Egyptian Journal of Anaesthesia (2015) **31**, 239–246

HOSTED BY

ELSEVIER

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

www.elsevier.com/locate/egja
www.sciencedirect.com

Research Article

Intra-articular versus intravenous magnesium-sulfate as adjuvant to femoral nerve block in arthroscopic knee surgery under general anesthesia: Randomized controlled trial

Mohamed Abdulatif, Shereen Mostafa Maher Amin, Amina Aboul-Ela, Engy Wagdy Megalley Samuel *, Sarah Mohammed Amin Abdel-Hakim

Department of Anesthesiology, Faculty of Medicine, Cairo University, Egypt

Received 13 January 2015; revised 8 April 2015; accepted 22 April 2015
Available online 5 June 2015

KEYWORDS

Intra-articular magnesium sulfate;
Intravenous magnesium sul fate;
Femoral nerve block;
Postoperative analgesia;
Arthroscopic knee surgery

Abstract *Background:* The combined use of intra-articular (IA) or intravenous (IV) magnesium-sulfate (mgso4) with femoral nerve block might be associated with additive effects on the duration and quality of postoperative analgesia in arthroscopic knee surgery.
Patients and methods: This randomized controlled double-blind study included 90 patients. Femoral nerve block was performed in all patients using 20 ml 0.25% bupivacaine before induction of general anesthesia. At the end of surgery patients were randomly allocated into: Group-IA (intra-articular 1 g $MgSO_4$ in 20 ml), Group-IV (intravenous 1 g $MgSO_4$ in 20 ml), and Group-P (20 ml intra-articular and 20 ml intravenous normal saline). 20 ml normal saline was given IV in IA group and IA in IV group. Visual analogue pain score (VAS) at rest, with movement, time to first post-operative rescue analgesia, total postoperative diclofenac consumption, and the number of meperidine rescue doses during the first 24 h postoperatively were measured.
Results: Pain scores were comparable in the three groups at 2 and 4 h and were significantly higher in the control group at 6 h and over 24 h. Group IA had the lowest pain scores. Duration of analgesia was significantly higher [11.6 (4.5) h] in IA group compared to [7.5 (3.6) h] in IV group and [5.2 (2.3) h] in control group ($p < 0.01$). Total Diclofenac over 24 h was significantly lower in IA group [73.8 (50.9) mg] versus [138.4 (51.6) mg] in IV group and [186.0 (43.9) mg] in the control group ($p < 0.01$).

* Corresponding author. Tel.: +20 1224448234.
E-mail address: engysamuel@gmail.com (E.W.M. Samuel).
Peer review under responsibility of Egyptian Society of Anesthesiologists.

http://dx.doi.org/10.1016/j.egja.2015.04.005

Conclusion: The combined use of femoral nerve block with IA or IV $MgSO_4$ is associated with significant reduction of the intensity and duration of postoperative pain and postoperative analgesic requirements in patients undergoing arthroscopic knee surgery with the IA $MgSO_4$ being superior to IV route of administration.

1. Introduction

Acute pain from anterior cruciate ligament (ACL) reconstruction surgery has three major components: tissue injury, nociceptor sensitization, and activation of a central pathway [1,2]. Good-quality postoperative analgesia is essential for early rehabilitation after arthroscopic knee surgery [3]. Local anesthetics [4,5], opioids [6], alpha-2 adrenoceptor agonists [7,8], and magnesium sulfate $MgSO_4$ [9,10] have all been tried intra-articularly either as sole agents or in combination, to provide effective postoperative analgesia [3]. However, there is increasing evidence of a potential toxic effect of local anesthetic agents to chondrocytes within the articular cartilage [11]. In contrast, several reports have confirmed the safety of intra-articular $MgSO_4$ at the chondrocyte level [12,13]. Furthermore, intra-articular $MgSO_4$ appears to have protective effects on chondrocytes when co-administered with local anesthetics [12].

It has been reported that intra-operative intravenous $MgSO_4$ reduces analgesic requirements and improves postoperative analgesia [14]. Although the majority of studies have concluded that magnesium sulfate has a positive analgesic effect, some have produced negative results [15]. The mechanism underlying the analgesic effect of magnesium is unclear. Magnesium acts as an antagonist at N-methyl-D-aspartate (NMDA) type glutamate receptors [15]. Block of NMDA receptors is known to inhibit the induction and maintenance of central sensitization to nociceptive stimuli [15]. N-methyl-D-aspartate receptors are present in the peripheral terminal of articular primary afferent fibers and on cellular elements within the knee joint [14].

Femoral nerve block provides a superior analgesic effect for patients undergoing ACL reconstruction surgery than placebo [2]. However, when applied alone, femoral nerve block does not facilitate early recovery [2]. The outcome with continuous femoral nerve block has been shown to be better than "single shot" femoral nerve block (SFNB) and continuous epidural anesthesia [16]. Nevertheless, continuous femoral nerve block for postoperative analgesia induces a frequent rate of catheter colonization [17]. The concomitant use of single-shot femoral nerve block and intravenous or intra-articular adjuvants appears to be a logical alternative to continuous catheter techniques.

