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The effect of magnesium added to levobupivacaine for femoral nerve block on postoperative analgesia in patients undergoing ACL reconstruction

Perihan Ekmekci · Zuleyha Kazak Bengisun · Burak Akan · Baturay Kansu Kazbek · Kemal Sefa Ozkan · Arif Hikmet Suer

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Abstract
Purpose The aim of this prospective randomised double-blind study is to investigate the effect of magnesium added to local anaesthetics on postoperative VAS scores, total opioid consumption, time to first mobilisation, patient satisfaction and rescue analgesic requirements in arthroscopic ACL reconstruction surgery.
Methods A total of 107 American Society of Anaesthesiologists physical status grade I and II patients between 18 and 65 years of age who were scheduled to undergo elective anterior crucial ligament (ACL) reconstruction with hamstring autografts were enrolled in the study. The patients were randomly allocated to Groups L (n = 51) and LM (n = 56) using the closed-envelope method. Group LM was administered 19 ml of 0.25 % levobupivacaine and 1 ml of 15 % magnesium sulphate, while Group L was administered 20 ml of 0.25 % levobupivacaine for femoral blockade. General anaesthesia was administered using laryngeal airway masks following neural blockade in both groups. The patients were evaluated for heart rate and mean arterial pressure, oxygen saturation, visual analogue score (VAS), verbal rating scale (VRS), rescue analgesic requirements, total opioid consumption, side effects and time to first mobilisation at the 1st, 2nd, 4th, 6th, 12th and 24th hours postoperatively.
Results There was no statistically significant difference in terms of demographic data, mean arterial pressure, heart rate or oxygen saturation between groups. The area under the curve VAS and VRS scores were lower at 4, 6, 12 and 24 h in Group LM ($p = 0.001$, $p = 0.016$, respectively). The rescue analgesic requirement and the total opioid consumption were significantly lower in Group LM ($p = 0.015$, $p = 0.019$, respectively). The time to first mobilisation and the Likert score (completely comfortable; quite comfortable; slight discomfort; painful; very painful) were higher, and the block onset time was lower in Group LM ($p = 0.014$ and $p = 0.012$, respectively). There was no difference in terms of side effects.
Conclusions The addition of magnesium to levobupivacaine prolongs the sensory and motor block duration without increasing side effects, enhances the quality of postoperative analgesia and increases patient satisfaction; however, the addition of magnesium delays the time to first mobilisation and decreases rescue analgesic requirements.

Keywords Postoperative analgesia · Femoral block · Magnesium sulphate · Anterior cruciate ligament reconstruction

P. Ekmekci · Z. K. Bengisun · B. K. Kazbek · K. S. Ozkan · A. H. Suer
Department of Anaesthesiology and Reanimation, Faculty of Medicine, Ufuk University, Ankara, Turkey

B. Akan (✉)
Department of Orthopaedic and Traumatology, Faculty of Medicine, Ufuk University, Evleri 9/B No 28 Keklikpinari Cankaya, Ankara 06420, Turkey
e-mail: burakakan1977@yahoo.co.uk

Introduction

Arthroscopic knee surgery is an outpatient surgery that is commonly performed. In addition to postoperative analgesia with narcotic analgesics and postoperative intraarticular local anaesthetic infiltration [12, 16] and hamstring donor-site block [3], femoral nerve block is an effective technique for analgesia following arthroscopic knee surgery [7, 14, 20]. Agents such as clonidine and magnesium are used as adjuvants in peripheral nerve blockade [6, 19].

In vivo and in vitro studies have shown that magnesium enhances the effect of local anaesthetics on peripheral nerves [1, 8, 9]. Studies evaluating the mechanism of action of magnesium in perineural applications have shown that it acts directly on peripheral nerves [6]. The antinociceptive effect of magnesium is linked to its N-methyl D-aspartate (NMDA) receptor blocker effect and its physiological effects as a calcium antagonist [6].

The hypothesis that the addition of magnesium sulphate to femoral nerve block in patients undergoing arthroscopic knee surgery provides better pain relief and decreases opioid consumption. The primary endpoint of this prospective randomised double-blind study is to investigate the effect of adding magnesium to local anaesthetics on postoperative VAS scores. The secondary endpoints were patient satisfaction and rescue analgesic requirements.

