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The Additional Effect of Magnesium Sulfate to Lidocaine in Spinal Anesthesia for Cesarean Section

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Abstract: Different additives have been used to prolong spinal anesthesia. We designed a prospective, randomized, double-blind study to evaluate the effect of spinal anesthesia. Eighty patients scheduled for first cesarean surgery were randomly allocated into 2 groups to receive either 1.5 mL lidocaine 5% with 0.5 mL sterile water (control group, n = 40) or 1.5 mL lidocaine 5% with 0.5 mL preservative-free magnesium sulfate 10% (magnesium group, n = 40). Neither epinephrine nor opioid was added to the treatment mixture. The duration of analgesia after spinal anesthesia (the time from local anesthetic injection to the first opioid request) and the duration of analgesia after surgery (the time between termination of the procedure and the time at which the first dose opioid was requested) were compared. The durations of analgesia after spinal anesthesia was significantly longer in the magnesium (160.8±49.1) than in the control group (113.3±27.3) and the durations of analgesia after surgery was significantly longer in the magnesium (74.5±47.5) than in the control group (26.6±25.1), (p = 0.001). There was no associated increase in adverse events in the group receiving intrathecal magnesium.

Key words: Anaesthetic techniques, regional, spinal, magnesium, lidocaine

INTRODUCTION

Spinal anesthesia is a well known technique for cesarean section, which is of rapid onset, provides a superior block Addis more cost-effective (Riley *et al*., 1995). The quality of the spinal anesthesia has been reported to be improved by the addition of opioids (such as morphine, fentanyl and sufentanil) and other drugs (such as epinephrine, clonidine, neostigmine, adenosine, ketorolac and midazolam) (Rathmell *et al*., 2005).

Magnesium, the fourth most common cation in the body, has numerous physiological activities (James, 1992). Magnesium antinociceptive effects appear to be relevant not only to chronic pain (Feria *et al*., 1993; Tramer *et al*., 1996), but if also determines in part, the duration and intensity of postoperative pain (Woolf and Thompson, 1991). These effects are primarily based on the regulation of calcium influx into the cell, i.e., natural physiological calcium antagonism (Iseri and French, 1984) and antagonism of the N-methyl-D-aspartate (NMDA) receptor. NMDA receptors mediate neuronal signaling and therefore perform critical roles in CNS functioning. Because of their role in CNS function and particularly its involvement in pain processing, blocking NMDA receptors promises to be useful in preventing development of prolonged pain states. No selective NMDA receptor antagonists are available for clinical use. However, several compounds approved for use in humans for other indications have significant NMDA receptor-blocking properties (Lodge and Johnson, 1990). Of these, Mg^{2+} is of most interest.

The present placebo-controlled clinical trial evaluates the effect of magnesium sulfate added to lidocaine on the durations of analgesia after spinal anesthesia and after surgery to prolong the duration of spinal analgesia and decrease the opioid and analgesic drugs requirement in the patients undergoing their first caesarian.

MATERIALS AND METHODS

After institutional approval and obtaining informed patient consent, 80 ASA physical status I-II patients aged 18-45 year, height 160-190 cm and weight 50-90 scheduled for cesarean section under spinal anesthesia in Dr. Ali Shariati Hospital 2006 were included in the study. Patients with a history of opium addiction, sedative drugs

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consumption, contraindication for spinal anesthesia, failure of spinal block and the need for general anesthesia were excluded from the study. Patients were randomly assigned into two groups of either control (Group c, n = 40) or magnesium (Group m, n = 40) using a computer-generated randomization list.

Neither epinephrine nor opioid were added to the mixtures. All local anesthetic solutions and adjuvant drugs were prepared by an anesthesiologist not involved in the performance of spinal anesthesia, patient care, or data collection.

On arrival at the operating room, standard monitoring was established and all the patients received 10 mL kg^{-1} Ringer's lactate solution. Then, using an aseptic technique, a 25-gauge Quincke needle was inserted intrathecally via a midline approach into the L3-4 or L4-5 interspace with the patient in the left lateral decubitus position. After a successful dural puncture, the patients in group c received 1.5 mL lidocaine 5% with 0.5 mL of distilled water and those in group m received 1.5 mL lidocaine 5% with 0.5 mL of preservative-free solution of magnesium sulfate 10% (50 mg). After intrathecal injection, the patient was positioned supine and pelvic tilt used to minimize vena caval occlusion. Pin-prick test (Hollmen grade 2) was used for estimating level of anesthesia in the midclavicular line. The duration of analgesia after spinal anesthesia (the time from local anesthetic injection to the first opioid request) and the duration of analgesia after surgery (the time between termination of the procedure and the time at which the first dose opioid was requested) were recorded.

Present method was similar to Buvanendran study which was the only intrathecal magnesium human study and our drug dosage was exactly the same.

Complications such as nausea, vomiting, dyspnea during the surgery and in the recovery room andhypotension (>20% decline in systolic arterial blood pressure) during surgery were treated and recorded. Also, the patients were observed for sensory-motor complications until 24 h after surgery for any neurological symptoms.

