

Effects of Intra-articular Magnesium Sulfate Injection in Post-operative Pain in Knee Arthroscopy: A Prospective Comparative Study

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Abstract

Background and Objective: Intra-articular magnesium sulfate, an *N*-methyl-d-aspartate receptor blocker, would be of particular interest in either producing post-operative analgesia or enhancing the analgesic effect of intra-articular bupivacaine. This study was aimed to investigate the efficacy of intra-articular magnesium sulfate injection as post-operative analgesic agent knee arthroscopy. A decrease in visual analog scale (VAS) score followed by a decrease in analgesic requirement and subsequently less analgesic requirement. **Materials and Methods:** This is a randomized, prospective, double-blinded clinical trial conducted on patients undergoing arthroscopic partial meniscectomy referred to Ahvaz Razi Hospital, Iran. 94 patients were randomly divided into two parallel groups. The saline placebo group received 20 ml of isotonic saline, and the magnesium sulfate group received 20 ml of isotonic saline containing 1 g magnesium sulfate. The post-operative analgesia was assessed using VAS recorded at 5, 60, 120, and 240 min post-surgery. Patients were evaluated at rest and under movement. **Results:** The magnesium sulfate group showed a significant reduction in VAS score, a significantly increased time to first post-operative analgesic request, as well as significantly reduced total analgesic requirement than the control group. **Conclusion:** Magnesium sulfate produces a reduction in post-operative pain when given intra-articularly in comparison to saline placebo.

Key words: Analgesia, knee arthroscopy, magnesium sulfate

INTRODUCTION

Arthroscopic knee procedures are commonly performed in the outpatient setting. Unrelieved post-operative pain may delay discharge and prolong hospital stay. Intra-articular local anesthetics are often used for prevention of pain after arthroscopic knee surgery.^[1,2] However, the mean duration of analgesia provided by local anesthetics is short, and patients may need opioid analgesia, possibly delaying their discharge. To overcome this, various drugs such as opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), clonidine, neostigmine, and ketamine have been used with variable effects.^[3-5]

Recent evidence suggests that *N*-methyl-d-aspartate (NMDA) receptors located in the peripheral somatic and visceral pain pathways play an important role in nociception.^[6] NMDA receptors have been found in joints as demonstrated in a rat model in a study conducted by Yu *et al.*^[7]

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Despite recently intra-articular injection of magnesium sulfate had been shown to have post-operative analgesia after arthroscopy,^[8] but the effect of magnesium sulfate as a NMDA receptor antagonist intra-articularly in reducing pain sensation, or as an adjunct to the local intra-articular anesthetic, is not known. This randomized, prospective, double-blinded study investigated whether magnesium sulfate results in a decrease in visual analog scale (VAS) scores followed by a reduction in analgesic requirement and providing more reduction in VAS and subsequently less analgesic requirement.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of the Ahvaz Jundishapur University of Medical Sciences, Iran, and the authors have no conflict of interest. All of the patients gave written consent to participate in the study. This study was conducted in accordance with the Declaration of Helsinki and good clinical practice according to the International Conference on Harmonization guidelines. The Ethics Committee of Jundishapur University of Medical Sciences, Ahvaz, Iran, approved this study. The study was designed as a randomized, clinical trial and performed in Razi Educational Hospital in Ahvaz (IRCT: IRCT2017012232117N1).

The inclusion criterion was as follow as patients 18-45 years of age who were candidate for arthroscopic partial meniscectomy and evidences of meniscus rupture proven in magnetic resonance imaging. Exclusion criteria were patients undergoing simple diagnostic procedures, biopsy, as well as patients younger than 18-year-old and patients already taking opioid analgesics, tramadol, or NSAIDs. Patients with renal failure, advanced atrioventricular conduction abnormalities or contraindication for the use of magnesium sulfate were also excluded. Based on a study by Chen *et al.*^[9] with a power of 80% and a significance level of 0.05, a sample size of 106 patients was calculated for this study who were randomly assigned to two groups.

