Intra-articular magnesium is effective for postoperative analgesia in arthroscopic knee surgery†

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Background. Several medications are commonly injected intra-articularly for postoperative analgesia after arthroscopic knee surgery. Among the potentially efficient substances, magnesium could be of particular interest through its NMDA-receptor blocking properties.

Methods. A total of 60 patients undergoing arthroscopic knee surgery were randomly and double-blindly assigned to two groups to receive intra-articular injection of either 10 ml of magnesium sulphate (MgSO4) (50 mg ml−1) (Group M) or 10 ml of normal saline (Group C). Analgesic effect was evaluated by measuring pain intensity (visual analogue scale; VAS) 1, 2, 6, 8, 12, 18 and 24 h after operation and the time delay between MgSO4 or saline administration and the first requirement of supplementary analgesic medication by the patient (diclofenac).

Results. Intra-articular magnesium administration resulted in a significant reduction in pain scores in Group M compared with Group C 1, 2, 6 and 8 h after the end of surgery [1.7 (0.59), 2.2 (0.69), 2.8 (1.01) and 3.5 (1.10) in Group M; 8.0 (1.25), 5.9 (1.12), 4.4 (0.67) and 4.5 (1.13) in Group C, respectively]. A longer delay between intra-articular injection of the study medication and first administration of diclofenac was observed in Group M [667 (198) min] as compared with Group C [49 (13) min]. Total diclofenac consumption was significantly lower in Group M [37.5 (38.14) mg] than in Group C [117.5 (46.95) mg]. No early side-effects were noted.

Conclusion. Intra-articular magnesium is effective for postoperative analgesia in arthroscopic knee surgery.

Keywords: analgesia, knee surgery; analgesia, postoperative; magnesium, intra-articular; receptor, NMDA; surgery, knee

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Various drugs are commonly administered intra-articularly to provide postoperative analgesia after arthroscopic knee surgery. Among them, bupivacaine,1 morphine2 and clonidine3 have been shown to reduce postoperative pain.

N-methyl-D-aspartate (NMDA) receptors play a major role in central nociceptive transmission, modulation and sensitization of acute pain states.4 In addition to their central location, recent studies identified NMDA receptors peripherally in the skin,5 muscles6 and knee joints,7 and found that they play a role in sensory transmission of noxious signals. In its inactive state, the NMDA receptor is blocked by the presence of a centrally positioned magnesium ion. Afferent activity in nociceptor fibres dislodges the central magnesium ion from the NMDA receptor, therefore allowing calcium influx into the cell.8

Magnesium can be considered as a physiological blocker of NMDA receptors.9 Magnesium therapy has been shown to be potentially beneficial in eclampsia,10 headache,11 and acute migraine attacks.12 More recently, it has been demonstrated to reduce postoperative analgesic requirements.13 14

The aim of this study was to investigate the potential analgesic effect of magnesium when administered intra-articularly at the end of arthroscopic knee surgery.

Patients and methods

The study was conducted in the Orthopaedic Department of Ain-Shams University Hospital. After approval from the

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local Ethics Committee and informed consent, 60 ASA I–II patients undergoing elective arthroscopic meniscectomy were enrolled in the study. All surgical procedures were performed by the same surgeon (A.M. Abd El-Hady). After placement of routine monitors, induction of anaesthesia was achieved using i.v. thiopental (4 mg kg\(^{-1}\)) and fentanyl (2 \(\mu\)g kg\(^{-1}\)). No further opioid doses were administered during the surgical procedure. Anaesthesia was maintained with 60% nitrous oxide in oxygen and isoflurane (1.0–2.0% inspired concentration). Patients were randomly allocated to one of two groups using a computer-generated randomization list (n=30 for each group). Numbered, sealed and coded medical packs, each of which contained one syringe with active drug or placebo, were available. The anaesthetist, surgeon and observer were all unaware of the nature of the drug in each syringe, and the master codes were held by a personnel who did not participate in the observation. At the end of the surgery when skin was closed and before tourniquet release, the test solution was injected into the joint space. Group M patients received 10 ml of magnesium sulphate (MgSO\(_4\), 50 mg ml\(^{-1}\), that is 500 mg 5 ml\(^{-1}\) of a MgSO\(_4\) 10% solution diluted to 10 ml using saline) intra-articularly; Group C patients received 10 ml of normal saline intra-articularly. All patients were blinded to the treatment. An observer blinded to the patient’s study group assisted the patients in recording their pain scores. Pain intensity was assessed with a 10-point linear visual analogue scale (VAS). A score of 0 was described as no pain, and a score of 10 as the worse imaginable pain. Pain was scored 1, 2, 6, 8, 12, 18 and 24 h after operation.

Diclofenac sodium (75 mg) was administered i.v. as an analgesic supplement if the recorded VAS pain score was 5 or greater. Bearable pain period of time was considered as the time from intra-articular injection of the study drug to the first requirement of diclofenac. The total diclofenac consumption was also recorded. Side-effects such as flushing, sedation and reduction in heart rate and arterial pressure by more than 15% of baseline values were recorded at the same time points as those defined for VAS assessment.