The combination of a local anaesthetic and magnesium sulphate demonstrates excellent safety and efficacy profiles, ensuring better postoperative pain control. Indeed, adding magnesium sulphate to femoral nerve block in patients undergoing knee surgery decreases rescue analgesic and opioid requirements. Thus, magnesium can shield patients from the side effects of analgesics and opioids.

Materials and methods

After obtaining approval from the Ufuk University Faculty of Medicine ethics committee (ID number: 08072) and written informed consent from patients, 107 American Society of Anaesthesiologists (ASA) physical status grade I and II patients between 18 and 65 years of age who were scheduled to undergo elective arthroscopic anatomic single bundle anterior crucial ligament (ACL) reconstruction were enrolled in the study.

One surgeon performed all the surgical procedures. Hamstring autografts were used in all patients, and there were no complications during surgery. Graft fixations were achieved using loop EndoButton CL® (Smith and Nephew, Mansfield, MA, USA) for the femoral fixation. Tibial fixation was performed with an oversized bioabsorbable screw (Bio-RCI HA® Smith and Nephew, Mansfield). An above-knee tourniquet was applied at 300 mm/Hg during the procedure. Patients who underwent meniscal repair, developed microfractures or exhibited Outerbridge grade III or greater chondrosis were not included in the study. Of the 23 patients with Outerbridge grade I or II chondrosis, 17 had concomitant meniscal tears. The presence of Outerbridge grade I or II chondrosis was not statistically significant. Of the 107 total patients, 23 underwent partial meniscectomy. The difference in whether partial meniscectomy was performed or not was not statistically significant (n.s.).

Additional exclusion criteria were as follows: calcium-channel or beta-blocker usage, a history of advanced renal, cardiac or hepatic disease, pregnancy, known allergy to study drugs, central or peripheral neurological disease, localised infection at the site of the femoral blockade and bleeding diathesis, obesity (BMI > 25) and a previous operation on the same knee.

The patients were randomly allocated to Group LM and were administered 19 ml of 0.25 % levobupivacaine and 1 ml of 15 % magnesium sulphate. Group L was administered 20 ml of 0.25 % levobupivacaine for femoral blockade using the closed-envelope method.

The patients were premedicated using intramuscular midazolam 0.01 mg/kg before the femoral block. Following sterilisation of the block site using povidone iodine, the block was performed 1 cm lateral to the femoral artery and 2 cm inferior to the inguinal ligament. This tissue was infiltrated with 1 ml of 2 % lidocaine using a 50 mm 22G atraumatic nerve stimulator needle (Stimuplex D, B.Braun, Melsungen Germany). The location of the femoral nerve was identified using a nerve stimulator by eliciting motor responses from the quadriceps femoris muscle and patellar motion (dancing patella) on 0.4–0.5 mA impulses. All the blocks were performed by the same experienced anaesthesiologist, who was blinded to the solution used for the femoral blockade. The development of the block was evaluated and recorded using pin-prick tests for sensory block. The Bromage scale (0: no motor block, 1: inability to raise extended legs, 2: inability to flex knees, and 3: inability to flex ankle joints) was used to determine the degree of motor block at 1, 3, 5, 10, 15 and 20 min. The authors collecting the postoperative VAS and VRS values (P.E and Z.K) were blinded to the study groups. All patients were monitored for pain intensity by using a 100 mm VAS (0 = no pain, 100 = worst pain imaginable), VRS (0 = no pain, 4 = worst pain imaginable) for pain at rest. No intraarticular injection was administered. General anaesthesia was administered using a laryngeal mask airway following neural blockade in both groups.

Propofol (3 mg/kg) was used for anaesthesia induction, and a 50–50 % oxygen-air mixture and sevoflurane 2–3 % were used for anaesthesia maintenance. Patient controlled analgesia (PCA) was initiated for postoperative analgesia (4 mg/ml tramadol in 100 cc of 0.9 % normal saline, 10 mg/h infusion, 20 mg bolus with a 15-minute lock-out time and no 4-hour limit).

