A Prospective Randomized and Double-blind Study to evaluate the Efficacy of Magnesium Sulfate on Postoperative Analgesic Requirement in Patients undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Background and aims: Magnesium sulfate has recently gained popularity as an adjuvant to general anesthesia. It acts as a blocker of N-methyl D-aspartate (NMDA) antagonist and hence may have a potential role in the prevention of postoperative pain. The aim of the present prospective, randomized, double-blind, and placebo-controlled study was to evaluate the efficacy of injection magnesium sulfate 50 mg/kg as premedication upon postoperative pain and analgesic requirement in patients undergoing elective laparoscopic cholecystectomy under general anesthesia.

Materials and methods: After obtaining institutional ethical committee approval, 100 patients of American Society of Anesthesiologists (ASA) grade 1 and 2 undergoing laparoscopic cholecystectomy under general anesthesia were randomly allocated into two groups to receive either 50 mg/kg magnesium sulfate in normal saline to a total volume of 5 mL (group M, n = 50) or 5 mL of normal saline (group S, n = 50) as premedication prior to general anesthesia. The patients were continuously monitored for postoperative pain using visual analog scale (VAS) in the immediate postoperative period and subsequently at 2-hour intervals for the next 24 hours. Injection tramadol 1 mg/kg was given as the rescue analgesic (VAS ≥ 4).

Results: Both the groups were comparable with respect to demographic variables. There was no statistically significant difference in the postoperative VAS scores (p = 0.489) and tramadol requirement among the groups (p = 0.38).

Conclusion: Magnesium sulfate 50 mg/kg premedication is ineffective in reducing postoperative pain and analgesic requirement in patients undergoing laparoscopic cholecystectomy under general anesthesia.

Keywords: Adjuvants, Analgesia, Magnesium sulfate, N-methyl D-aspartate antagonists, Pain, Postoperative.

INTRODUCTION

Pain is one of the most common and feared side-effect postoperatively. Postoperative pain is associated with not only adverse physiological but also psychological (posttraumatic stress disorder) sequelae. Unrelieved pain in the immediate postoperative period can also lead to the development of chronic pain, such as chronic postherniorrhaphy pain. Peripheral sensitization, chronic sensitization, and intraoperative nerve damage may singly or in combination act as the inciting causes for the above. On the contrary, an effective postoperative pain management not only retards the above adverse sequelae but also leads to early recovery, early mobilization, reduced hospital stay, and improved patient satisfaction.

Opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) are the most common analgesics used for the management of postoperative pain but are not devoid of side-effects. The goal of postoperative pain management is alleviation of pain, its associated suffering, and at the same time, minimizing the dose and the side-effects of the analgesics. Preemptive analgesia that is administered prior to nociceptive stimulus prevents development of altered signal processing of afferent inputs from injuries. A number of drugs, such as NSAIDs, opioids, N-methyl D-aspartate (NMDA) antagonists, alpha-2 receptor blockers, etc. have used as preemptive adjuvants so as to reduce the requirement of postoperative analgesics. Magnesium sulfate has been used since many years as an antiarrhythmic as well as for prophylaxis and treatment of seizures in preeclampsia and eclampsia respectively. Among its numerous physiological actions, the ones that are most commonly exploited in the clinical practice include calcium channel antagonism, NMDA receptor antagonism, prevention of catecholamine release from adrenal.
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Materials and Methods

After obtaining approval from institutional ethics committee and written informed consent, 100 consecutive American Society of Anesthesiologists (ASA) grade I and II adult patients of age group between 18 and 60 years, of either sex undergoing laparoscopic cholecystectomy under planned general anesthesia were included in the study. Patients with uncontrolled hypertension, diabetes mellitus, cardiovascular, respiratory or renal comorbidities, allergy to any of the study drug and hypomagnesemia were excluded from the study. Pregnant and lactating mothers and patients who refused to participate in the study were also excluded. A thorough preanesthetic checkup inclusive of history, history of previous anesthesia, and 24 hours postoperatively. The intensity of pain was assessed using an 11-point NRS (0–11, 0: No pain and 10: Worst possible pain) at 0 (immediately after extubation), 2, 4, 6, 8, 12, and 24 hours postoperatively. The intensity of pain was classified using the following scoring system:

0: No pain,
1–3: Mild pain,
4–6: Moderate pain, and
7–10: Severe pain.19

The patients as well as the trained nurse involved in postoperative monitoring were unaware of the group allocation. Injection tramadol 1.5 mg/kg IV was administered as the rescue analgesic whenever NRS score was ≥7 and 24-hour consumption of tramadol was recorded.