This study was designed to investigate the potential analgesic effect of intra-articular or intravenous $MgSO_4$ as adjuvant to femoral nerve block in adult patients undergoing arthroscopic ACL reconstruction under general anesthesia.

2. Patients and methods

Ninety patients with ASA physical statuses I and II aging from 18 to 60 years scheduled for arthroscopic ACL reconstruction were enrolled in this randomized controlled double-blinded study. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from each patient and is registered in the Pan African Clinical Trial Registry with an identification number (PACTR201503001053196). The study was conducted in the Orthopedic Surgical Theatre in Cairo University Hospitals. Online randomization program (http://www.randomizer.org/) and the sealed envelope method were used to allocate patient in the three study groups and to conceal this allocation.

Patients with hepatic, renal, cardiac, hematological, or respiratory impairment, diabetic patients, morbidly obese and pregnant patients with history of neuropathy, myopathy and neuromuscular diseases, patients with prior treatment with corticosteroids, calcium channel blockers, and opioids and patients with cognitive dysfunction that may interfere with the patient ability to provide reliable information about their postoperative pain all were excluded from the study.

No premedication was given to allow for reliable assessment of the femoral nerve block. Standard monitoring was applied. Femoral nerve block was performed using 20 ml bupivacaine 0.25% before induction of general anesthesia. A peripheral nerve stimulator (STIMUPLEX HNS12, B Braun, Germany) was used to localize the femoral nerve. A 22-gauge, 5-cm Contiplex® D fully insulated atraumatic needle (B Braun, Germany), was used for bupivacaine injection. Over a period of 30 min after injection of peri-neural bupivacaine and prior to induction of anesthesia, a blinded investigator assessed sensory block by testing the pinprick sensation along the medial aspect of the leg. The sensory block was graded as follows: grade 0, normal sharpness sensation (compared with the contralateral side); grade I, reduced sharpness or a non-sharp sensation (touch or pressure); and grade II, unable to recognize pinprick sensation. For motor block assessment, the patient's knee was fully flexed, and the patient was then asked to extend it. The motor block was classified as follows: grade 0, normal muscle power; grade I, motor weakness; and grade II, complete motor paralysis [9]. At the end of the 30 min assessment period, patients with inadequate femoral nerve block were excluded from the study.

After adequate assessment of femoral nerve block, general anesthesia was induced using fentanyl 2 μg/kg and propofol 2 mg/kg. An appropriately sized laryngeal mask airway (LMA) was inserted and patients were allowed to breathe spontaneously and the tidal volume was augmented with the use of pressure support ventilation mode. Anesthesia was maintained using isoflurane 2–3% end-tidal concentration in oxygen adjusted to maintain the heart rate and mean arterial blood pressure within ± 10% of their baseline values. No other analgesics were given intraoperatively.

At the conclusion of surgery, patients were randomized to one of three equal groups (n = 30): Group-IA received 20 ml intra-articular $MgSO_4$ (10 ml 10% $MgSO_4$ "1 g" diluted in

10 ml normal saline) plus 20 ml intravenous normal saline, Group-IV received Intravenous 20 ml $MgSO_4$ (10 ml 10% "1 g" $MgSO_4$ diluted in 10 ml normal saline) plus 20 ml IA normal saline, and Group-P received 20 ml intra-articular and 20 ml intravenous normal saline and served as the control group. Intravenous medications were given over 10 min.

All patients were evaluated at scheduled post-operative follow-up visits (2, 4, 6, 12, and 24 h) to assess and manage post-operative pain and to record the study outcome measures over 24 h. The primary outcome measure of this study was the intensity of postoperative pain at rest as assessed by 0–10 visual analogue pain score (VAS) where 0 = no pain and 10 = the worst unbearable pain. Secondary outcome measures were dynamic visual analogue pain score with movement (knee flexion) and the period of bearable pain (the time interval from completion of surgery until the first rescue analgesic dose was required). Diclofenac sodium (75 mg) was administered intramuscularly as an analgesic supplement if the recorded VAS pain score was 3 or greater at rest. The maximum 24 h dose of diclofenac was 200 mg. Persistent inadequate analgesia despite a maximum diclofenac dose was managed by intramuscular meperidine 1 mg/kg. The total postoperative analgesic doses of diclofenac and the number of meperidine rescue doses required during the first 24 h postoperatively were recorded. Side-effects such as shivering, flushing and reduction in heart rate and arterial pressure by more than 15% of baseline values were recorded and managed at the same time intervals as those defined for VAS assessment.

Serum magnesium levels were measured preoperatively and one hour after I.V. or intra-articular $MgSO_4$.

Based on the results of two previous studies [18,19] and assuming a SD of 1 cm in pain score, we calculated a sample size of 25 patients in each study group would be sufficient to detect a difference of 1 cm on the visual analogue score (VAS) at an α threshold of 0.05 with power of 90%. We have increased our sample size in each group to 30 patients to allow for possible dropouts.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS). Patients' demographics, time to first analgesic requirement, pain scores, and amount of postoperative analgesics were compared using One-Way Analysis of Variance (ANOVA) and Bonferroni post hoc test. Repeated measure ANOVA was used to test for significant differences over time within each of the three study groups. Chi square and Fisher Exact tests were used as appropriate for comparison of categorical data. Continuous data are reported as mean (SD). Nominal data are presented as numbers. Differences were considered statistically significant if a P of <0.05 was obtained.