The patients were evaluated for mean arterial pressure (MAP), heart rate (HR), oxygen saturation, VAS, VRS, rescue analgesic requirements, side effects after 1, 2, 4, 6, 12 and 24 h postoperatively and time to the first mobilisation. Both groups received PCA with tramadol for postoperative analgesia, and the total tramadol consumption was recorded. Total opioid consumption was calculated by multiplying the number of boluses by the amount of opioid in each bolus in milligrams. Lornoxicam (8 mg) was administered intravenously as a rescue analgesic when VAS values were $\geq$40. The patients were asked to grade their satisfaction at the 24th postoperative hour. Patient satisfaction was evaluated with a five-point Likert score (completely comfortable; quite comfortable; slight discomfort; painful; very painful).

Statistical analysis

SPSS for Windows version 15.0 was used for the statistical analyses. Quantitative variables were shown as the means, standard deviations, medians, numbers and percentages. The difference in quantitative variables between groups was calculated using the t test or the Mann–Whitney test, depending on the normal distribution, and the chi-squared test was used for qualitative variables. Variance analysis was used for repeated measurements of HR and MAP. The Mann–Whitney test was used to determine differences between groups in terms of VAS and VRS values, and the Friedman test was used to evaluate changes in each group. The level of statistical significance was set at $p = 0.05$.

Group sample sizes of 56 and 51 achieve 73 % power to detect a VAS difference of 5.0; the null hypothesis was that both group means were 10.0, and the alternative hypothesis was that the mean of group 2 is 15.0, with estimated group standard deviations of 8.0 and 11.0 and with a significance level (alpha) of 0.05 when using a two-sided Mann–Whitney test, assuming that the actual distribution is normal.

Results

A total of 107 patients were included in the study. The following patients were excluded: 4 because they underwent meniscal repair, 2 because of a failed block and 1 because of a failure to communicate in Group LM. As a result, data from 100 patients, 50 from each group, were evaluated. There was no statistically significant difference in the demographical data (Table 1) or the MAP, HR or oxygen saturation between the groups.

There was no difference in the side effects between the groups. Three patients complained of nausea, and 1 patient vomited in Group LM; in Group L, 4 patients complained of nausea and 2 patients vomited.

Twenty-one patients in Group L and 10 patients in Group LM required rescue analgesics during the postoperative period (168 mg of lornoxicam in Group L and 80 mg of lornoxicam in Group LM), ($p = 0.015$) (Table 1). The postoperative area under the curve (AUC) for the VAS, and VRS values were lower in the 4th, 6th, 12th and 24th hours in Group LM (Table I) ($p = 0.001$, $p = 0.016$, respectively). The total opioid consumption was 391.8 ± 171.7 mg and 558.8 ± 357.3 mg of tramadol in Group LM and Group L, respectively ($p = 0.019$) (Figs. 1, 2).

The block onset time was 5.8 ± 3 min and 8.7 ± 5.8 min ($p = 0.012$) in Group LM and Group L, respectively; the time to first mobilisation was 9.1 ± 6.6 and 6.0 ± 4.1 h in and Group LM and Group L, respectively ($p = 0.003$) (Table 1).

Patient satisfaction was higher in Group LM compared with Group L, ($p = 0.014$) (Table 2).

Discussion

The most important finding of the present study was that the addition of magnesium to levobupivacaine prolongs sensory and motor block duration without exacerbating the side effect profile and increases postoperative analgesia quality and patient satisfaction; however, the addition of magnesium delays the time to first mobilisation and decreases the rescue analgesic requirement.

The effectiveness of a single-shot femoral block for postoperative pain treatment in ACL reconstruction has been proven. Wulf et al. [20] reported that a single-shot femoral nerve block in 280 patients who were scheduled for ACL reconstruction provided effective postoperative analgesia.

Levobupivacaine, which is the S-enantiomer of bupivacaine, is considered a safer choice, especially in interventions involving volumes larger than 20 ml, due to its lower affinity and side effect profile in the central nervous system and the cardiovascular system [13, 15]. A study conducted by Urbanek et al. [18], in which 20 ml of 0.5 % levobupivacaine and 0.5 % bupivacaine was compared with 20 ml of 0.25 % levobupivacaine and 0.5 % bupivacaine in 60 patients scheduled for lower extremity surgery, showed that 0.25 % levobupivacaine provided a similar analgesic quality and block onset time. The present study showed that 20 ml of 0.25 % levobupivacaine also provided adequate analgesia.