After matching the patients in terms of age, gender, and underlying diseases, they were randomized into two groups, Group M, 51 patients, received magnesium sulfate before surgery and Group S, 43 patients, received standard normal saline at the end of the procedure. 12 patients were excluded: 7 patients refused to participate in the study, 3 patients had insufficient baseline pain recording, and 2 patients underwent simple diagnostic procedures.

Pre-operative tests included measurement serum levels of hemoglobin, bilirubin total and direct, aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase, blood urea nitrogen and creatinine, and serum magnesium level all before and after interventions.

After admission, the patients were instructed to use a 10-point linear VAS and were asked to record his or her level

of perceived pain intensity on the scale from 0 to 10, with the zero representing no pain and the 10 representing the worst pain possible preoperatively. Patients were monitored using standard monitoring (pulse oximetry, electrocardiogram, noninvasive arterial blood pressure monitoring, and capnography). No premedication were administered for the patients. Patients received a similar anesthetic technique, after placement of routine monitoring. Induction of anesthesia was achieved with propofol (2 mg/kg) and fentanyl (1.5 µg/kg). No further opioid analgesics were administered during the intraoperative period. Anesthesia was maintained with nitrous oxide (67%) in oxygen and isoflurane (1% inspired concentration).

Before surgical incision, a pneumatic tourniquet was inflated to 350 mmHg, and the surgeon performed arthroscopic partial meniscectomy using the motorized shaver. Patients were randomized using a computer-generated randomization list into one of two groups (placebo saline group [Group S] – $n = 43$, magnesium sulfate group [Group M] – $n = 51$). Each patient received 20 ml of isotonic saline alone or containing 10 ml 10% magnesium sulfate. Study drug was injected into patient's joint by the surgeon through the arthroscope 10 min before deflation of the tourniquet. Both the anesthesiologist in charge and the surgeon were unaware of the study medication.

Pain scores were recorded by a blinded observer 5, 60, 120, and 240 min after injection of the study drug. Pain scores at rest and with the movement were recorded during each of these evaluations. A 10-cm linear VAS was used for this measurement (0 = No pain and 10 = the worst imaginable pain). Patients were discharged when they were oriented to time and place, able to void, had stable vital signs, and could ambulate with the assistance of crutches.

The first time they required additional analgesia (either intravenous [IV] opioid agents or oral analgesics) and the total analgesic requirement during the initial 24 h after surgery were documented.

Discharge time was defined as the time from the end of surgery until the patients met the discharge criteria. On discharge from the hospital, patients were instructed to take naproxen 500 mg capsule as needed for pain. Outpatient visits were scheduled at 2, 6, and 12 weeks after discharge. A standardized evaluation of symptoms and, if indicated, laboratory tests and radiologic studies were performed at each visit. In addition, data regarding hospital admissions and all performed procedures were collected, with special attention to any complication, including all additional surgical procedures.

Data are expressed as median and mean and standard deviation. Statistical significance was set at <0.05 . The calculations were performed with use of SPSS version 22.0 for Windows statistical software (SPSS Inc., Chicago, IL, USA).

RESULTS

All patients underwent knee arthroscopic partial meniscectomy performed by the same surgeon. No patient experienced hypotension (mean arterial pressure <20% baseline), hypoxemia (SpO₂ <90%), or bradycardia (heart rate <60). No patient complained of sedation, flushing or pruritus. The groups were comparable with respect to age (ages ranged from 18 to 45 years), weight range (between 56 and 110 kg) and gender distribution [Table 1].

Pain scores were significantly different among the groups both at the times 5, 60, 120, and 240 min postoperatively. Pain scores were significantly lower in Group M compared with Group S [Table 2].