3. Results

Ninety patients fulfilled the study inclusion criteria. However, 81 patients completed the study. Details of allocation, randomization, exclusion, and final number of patients analyzed in the three study groups are provided in Fig. 1. Patients in the three study groups were comparable with respect to demographic data and duration of surgery (Table 1).

Resting visual analogue pain scores were comparable in the three study groups at the 2 and 4 h assessment points. Starting at the 6 h assessment point and over the 24 h observation period, pain scores were significantly higher in the control placebo group compared to the intra-articular and intravenous $MgSO_4$ groups. Furthermore, at the 6, 12, and 24 h assessment points, the use of intra-articular $MgSO_4$ was associated with lower pain scores compared to the intravenous route of administration. The lowest pain scores in the control placebo and intravenous $MgSO_4$ groups were reported at the 2 h assessment point (Fig. 2). Dynamic pain scores adopted a similar pattern at different assessment points in the three study groups (Fig. 3).

The use of intra-articular and intravenous $MgSO_4$ was associated with significant ($p < 0.01$) prolongation of the time to first request to postoperative rescue analgesic [11.6 (4.5) h] and [7.5 (3.6) h] respectively as compared to [5.2 (2.3) h] in the placebo group. The longest duration was observed with the intra-articular MgSO4 route of administration. Intra-articular and intravenous $MgSO_4$ administration was associated with significant reduction in the total dose of diclofenac over 24 h. The least diclofenac requirements were encountered with the use of the intra-articular regimen (Fig. 4). Seven patients in the control group required rescue meperidine analgesia.

The postoperative heart rate and arterial blood pressure changes had a similar pattern in the three study groups (Figs. 5–7). At the 2 and 4 h postoperative assessment points, heart rate and arterial blood pressure values were comparable. At the 6, 12 and 24 h assessment points, heart rate and arterial blood pressure were significantly higher (but within normal limits) in the control group compared to the other two intervention groups. Furthermore, at the 6, 12 and 24 h assessment points in the control group, heart rate and arterial blood pressure were significantly higher compared to the other assessment points.

There were no episodes of hypotension or bradycardia in any patient in the three study groups. Flushing was reported in 15 patients in the intravenous $MgSO_4$ group. In contrast, intra-articular $MgSO_4$ and normal saline were not associated with flushing. Postoperative shivering was observed in 12 and 10 patients in the intra-articular and control placebo groups, respectively. None of the patients included in the intravenous $MgSO_4$ group developed postoperative shivering.

Preoperative serum magnesium levels were comparable in the three study groups. Intra-articular and intravenous administration of magnesium was not associated with significant increase in serum magnesium levels compared to the control placebo group. There was an expected trend to higher serum magnesium level in the intravenous magnesium group. However, this increase did not reach statistical significance (Table 2).

4. Discussion

The Main finding of this study is that, compared to a single injection femoral nerve block, the combined use of nerve block with equal doses of intra-articular or intravenous $MgSO_4$ in patients undergoing arthroscopic anterior cruciate ligament reconstruction is associated with significant improvement in the intensity of postoperative pain, extension of the duration of postoperative analgesia, and reduced postoperative analgesic requirements. The postoperative analgesic effects of intra-articular $MgSO_4$ were superior to the intravenous route

