose of rescue analgesia in the first 24 hours with a longer delay in the need for that analgesia (20).

In conclusion, it seems that incisional injection of magnesium sulfate in post-cesarean section pain management can be safe and useful. Further studies are required to evaluate other doses as well as toxicity in longer durations than the first postoperative day.

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## Authors' Contributions

Mehri Jamilian: Contributed to the design of the study, acquisition and interpretation of the data, carried out the C/S and drafted the paper for important intellectual content; Shirin Pazoki: Contributed to the design of the study, carried out the anesthesia and incisional injection, and drafted the paper for important intellectual content; Majid Golestani Eraghi: Contributed to the design of the study, carried out the anesthesia, interpretation of the data, and drafted the paper for important intellectual content.

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