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Research Article

Preemptive use of epidural magnesium sulphate to reduce narcotic requirements in orthopedic surgery

Abir Hassan Aly Kandil *, Raafat Abd El Azim Hammad, Mohammed Anwar El Shafei, Reem Hamdi El Kabarity, Hala Salah El Din El Ozairy

Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, Egypt

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KEYWORDS

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Abstract *Background and objectives:* As pain is one of the most common problems challenging the anesthetist, and as regional anesthesia is a safe, inexpensive technique with the advantage of prolonged postoperative analgesia. Also, we all know that Magnesium is the fourth most plentiful cation in the body with antinociceptive properties arising from being the natural physiological calcium antagonist and the antagonism to N-methyl-D-aspartate (NMDA) receptor. Thus, the study is a prospective, randomized, double-blind study designed to evaluate analgesic efficacy of magnesium sulphate when added to epidural bupivacaine in patients undergoing orthopedic surgery in the lower limb.
Methods: After approval of the ethical committee and informed written consent 60 patients ASA I and II, undergoing orthopedic surgery in the lower limb were enrolled to receive either bupivacaine 0.5% or bupivacaine 0.5% plus magnesium sulphate 50 mg as an initial bolus dose followed by a continuous infusion of 10 mg/h as intraoperative epidural analgesia. Postoperatively, all patients were equipped with a patient-controlled epidural analgesia device. Heart rate, mean arterial pressure, oxygen saturation, respiratory rate, pain assessment using a visual analogue scale (VAS), sedation score, the first time patient ask for analgesics and postoperative fentanyl consumption were recorded.

* Corresponding author. Address: PO Box 60679, Danah Homes Unit 902, Riyadh 11555, Saudi Arabia. Tel.: +966 507580152, +966 12379315.
E-mail address: abirkandil@gmail.com (A.H. Aly Kandil).

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Results: VAS was significantly less in the magnesium group during 15 and 30 min intra-operatively and in the first and third hour post-operatively. The postoperative rescue analgesia, as well as the PCEA fentanyl consumption, was significantly reduced in the magnesium group.
Conclusion: Co-administration of epidural magnesium provides better intraoperative analgesia as well as the analgesic-sparing effect on PCEA consumption without increasing the incidence of side-effects.

1. Introduction

The goals of pre-emptive analgesia are to decrease acute pain after tissue injury, prevent pathologic modulation of central nervous system caused by pain, and prevent the development of chronic pain. Regional anesthesia is an effective technique, in this regards due to its safety, efficiency, and long duration of action [1]. Research continues concerning different techniques and drugs that could prolong the duration of regional anesthesia and postoperative pain relief with minimal side effects [1]. Magnesium is the fourth most plentiful cation in the body. It has antinociceptive effects in animal and human models of pain [2,3]. Previous studies had proved that intrathecally administered magnesium prolonged the duration of action of intrathecal opioid without increasing its side effects [3]. These effects have prompted the investigation of epidural magnesium as an adjuvant for postoperative analgesia [4].

The purpose of this study is to detect the analgesic efficacy of epidural magnesium when administered with bupivacaine in patients undergoing orthopedic surgery in the lower limb.

2. Methods

After obtaining the approval of the Hospital Research & Ethical Committee and patient's informed consent, 60 ASA I and II patients of both sexes, aged 20–70 years undergoing orthopedic surgeries of the lower limb were enrolled in this randomized, double blinded placebo-controlled study. Those who had renal, hepatic impairment, cardiac disease, coagulopathy or receiving anticoagulants, spine deformity or neuropathy for any cause were excluded from the study.

Prior to surgery, we explained to the patients the epidural technique as well as the visual analogue scale (VAS; 0: no pain; 10: worst pain) and the patient-controlled epidural analgesia device (PCEA).

All the patients were assessed as regards the hemodynamics including the heart rate (HR), mean arterial pressure (MAP) and oxygen saturation (SpO2). Intravenous access had been established and an infusion of crystalloid commenced.

Before the induction of anesthesia, an epidural catheter was placed at the L3–L4 or L4–L5 intervertebral space under local anesthesia with the use of loss of resistance technique, and correct position was confirmed by injection of lidocaine 2% (3 ml) with epinephrine in concentration 1:200,000. An epidural catheter was then inserted into the epidural space. The level to be blocked was up to T10. The study was done in a double blind method using a sealed envelope technique. Patients were randomly allocated to one of two equal groups. First group (control group) received 10 ml saline via epidural catheter followed by infusion of saline 2 ml/h during the surgery. Second group (Mg group) received 50 mg magnesium sulphate ($MgSO_4$) in 10 ml as an initial bolus dose followed by infusion of 10 mg/h (2 ml/h) during the surgery. All patients received epidural bupivacaine 0.5% in a dose of 1 ml/segment.