Magnesium is an adjuvant that has been shown to decrease anaesthetic and analgesic requirements in various analgesia applications (intravenous, intrathecal, epidural and peripheral nerve blockade) [11]. Koinig et al. [10] have shown that the combination of preoperative (50 mg/kg) and postoperative (8 mg/kg/h) magnesium infusion decreases both intraoperative and postoperative analgesic requirements in a study involving 46 patients who were scheduled for elective arthroscopic knee surgery under general intravenous anaesthesia. Similarly, Anbarci et al. [2] have shown that a 5 mg/kg bolus and a 500 mg/h

Table 1 Demographic data

	Group LM ($n = 56$)	Group L ($n = 51$)	p
Age (year)	49.6 ± 12.1	49.3 ± 10.2	n.s.
Weight (kg)	80.8 ± 12.7	76.9 ± 13.8	n.s.
Height (cm)	166.6 ± 9.1	163.7 ± 8.8	n.s.
Gender (female/male)	34/22 (60.7 %/39.3 %)	36/15 (70.6 %/29.4 %)	n.s.
ASA (I/II)	30/26 (53.6 %/46.4 %)	29/21 (58 %/42 %)	n.s.
Duration of surgery (min)	49.4 ± 23.5 (45.0)	43.9 ± 13.3 (40.0)	n.s.
Time to mobilisation (hr)	9.1 ± 6.6 (6.0)	6.0 ± 4.1 (4.0)	0.003
Rescue analgesics	46/10 (82.1 %/17.9 %)	30/21 (58.8 %/41.2 %)	0.015
Total opioid consumption (tramadol) (mg)	391.8 ± 171.7 (380)	558.8 ± 357.3 (540)	0.019
Block onset time (min)	5.8 ± 3.0 (5)	8.7 ± 5.8 (6)	0.012
Area under curve (VAS)	55.1 ± 32.0	81.9 ± 50.0	0.001
Area under curve (VRS)	4.9 ± 1.7	5.8 ± 1.7	0.016

Group LM: 19 ml 0.25 % levobupivacaine and 1 ml 15 % magnesium sulphate for femoral blockade

Group L: 20 ml 0.25 % levobupivacaine for femoral blockade

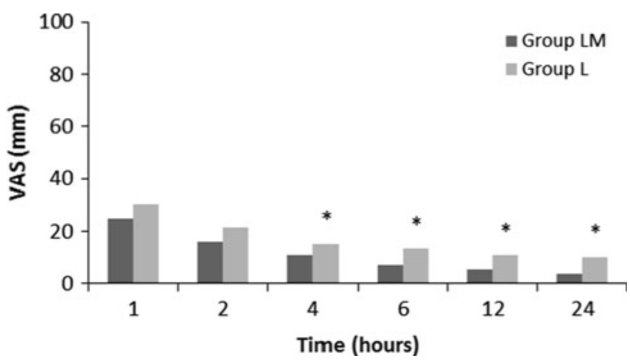

Fig. 1 Postoperative visual analogue score (VAS) values at rest among the study groups (mean ± SD). Group LM received 19 ml 0.25 % levobupivacaine and 1 ml 15 % magnesium sulphate for femoral blockade, Group L received 20 ml 0.25 % levobupivacaine for femoral blockade. *$P < 0.05$ Group LM versus Group L

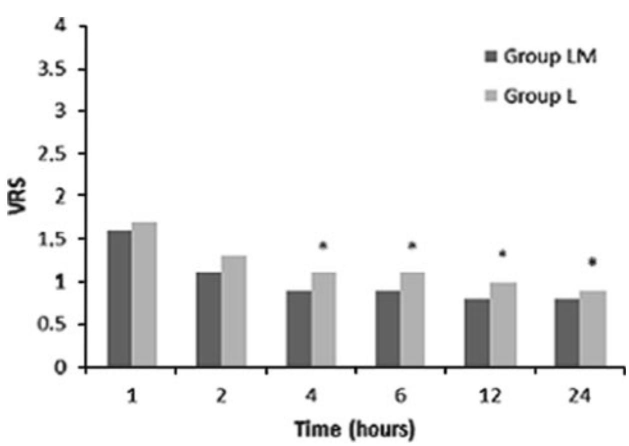

Fig. 2 Postoperative verbal rating score (VRS) values at rest among the study groups (mean ± SD). Group LM received 19 ml 0.25 % levobupivacaine and 1 ml 15 % magnesium sulphate for femoral blockade, Group L received 20 ml 0.25 % levobupivacaine for femoral blockade. *$P < 0.05$ Group LM versus Group L

