Journal of Clinical Anesthesia (2016) 34, xxx–xxx

ELSEVIER

Journal of Clinical Anesthesia

Original Contribution

Magnesium sulfate improves postoperative analgesia in laparoscopic gynecologic surgeries: a double-blind randomized controlled trial☆,☆☆

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Received 30 June 2015; revised 26 April 2016; accepted 2 May 2016

Keywords:
Magnesium sulfate;
Acute pain;
Analgesia, patient controlled;
Postoperative period;
Ketorolac;
Laparoscopy

Abstract

Study objective: The aim of this study is to compare the analgesic effect of intravenous infusion of magnesium sulfate to ketorolac during laparoscopic surgeries.
Design: Double-blind randomized controlled trial.
Setting: University-affiliated teaching hospital.
Patients: Sixty women submitted to laparoscopic gynecologic oncology surgeries.
Interventions: Intravenous ketorolac 30 mg in bolus followed by saline infusion (group K), intravenous magnesium sulfate 20 mg/kg in bolus followed by magnesium 2 mg kg^{-1} h^{-1} (group M) or intravenous saline solution 20 mL in bolus followed by saline infusion during the entire procedure (group S).
Measurements: Postoperative pain, nausea, vomiting, sedation, opioid consumption, time to first dose of analgesic.
Main results: Magnesium sulfate reduced opioid consumption compared with placebo in the postoperative, but not in the intraoperative, period. Nausea, not vomiting, was reduced in ketorolac but not in the magnesium group. Pain intensity was higher in placebo than in the other 2 groups during all periods of observation. In the first 60 minutes, pain intensity was lower in the magnesium than in the ketorolac or the placebo group.

☆ Conflicts of interest: The authors declare no conflicts of interest.
☆☆ Funding: No funds provided.

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http://dx.doi.org/10.1016/j.jclinane.2016.05.006

Conclusion: Intraoperative magnesium sulfate improves postoperative pain control, acting as an opioid-sparing adjuvant, and is similar to ketorolac 30 mg administered in the beginning of surgery.

1. Introduction

Magnesium is an important ion in the body and has key roles in several physiological processes. It has been reported to potentiate lidocaine [1], induce analgesia during spinal anesthesia [2,3], improve morphine analgesia in animals [4]and humans [5], and reduce postoperative morphine consumption [6,7]. Several trials with different doses, routes, and methods of administration of magnesium have been reported, some with conflicting results [8–12].

The analgesic effect of nonsteroidal anti-inflammatory drugs (NSAIDs), on the other hand, is well documented. Nonsteroidal anti-inflammatory drugs alleviate postoperative pain by inhibiting cyclooxygenases-1 and cyclooxygenases-2 with subsequent reduction of prostanoids [13] and induction of analgesia. However, some gastrointestinal (GI), renal, and cardiovascular adverse effects prevent the use of these drugs [14].

The search for alternatives to NSAIDs as analgesics leads us to investigate magnesium sulfate, an inexpensive, safe, and easy-to-use drug that can be administered by intravenous route during the perioperative period. Few studies compared magnesium sulfate to NSAIDs [15,16].

The objective of this study is to quantify the effect of intraoperative magnesium sulfate in postoperative pain and compare these effects with saline and NSAIDs.

2. Materials and methods

After approval from the local ethics committee, written informed consent was obtained from all patients (CEP 003/11). Sixty American Society of Anesthesiologists (ASA) I-II patients undergoing laparoscopic gynecologic oncology surgeries were enrolled in this study. Exclusion criteria were as follows: chronic pain, cardiovascular, hepatic or renal disease, neuromuscular disease, diabetes, drug or alcohol abuse, obesity, patients treated with calcium channel blockers or magnesium, allergy, or contraindication to any of the drugs studied.

Patients were randomized to receive either intravenous ketorolac 30 mg in bolus followed by saline infusion (group K), intravenous magnesium sulfate 20 mg/kg in bolus followed by magnesium 2 mg kg^{-1} h^{-1} (group M), or intravenous saline solution 20 mL in bolus followed by saline infusion during the entire procedure (group S). The study used a double-blinded methodology with random allocation into 1 of the 3 groups, using sealed opaque envelopes numbered 1 to 60, containing the instructions for the study. An independent anesthesiologist not involved in the study prepared the solutions, and an observer who was also blinded to the patient's group recorded the data.

In the preoperative visit, patients who agreed to participate were instructed about visual analog scale (VAS; 0 = no pain, 100 = worst possible pain) and the patient-controlled analgesia (PCA) device.

The night before surgery, patients were premedicated with midazolam 7.5 mg per os. Upon arrival in the operating room, monitoring devices (electrocardiogram, noninvasive arterial pressure, capnography, and pulse oximetry) and a bispectral index monitor were established. An intravenous line was secured and general intravenous anesthesia was induced with target infusion remifentanil and propofol, and these drugs were adjusted according to variation in heart rate and mean arterial pressure. Cisatracurium besylate (0.5 mg/kg) was given to facilitate tracheal intubation, and controlled ventilation was adjusted to maintain normocapnia with an Fi_{O_2} of 0.5. Afterward, the study medications were administered in bolus for 20 minutes, followed by continuous infusion of the specific solution, according to the study group to which the patient belonged, as described before.

At the end of the surgery, the study drugs were discontinued before the patient was extubated. If patients presented clinical signs of residual neuromuscular blockade, they received atropine 0.01 mg/kg and neostigmine 0.04 mg/kg. All patients received dypirone 30 mg/kg in bolus, and a PCA device was connected to the intravenous line before discharge to the post anesthesia care unit (PACU). The PCA solution contained morphine 1 mg/mL in 0.9% saline, set to give bolus of 2 mL (2 mg) with a 10-minute lockout interval.

In the postoperative period, the anesthesiologist responsible for the study questioned the patients about intensity of pain, using 2 methods: VAS (0 = no pain and 100 = worst pain imaginable) and descriptive verbal scale (no pain, mild pain, moderate pain, or severe pain) at emergence from anesthesia and after 20, 30, and 60 minutes while in PACU. Time (in minutes) to the first morphine rescue, average pain intensity, and total consumption of morphine in the PACU were registered. Agitation and sedation were monitored using the Richmond Agitation-Sedation Scale [17], and patient was considered sedated if Richmond Agitation-Sedation Scale is −1 or less. Episodes of nausea, vomiting, respiratory depression, or pruritus were also recorded during PACU stay.

Patients were discharged to the ward after 60 minutes when minimum criteria for discharge were met [18].

Twenty-four hours after discharge from PACU, pain intensity score, adverse effects occurrence, and total morphine consumption were recorded. The PCA device was disconnected after 24 hours from surgery. Anesthesia and surgery duration,