Sensory block was assessed bilaterally by using loss of temperature sensation with an ice cube regarding the onset of analgesia and its duration. Motor block was evaluated using a modified Bromage scale (0: no motor block, 1: inability to raise extended legs, 2: inability to flex knees, 3: inability to flex ankle joints). During the course of operation, epidural bupivacaine 0.5% was given, if required, to achieve a block above T10 level. MAP, HR, SpO2 and respiratory rate (RR) were recorded before and after administration of the epidural medications and every 15 min till the end of the surgery.

When surgery was completed, all patients received PCEA using a PCEA device (Infusomat® Space, B. Braun Space, Germany) containing fentanyl 2 μg/ml and bupivacaine 0.03% (0.3 mg/ml). The PCEA was programmed to deliver 2.5ml/h infusion with a bolus dose of 1.5 ml on demand. The lockout interval between boluses was 6 min. The PCEA bolus volume was titrated according to the analgesic effect or appearance of side-effects. Patients' first analgesic requirement times were recorded. The time from end of surgery till the first use of medication by PCEA was defined as the time to the first requirement for postoperative epidural analgesia. A resting pain score of $\leqslant 3$ was considered as a satisfactory pain relief. If patients had inadequate analgesia, supplementary rescue analgesia with intramuscular pethidine 50 mg was available. MAP, HR, SpO2, RR and pain assessment using VAS were recorded on arrival to recovery, every hour for 6 h and every 6 h for 24 h in the postoperative period. Epidural fentanyl consumption was also recorded. Patients discharged to the ward when all hemodynamic variables were stable with fully resolved motor block, satisfactory pain relief, and absence of nausea and vomiting. Adverse events related with the epidural drugs (sedation, respiratory depression, nausea, vomiting, prolonged motor block) and epidural catheter were recorded throughout the 24 h study period. Sedation was assessed with a four-point Scale: 0: awake and alert, 1: mildly sedated, easily aroused, 2: moderately sedated, aroused by shaking, 3: deeply sedated, difficult to be aroused by physical stimulation. A blinded anesthesiologist who was unaware of the drug given, performed all assessments.

Statistical presentation and analysis of this study was conducted using the mean, standard error, student *t*-test, and chi square test whenever appropriate using SPSS v 17. A difference with p value < 0.05 was considered statistically significant.

3. Results

As regards the demographic data there was no significant difference between the 2 study groups (Table 1). As regards the intra-operative hemodynamics there is no significant difference between the 2 study groups (Figs. 1 and 2).

The intraoperative VAS was significantly less in magnesium group compared to control group after 15 and 30 min (Fig. 3). Whereas the postoperative VAS was significantly less in the magnesium group in the first and third postoperative hour compared to control group (Fig. 4).

The time of request for postoperative analgesia was significantly delayed and the number of patients requesting postoperative analgesia was significantly reduced in magnesium group (Fig. 5).

Moreover, the pethidine rescue analgesia consumption was significantly reduced in magnesium group compared to control group (Table 2 and Fig. 5).

The total amount of fentanyl infusion over 24 h post-operative is reduced in magnesium group than control group being 296.9 ± 56.86 μg in magnesium group and 420.67 ± 112.19 μg in control group with p value 0.0001.

No significant differences were recorded regarding the incidence of sedation or any adverse effects between groups (Table 3).

4. Discussion

The efficacy of postoperative pain therapy is a crucial issue in the functional outcome of the surgery [5]. It was evident that

Table 1 Demographic data.

	Control group (n = 30)		$MgSO_4$ group (n = 30)		
	No	%	No	%	p-Value
Gender					
Male	11	36.7	9	30.0	0.584
Female	19	63.3	21	70.0	
Age	61.9 ± 8.21	58.57 ± 7.99	0.12		
BMI					
Normal	0	0.0	2	6.7	0.152
Overweight	18	60.0	14	46.7	
Obesity	12	40.0	14	46.7	
Procedure					
Rt TKR	6	20.0	9	30.0	0.545
Lt TKR	7	23.3	7	23.3	
Bil TKR	17	56.7	13	43.3	
ORIF Tibia	0	0.0	1	3.3	
ASA					
I	7	23.3	8	26.7	0.766
II	23	76.7	22	72.2	
Duration of surgery (min)	40.3 ± 123		40.8 ± 129		0.72

TKR = Total knee replacement, ORIF = open reduction internal fixation, ASA = American society of anesthesiologist. Over weight = BMI of $>24\ Kg/m^2$, obesity = BMI of $>30\ Kg/m^2$. Morbid obesity = BMI of $>40\ Kg/m^2$. Duration of surgery expressed as mean ± SD.