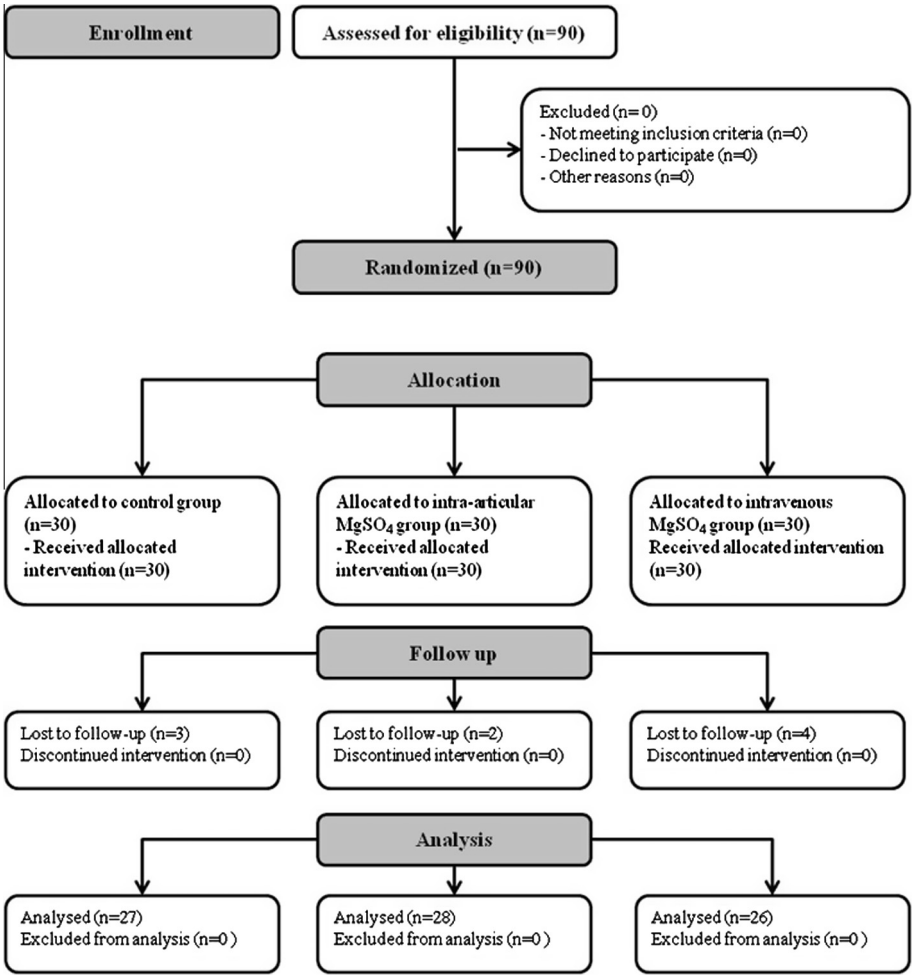

Figure 1 CONSORT flow diagram of the three study groups.

Table 1 Demographic characteristics of patients and duration of surgery. Values are means (SD) or numbers.

	Placebo (n = 27)	Intra-articular (n = 28)	Intravenous (n = 26)	P value
Age (y)	35.0 (10.4)	34.6 (9.3)	34.4 (8.3)	0.97
Weight (kg)	78.7 (11.7)	77.9 (10.7)	78.0 (11.1)	0.96
Sex (M/F)	20/7	17/11	20/6	0.61
ASA I/ASA II	18/7	17/8	19/6	0.82
Duration of surgery (min)	96.9 (9.5)	95.4 (10.8)	96.4 (7.5)	0.86

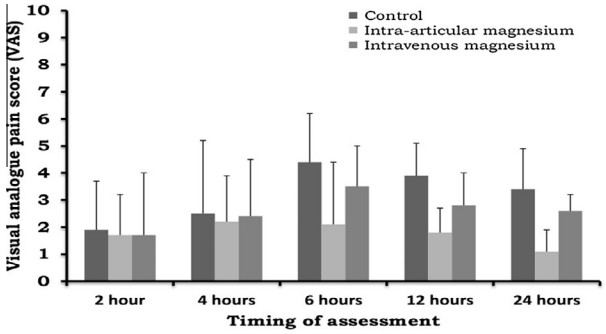

Figure 2 Visual analogue pain score at rest. Values are means and error bars represent the standard deviations.

of administration. The least postoperative analgesic requirements were encountered with the use of combined femoral nerve block and intra-articular $MgSO_4$.

This is the first report of the use of this multimodal postoperative analgesic regimen targeting pain pathway at the level of the main sensory nerve supply to the anterior aspect of the knee joint and at the peripheral receptors in the synovial membrane. Our results with intra-articular $MgSO_4$ are generally in agreement with previously published studies investigating a similar concept. Bondok and Abdel-Hady [18] studied the effect of intra-articular 500 mg $MgSO_4$ for postoperative analgesia in arthroscopic knee surgery. They reported significantly lower pain scores in the $MgSO_4$ group compared to the control group at 1, 2, 6 and 8 h after the end surgery. Radwan et al. [1] reported that intra-articular $MgSO_4$ provided postoperative analgesia after total knee arthroplasty and arthroscopic knee surgery comparable with that produced with intra-articular bupivacaine though significantly longer in duration. El-Sharnouby et al. [19], El-Bahnasawe et al. [20] and Hemida [21] in three separate studies reported more effective

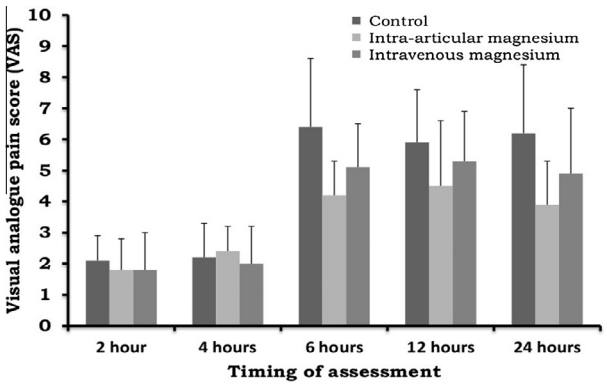

Figure 3 Dynamic visual analogue pain score. Values are means and error bars represent the standard deviations.

postoperative analgesia with the use of combination of intra-articular magnesium and bupivacaine compared to the isolated use of either medication. Intra-articular administration of $MgSO_4$ or morphine, with bupivacaine, had comparable analgesic effects [9,22]. However, the $MgSO_4$–morphine combination provided more effective postoperative analgesia than either drug alone. [22] The results obtained with the combined use of intra-articular $MgSO_4$ and bupivacaine were reproduced with the use of ropivacaine [14], and Levobupivacaine. [23].