magnesium infusion combined with a brachial plexus block using 40 ml of 1.25 % lidocaine prolongs sensorial block and decreases total opioid consumption in a study involving 70 patients who were scheduled for upper extremity surgery.

Magnesium was added to intrathecal fentanyl for labour analgesia in 52 patients; this approach increased median analgesia time without increasing the associated side effects [4]. Turan et al. [17] added 10 ml of 15 % magnesium to lidocaine in intravenous regional anaesthesia (IVRA) in patients who were scheduled for elective hand surgery. They demonstrated that the addition of magnesium to lidocaine in IVRA accelerates sensory and motor block onset, prolongs the block duration and the time to first analgesic requirement but decreases VAS scores and rescue analgesic consumption. Similarly, in the present study, it was observed that when added to local analgesics as an adjuvant, magnesium decreases block onset time and rescue analgesic requirement and increases the sensory and motor block. Although magnesium prolonged the time to first mobilisation because all patients were discharged at 24 h, this did not affect the overall hospitalisation duration. The AUC values for the VAS ($p = 0.001$) and VRS ($p = 0.016$) scores showed a significant reduction after the addition of magnesium to levobupivacaine.

Chanimov et al. [5] did not show neurotoxicity, based on histological examinations, in a rat model following repeated intrathecal magnesium injection. Gunduz et al. [6] have shown that 150 mg of magnesium added to axillary brachial plexus block prolonged sensory and motor block duration in 60 patients undergoing hand and forearm surgery. In the present study, 150 mg of

Table 2 Patient satisfaction (mean ± SD) *$P < 0.05$, group LM versus group L

		Group LM ($n = 56$)	Group L ($n = 51$)	p
Patient satisfaction	Completely comfortable	18 (32.1 %)	5 (9.8 %)	0.014
	Quite comfortable	13 (23.2 %)	7 (13.7 %)	
	Slight discomfort	10 (17.9 %)	12 (23.5 %)	
	Painful	6 (10.7 %)	11 (21.6 %)	
	Very painful	9 (16.1 %)	16 (31.4 %)	

Group LM: 19 ml 0.25 % levobupivacaine and 1 ml 15 % magnesium sulphate for femoral blockade

Group L: 20 ml 0.25 % levobupivacaine for femoral blockade

magnesium sulphate added to 20 ml of 0.25 % levobupivacaine in femoral nerve block prolonged the sensorial and motor block duration without any additional side effects.

The primary endpoint of this study was the effect of magnesium (when added to levobupivacaine in femoral block for ACL reconstruction) on postoperative analgesia, VAS scores. Furthermore, the secondary endpoints were patient satisfaction and rescue analgesic requirement.

The absence of a group that was administered systemic magnesium and the fact that only one dose of magnesium was evaluated can be considered limitations of this study. Further studies on the effects of different methods of magnesium administration and on different magnesium doses are necessary.

Magnesium, when added to local anaesthetics, can reduce postoperative analgesic requirements in clinical practice. Non-steroidal anti-inflammatory drugs have serious side effects; thus, magnesium can reduce the use of non-steroidal anti-inflammatory drugs and its side effects in postoperative pain management. Achieving early passive or active range of motion is very important for some knee surgeries such as total knee arthroplasty and ACL reconstruction; reducing postoperative pain may help achieve early passive or active range of motion.

Conclusions

In this study, the addition of magnesium to levobupivacaine prolonged the sensorial and motor block duration without increasing the side effect profile and improved postoperative analgesia quality and patient satisfaction; however, the addition of magnesium delayed the time to first mobilisation and decreased the rescue analgesic requirement.

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