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# Does magnesium sulfate reduce the short- and long-term requirements for pain relief after caesarean delivery? A double-blind placebo-controlled trial

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**KEY WORDS**
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**Objective:** The purpose of this study was to determine whether magnesium sulfate decreases postoperative pain and analgesic consumption.
**Study design:** Women who underwent elective cesarean delivery were randomized into groups according to high-dose magnesium sulfate (50 mg/kg load and 2 g/h), low-dose magnesium sulfate (25 mg/kg load and 1 g/h), or placebo. Before the delivery, the dose of patient-controlled opioid that was used and the visual analogs of pain during the first 48 hours after delivery and at 6 weeks were assessed.
**Results:** Forty-two women were assigned randomly to the high-dose arm; 38 women were assigned to the low-dose magnesium arms, and 40 women were assigned to the control arm. The cumulative opioid use ($P = .636$); pain scores at 6, 12, 24, and 48 hours at rest ($P = .786$) and with movement ($P = .179$); the use of analgesics after hospital discharge ($P = .711$); and wound pain with movement ($P = .429$) or pressure ($P = .144$) after 6 weeks were similar.
**Conclusion:** Magnesium sulfate does not reduce the severity of short-term or long-term (6 weeks) pain after cesarean delivery.


In pregnancies that are complicated by preeclampsia, magnesium sulfate is the drug of choice to prevent eclamptic seizure.[1] In the United States, it also is used commonly to treat preterm labor and to delay preterm delivery, to administer corticosteroids to enhance fetal lung maturity and lessen neonatal morbidity.[2] In addition to its actions in the prevention of seizures and relaxing a contracting uterus, magnesium sulfate is a voltage-gated antagonist at the N-methyl-D-aspartate receptor in the spinal cord. This antagonism alters pain processing and reduces the induction and maintenance of central sensitization from nociceptive stimulation. This has implications for the prevention of long-term and neuropathic pain, and there is experimental and clinical support that magnesium may play a role in the modulation of acute pain,[3] reducing postsurgical pain

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intensity or the dosage of analgesics.[4-10] Decreased pain might have functional benefits by permitting the parturient to ambulate or to be discharged from the hospital earlier. It is also possible that the number of women who continue to experience wound or abdominopelvic pain after cesarean delivery may be reduced.

The impact of pre- or perioperative magnesium sulfate on postoperative pain in obstetric patients is unknown. A Medline search from 1966 through September of 2004 with the search words *magnesium sulfate*, *pregnancy*, *pain management*, and *postoperative pain* revealed no articles that assessed the effect of magnesium sulfate on early or long-term postoperative pain. The preliminary report of a small retrospective study noted that parturients with preeclampsia who underwent cesarean delivery and were exposed to magnesium therapy had less postoperative pain than matched control subjects.[11]

The efficacy of magnesium sulfate for the management of postoperative pain in obstetric patients has not been studied. The primary purpose of our investigation was to determine whether magnesium sulfate could be used to decrease analgesic requirement after cesarean delivery. Secondary aims were to investigate whether the severity of early postoperative pain was reduced and to determine the incidence of residual wound pain at 6 weeks after surgery.

## Material and methods

This study was approved by the Ethics Committee of King Edward Memorial Hospital for Women. Women were recruited from the obstetric population who attended the clinics of and were delivered at King Edward Memorial Hospital.

The primary end point in the study was the cumulative meperidine use at the 24-hour postsurgical assessment. Secondary end points included visual analog scores of pain, the use of postoperative epidural meperidine at 48 hours, and the incidence of sensory changes at 6 weeks postpartum evaluations. Sample size estimation for the cumulative meperidine use at 24 hours was based on previous data for patient-controlled epidural analgesia at King Edward Memorial Hospital, where mean use was 365 $\pm$ 133 mg.[12] One hundred seventeen women (39 per group) were required to detect a 25% reduction in the amount of meperidine that was used in either of the treatment groups compared with the control arm, with a Kruskal-Wallis nonparametric analysis of variance with the overall significance level of 5% and power of 80%. This estimation allowed for 2 pairwise comparisons between control and either active group (Power and Sample Size Estimation Program, PASS 2002, Kaysville, UT). To allow for withdrawals, 130 women were recruited. Nonparametric analysis of primary outcome was anticipated to address the anticipated lack of normality of postoperative meperidine requirement, as indicated by previous data.[12]

Inclusion criteria were a maternal age of $\geq$18 years, a singleton pregnancy with no contraindication to magnesium sulfate therapy, a planned cesarean delivery (so that sufficient time was available to administer the magnesium sulfate 1 hour before surgery), and consent to a combined spinal-epidural anesthetic. Women were excluded if they refused study participation, underwent an urgent cesarean delivery at which there was insufficient time to give magnesium therapy before surgery, had heart block or renal impairment, were receiving a calcium-channel antagonist drug, or were receiving magnesium sulfate for preterm labor or preeclampsia. Participating women were discontinued from the study if they had an adverse reaction to magnesium sulfate, received magnesium sulfate for preterm labor tocolysis or preeclampsia prophylaxis, or requested discontinuation.

With a computer-generated random number sequence, with trial group allocation used coded intravenous infusion bags that were prepared by the Pharmacy Department, women were assigned randomly to 1 of 3 trial arms: (1) high-dose magnesium sulfate (50 mg/kg loading dose, then 2 g/h); (2) low-dose magnesium sulfate (25 mg/kg loading dose, then 1 g/h); or (3) a control group who received normal saline solution. All solutions were commenced 1 hour before scheduled surgery and continued for 24 hours after loading. Neither the patient nor the health care provider was aware of the content of the study solution, and the solution code remained unbroken until after the study was completed.

All women were monitored for evidence of magnesium toxicity by assessment of respiratory rate, vital signs, and patellar reflexes for the period of infusion. Respiratory depression or absence of the patellar reflexes was investigated by serum magnesium assay, and the infusion was ceased until it was confirmed that serum magnesium levels were subtoxic.

All women had the same method of spinal-epidural anesthesia for the cesarean delivery, with hyperbaric bupivacaine 0.5% and fentanyl 15 μg. A 0.5-mL sample of cerebrospinal fluid was taken for analysis of magnesium concentration before the intrathecal administration of drugs. Intravenous ephedrine 30 mg in 500 mL normal saline solution was infused prophylactically, and phenylephrine boluses were administered, as required, to maintain blood pressure within 20% of baseline. Blood loss at the time of cesarean delivery was estimated by the operating surgeon after evaluating the blood contained within the suction devices, drapes, and the number of and saturation of the laparotomy pads that were used at cesarean delivery. After the operative procedure, all women had the same analgesics made available, on an "as needed" basis, with the technique of meperidine patient-controlled epidural analgesia and regular oral