Our study demonstrated a relatively different postoperative pain profile; the resting and the dynamic visual analogue pain scores were comparable in the three study groups at 2 and 4 h assessment points. Starting at 6 h assessment point and over the 24 h observation period, pain scores were significantly higher in the control group compared to other two groups. The values for the resting and dynamic visual analogue pain score at 2, 4 and 6 h assessment points were lower than the values reported by the above mentioned studies. Both observations could be related to the residual effect of the intraoperative femoral nerve block.

Various factors have been implicated in the intensity of pain and the effectiveness of intra-articular analgesia after knee arthroscopy. These include preoperative pain scores [24], duration of anesthesia [24], type of surgery [25], volume injected [26,27], time of intra-articular injection in relation to tourniquet deflation [27], and pain assessment at rest and movement [28]. All these factors make the large number of studies difficult to compare [1]. Neuraxial block can affect the pain scores in the early postoperative time. Therefore, in the design of this study, we used general anesthesia to allow for rapid recovery and reliable assessment of the postoperative analgesia profile.

The peripheral analgesic effects of $MgSO_4$ were also reported at the neuraxial and peri-neural levels. A recent report by Ekmekci et al. [29] demonstrated that the addition of 150 mg of $MgSO_4$ to 20 ml to levobupivacaine 0.25% prolonged the sensory and motor block duration of femoral nerve block and reduced rescue analgesic requirements in patients undergoing ACL reconstruction. However, the addition of magnesium delayed the time to first mobilization. Similar observation was reported with the combined use of $MgSO_4$ and bupivacaine for interscalene brachial plexus block [30]. Two recent systematic reviews [31,32] concluded that co-administration of intrathecal or epidural $MgSO_4$ increases the duration of neuraxial blocks. It is to be noted however that the addition of intrathecal magnesium sulfate to spinal anesthesia is not desirable in patients undergoing knee arthroscopy due to the extended duration of motor block and delayed time to ambulation [33].

In contrast to the earlier reports of intra-articular $MgSO_4$, we have included a parallel intravenous administration group using the same dose level of magnesium. The use of low dose level of intravenous $MgSO_4$ in the present study was associated with potentiation of the postoperative analgesic effects of femoral nerve block. However, intra-articular administration was superior in this context. Similarly, postoperative intravenous $MgSO_4$ infusion increased time to first perception of postoperative pain and rescue analgesic request without significant effect on the time to motor block resolution in lidocaine-induced axillary brachial plexus block [34]. The effectiveness of perioperative administration of intravenous $MgSO_4$ as an analgesic sparing regimen is considered to be a controversial issue over the past few years. However, the most recent high quality evidence derived from well conducted meta-analyses and systematic reviews indicates that systemic administration of $MgSO_4$ reduces postoperative pain scores and opioid consumption [35]. The authors concluded that intravenous $MgSO_4$ should be considered as a strategy to mitigate postoperative pain in surgical patients [36].

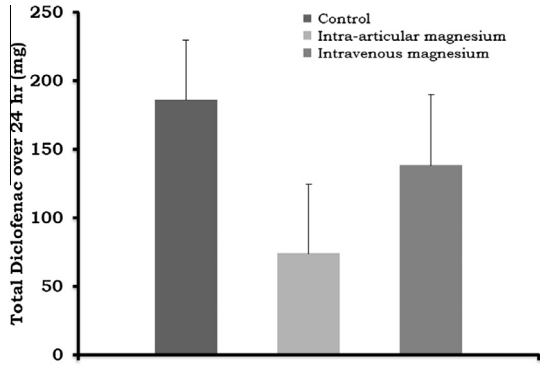

Figure 4 Total diclofenac requirements over 24 h. Values are means and error bars represent the standard deviations.

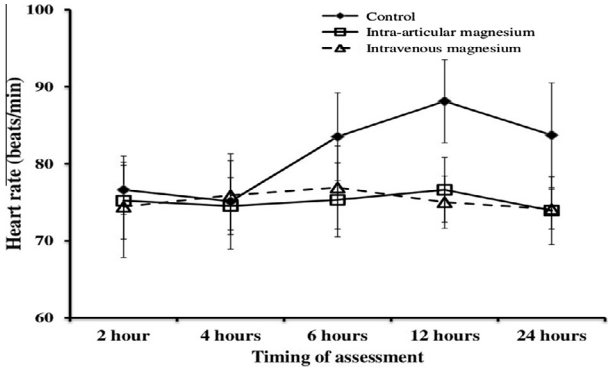

Figure 5 Postoperative heart rate changes in the three study groups. Values are means and error bars represent standard deviations.

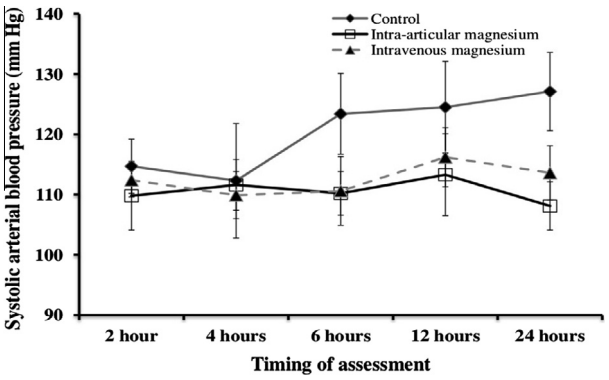

Figure 6 Systolic arterial blood pressure changes in the three study groups. Values are means and error bars represent standard deviations.