Our primary outcomes were postoperative pain scores and total 24-hour tramadol consumption. Our secondary outcomes were the HR and systolic blood pressure (SBP) response to endotracheal intubation.
Statistical Analysis

Statistical analyses were performed using SPSS 17.0 for Windows (Statistical Package for Social Sciences, Chicago, IL, USA). Continuous variables are presented as mean±SD or median (range) for non-normally distributed data. Categorical variables are expressed as frequencies and percentages. The normally distributed continuous variables for both groups were compared using analysis of variance. Non-normal distribution continuous variables were compared using Kruskal–Wallis test. Nominal categorical data between the groups were compared using chi-squared test or Fisher’s exact test as appropriate. For all statistical tests, a p-value of <0.05 and 0.001 was taken to indicate a significant and highly significant difference respectively.

RESULTS

A total of 100 patients were recruited and completed the study. Both the groups were comparable with respect to demographic variables (Table 1). The average age was 44.18 years in group C and 42.45 years in group M. The distribution of patients in the various age groups was also comparable among the groups (Table 2). The baseline vitals were comparable among the groups (Table 3). An increase in mean heart rate after intubation was observed in both the groups but the increase was found to be statically more significant in group C (from 75.56 ± 10.081 to 95.58 ± 11.76 mm Hg) compared to group M (from 79.56 ± 14.934 to 89.28 ± 12.657 mm Hg) (Graph 1, p = 0.0114). The mean SBP increased in both the groups after intubation and after creation of pneumoperitoneum but when compared there was a statistically more significant increase in group C compared to group M (p = 0.003 and 0.009 respectively) (Table 4 and Graph 2). The mean NRS was comparable among both the groups throughout the 24-hour postoperative period (Table 5). The mean NRS was 5.307 ± 1.339 and 5.286 ± 1.601 in groups C and M respectively. No episode of bradycardia, hypotension, or any other side-effect occurred in any of the groups.

DISCUSSION

Our study results show that single-dose (50 mg/kg) magnesium sulfate IV premedication prior to induction...
of anesthesia effectively attenuates the hemodynamic stress response to endotracheal intubation. The magnesium sulfate bolus pretreatment, however, did not confer any beneficial effect with respect to reduction in postoperative pain scores or analgesic (tramadol) consumption. The previous authors investigating the analgesic efficacy of magnesium sulfate have shown conflicting results. Lysakowski et al performed a meta-analysis of 14 randomized controlled trials (RCTs) evaluating the analgesic efficacy of magnesium sulfate. In 50 and 36% of the included RCTs, the magnesium sulfate pretreatment was unable to confer any advantage with respect to placebo in reducing either the postoperative pain or the analgesic requirements. Lysakowski et al concluded that there is no convincing evidence favoring the analgesic efficacy of preoperative magnesium sulfate. Our results are also in accordance with those of Tramer et al who also did not find any impact of preoperative magnesium sulfate on postoperative pain and analgesic requirements. However, Kiran et al evaluating the efficacy of 50 mg/kg magnesium sulfate preoperatively found the study group to have less postoperative pain after inguinal surgery. As magnesium administration potentiates the action of intraoperatively administered opioids and has an opioid sparing effect, the intraoperative administration of pethidine in their study might have resulted in superior pain relief in the magnesium sulfate group. Similar results have also been reported by other authors. However, most of the authors have used a continuous intraoperative infusion of magnesium sulfate in addition to bolus of magnesium sulfate. Since our primary objective was to evaluate the analgesic efficacy of a single dose of magnesium sulfate, we did not use a continuous infusion of magnesium sulfate.

A multitude of different doses (1.2–25 gm), regimens (bolus or bolus followed by continuous infusion) as well as magnesium preparations (magnesium levulinate/glucosate/sulfate) have been used by previous authors. The conflicting results might have been due to the above variations in the dose, regimens, and the chemical preparations of magnesium used by different authors. Laryngoscopy and intubation leads to sympathetic stimulation and release of catechol amines which can lead to adverse hemodynamic responses like tachycardia, hypertension, and transient arrhythmias. Magnesium reduces the release of catecholamine from adrenal medulla and nerve endings in response to stress like laryngoscopy and intubation. We observed statistically significant increase in HR and SBP in response to endotracheal intubation in the control group compared to the magnesium sulfate premedication group. Similar stabilization of hemodynamics with respect to endotracheal intubation has been demonstrated by other authors as well. No episode of hypotension or bradycardia occurred in any of the groups in our study. The hypotension observed with magnesium sulfate is a manifestation of its calcium channel blocking action and subsequent vasodilation. This rarely occurs at doses less than 60 mg/kg. The lower doses of magnesium sulfate (50 mg/kg) used in our study might have been the reason behind the absence of hypotensive effect. Our results are in accordance with those of other authors.

**LIMITATIONS**

The main limitation of our study is that we did not measure serum magnesium levels. However, measurement of serum magnesium is an imperfect measure of total body magnesium, majority of which is intracellular and there is an imperfect correlation between them.

**CONCLUSION**

We conclude by saying that magnesium sulfate 50 mg/kg IV premedication prior to induction of anesthesia is effective in attenuating the hemodynamic stress response to surgery but has no effect on the postoperative pain or the analgesic consumption. The use of 50 mg/kg magnesium sulfate is not associated with any side-effects.
REFERENCES