Data were analysed using computer statistical software system SPSS\textsuperscript{®} version 12.0 (SPSS Inc., Chicago, IL, USA). Numerical variables were examined for normality. Patient characteristics data, operative time and time delay between intra-articular injection and supplementary analgesic administration were analysed using two-tailed unpaired \(t\)-tests. Between group differences in pain scores and total diclofenac consumption were analysed using Mann–Whitney \(U\)-test. The number of patients requiring diclofenac was compared between groups using \(\chi^2\)-test with Yates correction. Descriptive data are expressed as mean (SD). Sample size was estimated using pain scores as the primary variable. Assuming a SD of 1 cm, we calculated a group size of 30 patients would be sufficient to detect a difference of 1 cm on the VAS at an alpha threshold of 0.007 with 90% power. A \(P\)-value lower than 0.05 was considered statistically significant and adjusted to a value of 0.007 when multiple comparisons were performed, according to Bonferroni.

**Results**

All 60 patients in this study underwent an arthroscopic knee meniscectomy. All participants were males. There was no statistical difference between the groups in terms of age [group M, 27 (4) yr; and group C, 25 (4) yr]. Mean operative duration was [32 (6) min] and [33 (4) min] in group M and C, respectively.

Pain scores were significantly lower in Group M than in Group C 1, 2, 6 and 8 h after the end of surgery [1.7 (0.59), 2.2 (0.69), 2.8 (1.01) and 3.5 (1.10) in Group M; 8.0 (1.25), 5.9 (1.12), 4.4 (0.67) and 4.5 (1.13) in Group C, respectively] (Fig. 1). The difference became less apparent thereafter.

A longer delay between intra-articular injection of magnesium or saline and first rescue diclofenac administration was observed in Group M [667 (198) min] as compared with Group C [49 (13) min] \((P<0.0001)\) (Fig. 2). Total diclofenac consumption over the 24 h study period was significantly lower in Group M [37.5 (38.14) mg] than in Group C [117.5 (46.95) mg] (Table 1). No side-effects were reported during the first 24 h after surgery. Arterial pressure and heart rate did not change significantly. No patient complained of sedation.

**Discussion**

In the present study, we have shown that intra-articular administration of MgSO\(_4\) (50 mg ml\(^{-1}\)) at the end of arthroscopic knee surgery improves postoperative pain scores when compared with a situation in which no specific analgesic medication is administered to patients. It also...
we were interested in postoperative analgesia through its voltage-dependent and intrathecal administration of magnesium enhances techniques for postoperative analgesia. Because systemic knee surgery, research has been directed toward new decreases the need for other analgesic medications.

increases the time to first rescue analgesic request and decreases the need for other analgesic medications.

In conclusion, attenuation of postoperative pain articular clonidine and bupivacaine 700 min. In another study by Joshi and colleagues, the time for first analgesic request for intra-articular bupivacaine was 280 min, intra-articular clonidine and bupivacaine 600 min, intra-articular bupivacaine and morphine 720 min and combined intra-articular clonidine, bupivacaine and morphine was 950 min. In the study by Dal and colleagues, the time for first analgesic request for intra-articular ketamine was 109 min and for intra-articular neostigmine 113 min. It seems that intra-articular magnesium is much more efficient than any other sole intra-articular agent, and compares with combined agents such as intra-articular clonidine and bupivacaine, or intra-articular bupivacaine and morphine, in spite of different mechanisms of action.

Lower pain scores were observed after intra-articular administration of magnesium as compared with intra-articular saline during the first 8 h after the end of surgery, and both groups were comparable thereafter. This is probably because of the effect of random administration of diclofenac sodium on the time course of the VAS, combined with a physiological reduction in nociceptive input.

The mechanism of peripheral antinociceptive effect of NMDA antagonism has not been precisely defined. It has been hypothesized to occur through an analgesic and anti-inflammatory effect. NMDA antagonists reduce the excitability of nociceptive input terminals of C-fibres, which play a role in the central processing of pain. The anti-inflammatory action in the peripheral tissues occurs through antagonizing the release of inflammatory mediators such as histamine, cytokines and serotonin, which in turn excite nociceptors.

The analgesic effect of intra-articular magnesium is evident. It seems likely that a local effect is at least partly responsible for this, as we did not observe the side-effects usually described after systemic administration of magnesium. Even though, it is still possible that magnesium analgesic effect occurs through systemic absorption. Further studies comparing groups receiving intra-articular magnesium and i.v. saline, intra-articular saline and i.v. magnesium and intra-articular saline with i.v. saline may help to resolve these questions.

Although these results are interesting and suggest a potential application for magnesium intra-articularly, there are concerns about exposing patients to the use of a drug in an area where there is little evidence to suggest its safety. MgSO₄ has a product licence for i.v. administration. However, it may cause less pain on injection when administered intra-articularly than i.v. Furthermore, we have shown here that low concentrations of intra-articular magnesium are efficient for pain relief. Those concentrations may be safe for intra-articular tissues in the future.

In conclusion, attenuation of postoperative pain through intra-articular magnesium administration suggests a new alternative for pharmacological reduction of postoperative pain.
References


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