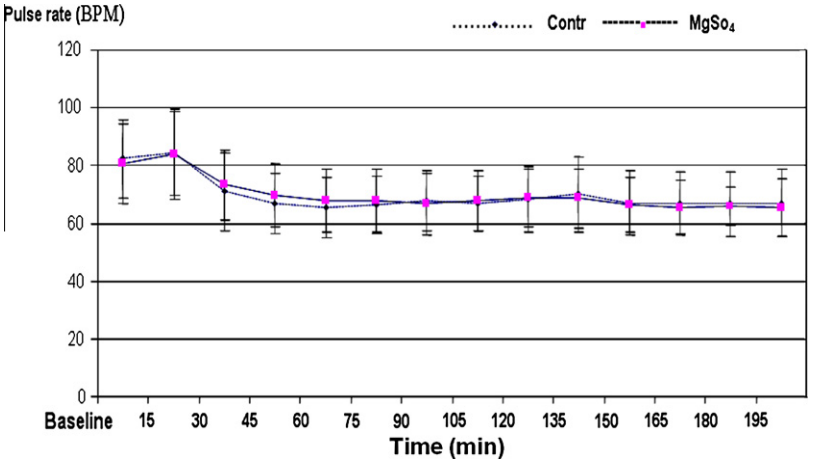

Figure 1 The intraoperative pulse rate of the study groups.

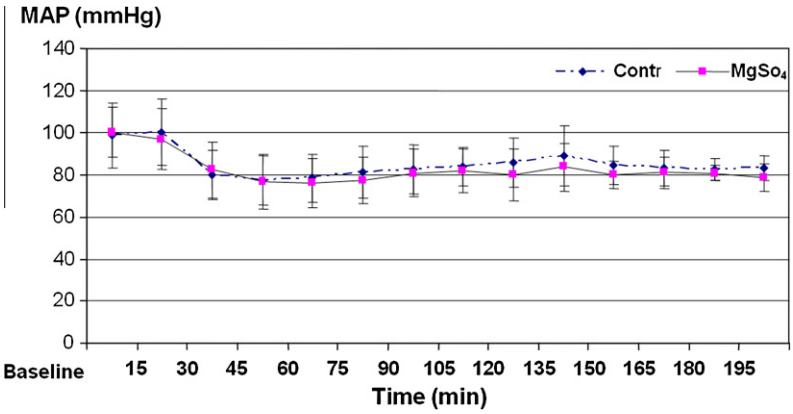

Figure 2 The intraoperative mean arterial blood pressure of study groups.

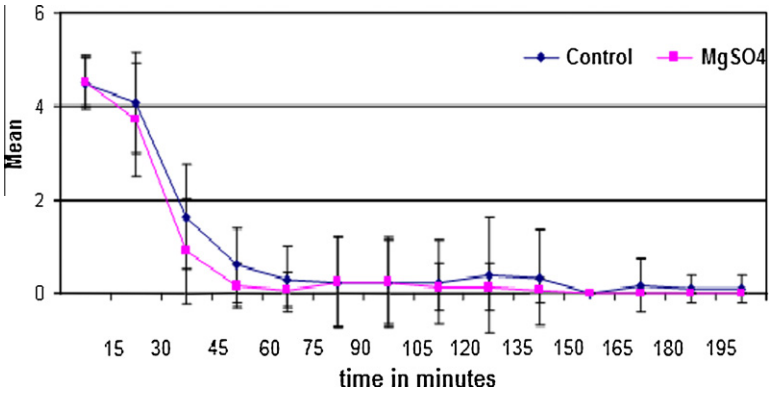

Figure 3 The intraoperative visual analogue scale of the study groups.

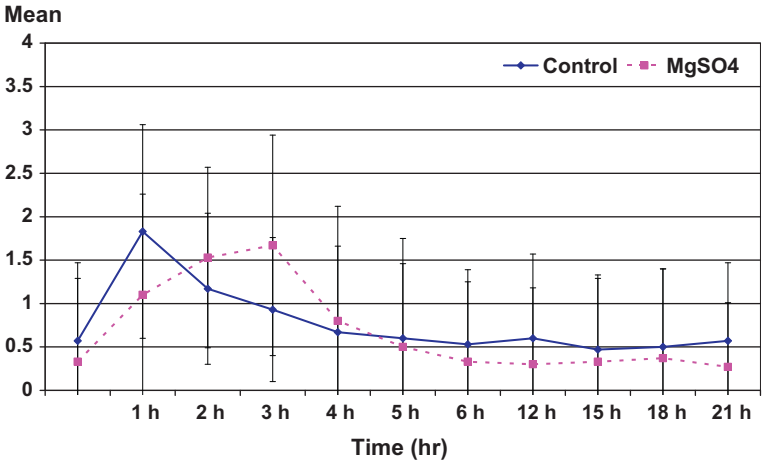

Figure 4 The postoperative visual analogue score of the study groups.

epidural analgesia regardless the agent used provides better postoperative analgesia than parental analgesia [6]. Merging of local anesthetics with adjuvants gained widespread popularity. It provides a significant analgesia which allows the reduction of the amount of local anesthetic and opioid administration for postoperative pain. Reducing the dose reduces the incidence of side effects [7].