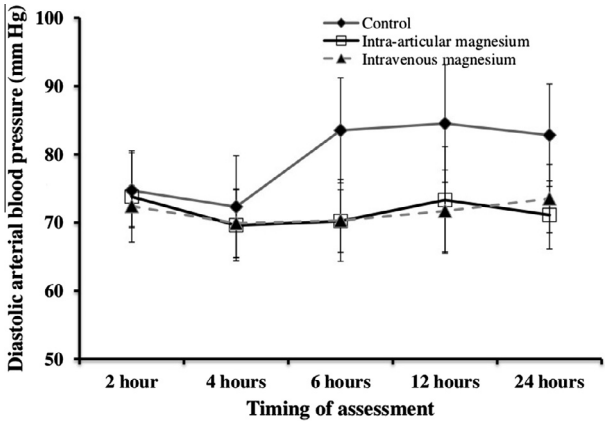

Figure 7 Diastolic arterial blood pressure changes in the three study groups. Values are means and error bars represent standard deviations.

Table 2 Serum magnesium level (mEq/L). Values are means (SD).

	Placebo (n = 27)	Intra-articular (n = 28)	Intravenous (n = 26)	P value
Preoperative	2.1 (0.12)	2.0 (0.22)	2.1 (0.28)	0.35
Postoperative	2.1 (0.2)	2.1 (0.19)	2.4 (0.18)	0.16

In the present study, the preoperative serum magnesium levels were comparable in the three study groups. Intra-articular and intra-venous administration of magnesium was not associated with significant increase in serum magnesium levels compared to the control placebo group. Trials reporting on serum magnesium concentrations in patients receiving perioperative systemic magnesium are too heterogeneous and data reporting was inconsistent to allow for a relationship between the degree of hypo-magnesemia and pain intensity [37].

In the present study, the postoperative heart rate and arterial blood pressure changes adopted a similar pattern in the three study groups. Heart rate and arterial blood pressure values were comparable at the 2 and 4 h postoperative assessment points. This is probably due to adequate postoperative analgesia provided by the residual effect of femoral nerve block. At the 6, 12 and 24 h assessment points, heart rate and arterial blood pressure were significantly higher (but within normal limits) in the control group compared to the other two intervention groups, suggesting an adequate analgesic effect of both the intra-articular and intravenous magnesium sulfate. Furthermore, in the control group, heart rate and arterial blood pressure at the 6, 12 and 24 h assessment points were significantly higher compared to the other assessment points. Inadequate control of postoperative pain is associated with increased levels of catecholamines [38].

Magnesium sulfate may induce hypotension by vasodilatation, sympathetic blockade and inhibition of catecholamine release [39]. However, no hypotensive episodes were observed with the use of the relatively low dose of intravenous $MgSO_4$. These results are supported by a study of Ozcan et al. [40] which used intravenous injection and infusion of $MgSO_4$ for patients undergoing thoracotomy.

Flushing was reported in 15 patients in the intravenous magnesium group. In contrast, none of the patients in the intra-articular magnesium or control placebo groups developed flushing. A Cochrane systematic review reported that flushing is the most common side effect of intravenous $MgSO_4$ therapy in pre-eclamptic patients [41]. The vasodilator effects of magnesium [42,43] could account for the high incidence of flushing with the use of the intravenous $MgSO_4$.

Postoperative shivering was observed in 12 and 10 patients in the intra-articular and control placebo groups, respectively. None of the patients included in the intravenous $MgSO_4$ group developed postoperative shivering. Tramér and Glynn [44] tested the effect of a single preoperative intravenous bolus of magnesium sulfate on postoperative pain and analgesic requirements in patients undergoing outpatient inguinal hernia and vein stripping surgery. They reported that postoperative shivering was significantly lower in magnesium group. Lysakowski et al. [37] performed a comprehensive search for randomized studies comparing the use of $MgSO_4$ and placebo in the surgical setting. They reported that $MgSO_4$ decreases the incidence of postoperative shivering.

The current study has some limitations: First, It is reported that the use of ultrasonography during peripheral blocks increases their effectiveness and decreases the amount of anesthetic required [45]. Ultrasound guidance for femoral nerve block was not used in the current study. Second, it would have been optimal to include two additional groups in the present study, namely intra-articular and intravenous $MgSO_4$ without femoral nerve block. This could have elucidated the approximate share of magnesium in the overall duration of postoperative analgesia. Lastly, we did not evaluate the preoperative visual analogue score for our patients. Orthopedic patients might have long standing pain states associated with central sensitization. Assessment of preoperative pain scores could have identified which patient has more potential to benefit from intra-articular $MgSO_4$ administration.

In conclusion, the combined use of femoral nerve block with equal doses of intra-articular or intravenous $MgSO_4$ in patients undergoing arthroscopic anterior cruciate ligament reconstruction under general anesthesia is associated with significant improvement in the intensity of postoperative pain, extension of the duration of postoperative analgesia, and

reduced postoperative analgesic requirements. The postoperative analgesic effects of intra-articular $MgSO_4$ were superior to the intravenous route of administration. The least postoperative analgesic requirements were encountered with the use of the intra-articular regimen.