The duration of analgesia was significantly different among the groups ($P=0.01$). Group M had a significantly longer time to first analgesic requirements than Group S. Group M had a significantly longer duration time to surgery requirement than Group S ($P=0.01$). Group M had significantly higher

magnesium serum level postoperatively than Group S ($P < 0.001$).

The 24 h consumption of ketorolac and opioid agents (such as pethidine) was significantly different among groups ($P < 0.001$) (Table 3). Group M consumed significantly lower doses than did Group S ($P < 0.001$). No side effects were detected from intra-articular injection of magnesium sulfate during the 24 h period after surgery, as no patient experienced a significant reduction in arterial blood pressure or heart rate (more than 15% from baseline), arrhythmia, flushing, central nervous system changes sedation, excitation, or respiratory depression. Values were recorded at the same time points as those for VAS.

CONCLUSION

This study revealed a significant analgesic benefit from the intra-articular administration of magnesium sulfate for post-operative analgesia after arthroscopic knee surgery. The analgesic effect of intra-articular magnesium sulfate after arthroscopic knee surgery has been confirmed by various studies.^[9] Patients in the group receiving intra-articular magnesium sulfate had reduced post-operative pain scores, a longer analgesic duration, and lower 24 h analgesic use compared with the other placebo group receiving intra-articular saline.

In our study, the analgesic effect of magnesium sulfate alone was significantly higher than saline, suggesting local anesthetic action as a mechanism for this analgesic effect.^[10] Patients received magnesium sulfate significantly needed lower doses of opioid agents for post-operative pain relief. The analgesic effect of magnesium may be the result of pharmacodynamics rather than a pharmacologic receptor effect. Calcium channel blockers have shown antinociceptive effects in animals and a morphine-enhancing effect in patients with chronic pain.^[11] Another study showed that using magnesium sulfate improved the quality of anesthesia and analgesia for IV regional anesthesia.^[12] Greater amounts of magnesium sulfate can be administered intra-articularly (1 g in a single joint whereas a typical systemic analgesia does would be 2 g for a 70 kg patient) may allow a much greater effect.^[13] This study, though placebo-controlled, lacked an active control for systemic magnesium sulfate effect. Perhaps, intramuscular (IM), or IV magnesium sulfate would have the same effect; thus, further studies comparing the effect of IV

Table 1: Age and gender of patients

Characteristics	Group M	Group S	P value
Age (years)	30.6±7.6	29.9±9.5	0.4
Gender, male:female	42:9	34:9	0.6
Body weight (kg)	77.9±16.9	76.4±12.6	0.9
BMI	25.8±5.4	26.3±5.2	0.5
Knee involved, right: left	30:21	21:22	0.3
Duration of surgery (min)	59.1±31	71.5±29	0.015
Time of first analgesia (min)	112.9±36.1	95.1±31.6	0.019

BMI: Body mass index

Table 2: VAS score of pain

Characteristics	Group M	Group S	P value
VAS score – 5 min	1.1±1.3	5.4±2.1	<0.001
VAS score – 60 min	0.9±1.4	4.4±2.0	<0.001
VAS score – 120 min	0.8±1.5	3.4±1.7	<0.001
VAS score – 240 min	0.2±0.9	1.9±1.7	<0.001

VAS: Visual analog scale

Table 3: Analgesics after surgery

Characteristics	Group M	Group S	P value
Magnesium serum level	1.9±0.2	1.8±31.9	<0.001
Pethidine – N, mg	3, 1.4±5.9	30, 25.8±24.4	<0.001
Ketorolac – N, mg	13, 7.6±13.2	28, 19.5±14.4	<0.001
Naproxen – N, mg	14, 127.4±214.3	19, 191.8±230.4	0.1

or IM magnesium to intra-articular injection of magnesium are also recommended. We conclude that magnesium sulfate produces a reduction in post-operative pain when given intra-articularly in comparison to saline placebo and improved post-operative analgesia. There was decrease need for post-operative analgesia and lower pain scores after arthroscopic knee surgery with no significant side effects.

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