A sample size of 40 in each group would be sufficient to detect a difference of 30 min in the mean of duration of the spinal anesthesia, assuming a standard deviation of 35 (based on a pilot study), a power of 95% and a significant level of 5%. Statistical analysis was performed with SPSS for windows (SPSS Inc., Chicago, IL), version 11.5. Statistical comparison was carried out using the Chi-square or Fishers exact tests and independent student's t-test (considering levene's test for equality of variances) where appropriate. Two tailed $p<0.05$ was taken as significant.

RESULTS AND DISCUSSION

No patients were excluded from the study. The mean patient characteristics, level of sensory blockade and the duration of surgery were similar in the two groups (Table 1). The duration of analgesia after spinal anesthesia (the time from local anesthetic injection to the first opioid request) and the duration of analgesia after surgery (the time between termination of the procedure and the time at which the first dose opioid was requested) were significantly longer in the m group than in the c group ($p = 0.001$) (Table 2).

Based on the results of our study, complications such as nausea, vomiting, dyspnea during the surgery and in the recovery room andhypotension (>20% decline in systolic arterial blood pressure) during surgery were not statistically different between two groups (Table 3). No neurological symptoms were seen until 24 h after surgery.

The present study indicates that the addition of 0.5 mL magnesium sulfate 10% to 1.5 mL lidocaine 5% for spinal anesthesia results in a significant increase in the duration of analgesia after spinal anesthesia and surgery. Although this analgesic effect was accompany with considerable decreased of nausea and vomiting during surgery but the difference was not statistically significant. In other mentioned complications (dyspnea and

Table 1: Patient characteristics

Characteristics	Control group	Magnesium group
Age (year)	25.0±5	27.0±6
Weight (kg)	75.0±16	80.0±12
Height (cm)	150.0±13	153.0±10
Gestation (weak)	39.0±1	39.0±2
Duration of surgery (min)	58.0±11	60.0±13
Sensory blockade level (T4/T6)	27/13	24/16

Values are expressed as mean±SD, There are no significant differences between groups

Table 2: Effect of intrathecal magnesium sulfate

Parameters	Control group	Magnesium group	PV
Duration of analgesia after spinal anesthesia (min)	113.3±27.3	160.8±49.1	0.001
Duration of analgesia after surgery (min)	26.6±25.1	74.5±47.5	0.001

Table 3: Comparison of patient complications

Parameters	Control group (n = 40)	Magnesium group (n = 40)	PV
Nausea during the surgery	29 (72.5%)	20 (50%)	0.07
Nausea in the recovery room	8 (20%)	7 (17.5%)	1.00
Vomiting during the surgery	16 (40%)	8 (20%)	0.08
Vomiting in the recovery room	3 (7.5%)	2 (5%)	1.00
Dyspnea during the surgery	4 (10%)	4 (10%)	1.00
Dyspnea in the recovery room	5 (12.5%)	2 (5%)	0.40
Hypotension during surgery	13 (32.5%)	8 (20%)	0.30

There are no significant differences between groups, Hypotension: >20% decline in systolic arterial blood pressure

hypotension during surgery and nausea, vomiting and dyspnea in the recovery room) there was no statistical difference between the two groups.

Intrathecal magnesium was used in order to increase analgesic duration of opioids in human and they demonstrated that addition of 50 mg intrathecal magnesium to intrathecal fentanyl led to increasing analgesic effect during painless delivery (Buvanendran *et al*., 2002). These results were compatible with animal studies and intrathecal magnesium caused increasing analgesic time due to opioids (Liu *et al*., 2001; Ishizaki *et al*., 1999; Karasawa *et al*., 1998).

Magnesium blocks NMDA channels in a voltage-dependent way and produces a dramatic reduction of NMDA-induced currents (Ascher and Nowak, 1987). Noxious stimulation leads to the release of glutamate and aspartate neurotransmitters, which bind to the NMDA receptor. NMDA receptor signaling may be important in determining the duration and intensity of postoperative pain (Woolf and Thompson, 1991). Selective NMDA receptor antagonists are not available for clinical pain management. However, several compounds approved for use in humans for other indications, such as magnesium, have significant NMDA receptor-blocking properties (Liu *et al*., 2001).

In a study, Tramer *et al*. (1996) showed that the group under treatment with magnesium sulfate needed less amounts of opioid during the first 48 h after surgery compared with control group. Also, this group had a decreased discomfort in the first two nights after the surgery. The rate of insomnia in the magnesium sulfate group was not altered, but it was increased in the control group. Although intravenous magnesium leads to decreased need of opioids during surgery and after surgery (Tramer *et al*., 1996) using 50 mg kg^{-1} intravenous magnesium before surgery and 8 mg kg^{-1} h^{-1} during surgery achieved considerable results about reducing patients pain (Koinig *et al*., 1998) but small doses of this drug pass the blood brain barrier and in order to obtain analgesic effect of intravenous magnesium sulfate, higher doses should be used which may cause complications.

In conclusion, we have demonstrated that the noncompetitive NMDA antagonist magnesium sulfate, administered intrathecally, prolongs the duration of spinal analgesia. Further studies are required to determine whether larger doses of intrathecally magnesium sulfate can produce greater potentiation of analgesia and reduce opioid requirements.

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