Conflict of interest

Authors state that there is no conflict of statement.

References

[1] Radwan YA, Alfeky AA, Faramawi MF. Analgesic effect of inta-articular magnesium sulphate compared with bupivacaine after knee arthroscopic menisectomy. J Adv Res 2012;4:355–60.

[2] Peng P, Claxton A, Chung F, Chan V, Miniaci A, Krishnathas A. Femoral nerve block and ketorolac in patients undergoing anterior cruciate ligament reconstruction. Can J Anesth 1999;46:919–24.

[3] Bhattacharjee DP, Biswas C, Haldar P, Ghosh S, Piplai G, Rudra JS. Efficacy of intraarticular dexamethasone for postoperative analgesia after arthroscopic knee surgery. J Anaesthesiol Clin Pharmacol 2014;30:387–90.

[4] Dahl MR, Dasta JF, Zuelzer W, McSweeney TD. Lidocaine local anesthesia for arthroscopic knee surgery. Anesth Analg 1990;71:670–4.

[5] Chirwaa SS, MacLeod BA, Day B. Intra-articular bupivacaine (Marcaine) after arthroscopic meniscectomy: a randomized double blind controlled study. Arthroscopy 1989;5:33–5.

[6] Stein C, Comisel K, Haimerl E, Yassouridis A, Lehrberger K, Herz A, Peter K. Analgesic effect of intra-articular morphine after arthroscopic knee surgery. New Engl J Med 1991;325:1123–6.

[7] Paul S, Bhattacharjee DP, Ghosh S, Dawn S, Chatterjee N. Postoperative analgesia for arthroscopic knee surgery: a comparison between intra-articular bupivacaine alone or in combination with magnesium sulphate or clonidine. Pharmacologyonline 2009;3:938–43.

[8] Pal S, Bhattacharjee DP, Ghosh S, Dawn S, Chatterjee N. Efficacy of intra-articular dexmeditomidine for postoperative analgesia in arthroscopic knee surgery. Ceylone Med J 2010;55:111–5.

[9] Bondok R, Abd El-Hady A. Intra-articular magnesium is effective for postoperative analgesia in arthroscopic knee surgery. Br J Anaesth 2006;97:389–92.

[10] Saritas TB, Borazan H, Okesli S, Yel M, Otelcioglu Ş. Is intra-articular magnesium effective for postoperative analgesia in arthroscopic shoulder surgery? Pain Res Manag 2015;20:35–8.

[11] Baker JF, Mulhall KJ. Local anaesthetics and chondrotoxicty: what is the evidence? Knee Surg Sports Traumatol Arthrosc 2012;20:2294–301.

[12] Baker JF, Byrne DP, Walsh PM, Mulhall KJ. Human chondrocyte viability after treatment with local anesthetic and/or magnesium: results from an in vitro study. Arthroscopy 2011;27:213–7.

[13] Baker JF, Walsh PM, Byrne DP, Mulhall KJ. In vitro assessment of human chondrocyte viability after treatment with local anaesthetic, magnesium sulphate or normal saline. Knee Surg Sports Traumatol Arthrosc 2011;19:1043–6.

[14] Chen Y, Zhang Y, Zhu YL, Fu PL. Efficacy and safety of an intraoperative intra-articular magnesium/ropivacaine injection for pain control following total knee arthroplasty. J Int Med Res 2009;37:1733–41.

[15] Na HS, Lee JH, Hwang JY, Ryu JH, Han SH, Jeon YT, Do SH. Effects of magnesium sulphate on intraoperative neuromuscular blocking agent requirements and postoperative analgesia in children with cerebral palsy. Br J Anaesth 2010;104:344–50.

[16] Dauri M, Sidiropoulou T, Fabbi E, Giannelli M, Faria S, Mariani P, Sabato AF. Efficacy of continuous femoral nerve block with stimulating catheters versus nonstimulating catheters for anterior cruciate ligament reconstruction. Reg Anesth Pain Med 2007;32:282–7.

[17] Cuvillon P, Ripart J, Lalourcey L, Veyrat E, L'Hermite J, Boisson C, Thouabtia E, Eledjam JJ. The continuous femoral nerve block catheter for postoperative analgesia: bacterial colonization, infectious rate and adverse effects. Anesth Analg 2001;93:1045–9.

[18] El-Sharnouby N, Eid H, Abou Elezz N. Intra-articular injection of magnesium sulphate and/or bupivacaine for postoperative analgesia after arthroscopic knee surgery. Anesth Analg 2008;106:1548–52.

[19] Taha AM, Abd-Elmaksoud AM. Lidocaine use in ultrasound-guided femoral nerve block: what is the minimum effective anaesthetic concentration (MEAC90)? Br J Anaesth 2013;110:1040–4.

[20] El-Bahnasawe N, Shams T, El-Masry R. Intra-articular injection of magnesium sulphate and/or bupivacaine is effective for postoperative analgesia after total knee arthroplasty. EJICT 2011;1:11–6.

[21] Hemida MR. Intra-articular magnesium sulphate versus bupivacaine for postoperative analgesia in outpatient arthroscopic knee surgery. Tanta Med Sci J 2006;1:32–40.