The study demonstrates a significant improvement in VAS in the magnesium group in the intraoperative as well as in the postoperative period. The study also showed a significant reduction in the number of patients requesting early postoperative analgesia as well as total fentanyl consumption. This is indicating better control of pain in the magnesium group during both intraoperative and postoperative periods.

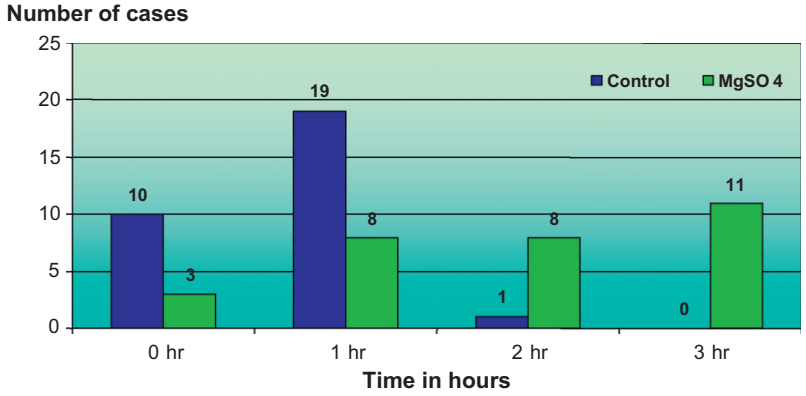

Figure 5 Time request for analgesia in study groups.

Table 2 The number of patients receiving pethidine used as rescue analgesia in the study group.

	Control		$MgSO_4$		*p*-Value
	No.	%	No.	%	
Pethidine given	21	70.0%	9	30.0%	0.002*
Amount (mg)	36.67 ± 26.04		15.00 ± 26.75		0.002*

Table 3 Complications in the study groups.

Complication	Control		$MgSO_4$		*p*-Value
	No	%	No	%	
No complication	22	73.3	24	80.0	0.753
Hypotension	5	16.7	4	13.3	
Bradycardia	2	6.7	2	6.7	
Wet tap	1	3.3	0	0.0	

The antinociceptive effects of magnesium are primarily based on the regulation of calcium influx into the cell, as a calcium antagonism and antagonism of N-methyl-D-aspartate (NMDA) receptor [1,8].

This agrees with a study done by Tanmoy and colleagues [9]. They evaluated the effect of the addition of $MgSO_4$ as an adjuvant to epidural Bupivacaine in the lower abdominal surgery. They reported reduction in the time of onset and establishment of epidural block.

Also, it agrees with Arcioni and colleagues [10] proved that combined intrathecal and epidural $MgSO_4$ supplementation reduce the postoperative analgesic requirements. Farouk and Ibrahim [11] found that the continuous epidural magnesium started before anesthesia provided preemptive analgesia, and analgesic sparing effect that improved postoperative analgesia. Also, Bilir and colleagues [4] showed that the time to first analgesia requirement was slightly longer with a significant reduction in fentanyl consumption after starting epidural $MgSO_4$ infusion postoperatively. While, Asokumar and colleagues [12] found that addition of $MgSO_4$ prolonged the median duration of analgesia after intrathecal drug administration.

On the other hand, Ko and colleagues [13] found that perioperative intravenous administration of magnesium sulfate 50 mg/kg does not reduce postoperative analgesic requirements which could be attributed to the finding that the perioperative intravenous administration of $MgSO_4$ did not increase CSF magnesium concentration due to inability to cross Blood brain barrier.

In the present study, there were no significant hemodynamic changes between groups. This is in agreement with many authors who used epidural $MgSO_4$ [4,14], and did not report any hemodynamic or respiratory instability during the observation period.

This study did not record any neurological or epidural drugs related complications postoperatively. The results agree with some of the trials that have previously examined the neurological complications of using the epidural $MgSO_4$ [4,11,12,14]. Moreover, Goodman and colleagues [15], found that inadvertent administration of larger doses MgSO4 (8.7 g and 9.6 g) through the epidural catheter did not reveal any neurological side effects.

The results did not reveal any significant difference regarding the sedation score. This is in agreement with Bilir et al. [4] and El-Kerdawy [14] who did not report any case with drowsiness or respiratory depression when using epidural magnesium.

In conclusion, co-administration of epidural magnesium provides better intraoperative analgesia as well as the analgesic-sparing effect on PCEA consumption without increasing the incidence of side-effects compared to bupivacaine alone in patients undergoing total knee replacement. The results of the present investigation suggest that magnesium may be one of the useful adjuvants to epidural analgesia.

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