[22] Farouk S, Aly A. A comparison of intra-articular magnesium and/or morphine with bupivacaine for postoperative analgesia after arthroscopic knee surgery. J Anesth 2009;23:508–12.

[23] Koltka K, Koknel-Talu G, Asik M, Ozyalcin S. Comparison of efficacy of intra-articular application of magnesium, levobupivacaine and lornoxicam with placebo in arthroscopic surgery. Knee Surg Sports Traumatol Arthrosc 2011;19:1884–9.

[24] Henderson RC, Campion ER, DeMasi RA, Taft TN. Post-arthroscopy analgesia with bupivacaine: a prospective, randomized, blinded evaluation. Am J Sports Med 1990;18:614–7.

[25] Haddox JD, Weissman SL, Denson DD, Hord AH, Hammonds WD. Analgesic effect of intra-articular morphine after knee surgery. New Engl J Med 1992;326:895.

[26] Heard SO, Edwards WT, Ferrari D, Hanna D, Wong PD, Liland A, Willock MM. Analgesic effect of intra-articular bupivacaine or morphine after arthroscopic knee surgery: a randomised, prospective, double-blind study. Anesth Analg 1992;74:822–6.

[27] Joshi JP, McCarroll SM, O'Brien TM, Lenane P. Intra-articular analgesia following knee arthroscopy. Anesth Analg 1993;76:333–6.

[28] Cook TM, Tuckey JP, Nolan JP. Analgesia after day-case knee arthroscopy: double-blind study of intra-articular tenoxicam, intra-articular bupivacaine and placebo. Br J Anaesth 1997;78:389–92.

[29] Ekmekci P, Bengisun ZK, Akan B, Kazbek BK, Ozkan KS, Suer AH. The effect of magnesium added to levobupivacaine for femoral nerve block on postoperative analgesia in patients undergoing ACL reconstruction. Knee Surg Sports Traumatol Arthrosc 2013;21:1119–24.

[30] Lee AR, Yi HW, Chung IS, Ko JS, Ahn HJ, Gwak MS, Choi DH, Choi SJ. Magnesium added to bupivacaine prolongs the duration of analgesia after interscalene nerve block. Can J Anesth 2012;59:21–7.

[31] Albrecht E, Kirkham KR, Liu SS, Brull R. The analgesic efficacy and safety of neuraxial magnesium sulphate: a quantitative review. Anaesthesia 2013;68:190–202.

[32] Morrison AP, Hunter JM, Halpern SH, Banerjee A. Effect of intrathecal magnesium in the presence or absence of local

anaesthetic with and without lipophilic opioids: a systematic review and meta-analysis. Br J Anaesth 2013;110:702–12.
[33] Dayioğlu H, Baykara ZN, Salbes A, Solak M, Toker K. Effects of adding magnesium to bupivacaine and fentanyl for spinal anesthesia in knee arthroscopy. J Anesth 2009;23:19–25.
[34] Anbarci O, Apan A, Sahin S. The postoperative analgesic effects of magnesium infusion on brachial plexus block. Agri 2007;19:26–31.
[35] Albrecht E, Kirkham KR, Liu SS, Brull R. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. Anaesthesia 2013;68:79–90.
[36] De Oliveira GS, Castro -Alves Jr LJ, Khan JH, McCarthy RJ. Perioperative systemic magnesium to minimize postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology 2013;119:178–90.
[37] Lysakowski C, Dumont L, Czarnetzki C, Tramer MR. Magnesium as an adjuvant to postoperative analgesia: a systematic review of randomized trials. Anesth Analg 2007;104:1532–9.
[38] Podder S, Wig J, Malhotra SK, Sharma S. Effect of pre-emptive analgesia on self-reported and biological measures of pain after tonsillectomy. Eur J Anaesthesiol 2000;17:319–24.
[39] Jee D, Lee D, Yun S, Lee C. Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy. Br J Anaesth 2009;103:484–9.
[40] Ozcan PE, Tugrul S, Senturk NM, Uludag E, Cakar N, Telci L, Esen F. Role of magnesium sulfate in postoperative pain management for patients undergoing thoracotomy. J Cardiothorac Vasc Anesth 2007;21:827–31.
[41] Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. Cochrane Database Syst Rev 2010;10.
[42] Dogan M, Peker RO, Donmez S, Gokalp O. Magnesium and diltiazem relaxes phenylephrine-precontracted rat aortic rings. Interact Cardiovasc Thorac Surg 2012;15:1–4.
[43] Landau R, Scott JA, Smiley RM. Magnesium-induced vasodilation in the dorsal hand vein. BJOG 2004;111:446–51.
[44] Tramér M, Glynn C. An evaluation of a single dose of magnesium to supplement analgesia after ambulatory surgery: randomized controlled trial. Anesth Analg 2007;104:1374–9.
[45] Akkaya A, Tekelioglu UY, Demirhan A, Ozturan KE, Bayir H, Kocoglu H, Bilgi M. Ultrasound-guided femoral and sciatic nerve blocks combined with sedo-analgesia versus spinal anesthesia in total knee arthroplasty. Korean J Anesthesiol 2014;67:90–5.