

Original article

EFFECTIVNESS OF DEXAMETASONE VS. MAGNESIUM SULPHATE IN POSTOPERATIVE ANALGESIA (DEXAMETASONE VS. MAGNESIUM SULPHATE)

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Summary

Introduction: Preoperative use of additive substances may be very helpful in perioperative acute pain management. Intravenous administration of dexametasonone in preoperative period prevents postoperative nausea and vomiting but also provides better pain relief. It is also well known that magnesium sulphate (the NMDA receptor's antagonist) by its central mechanism of action may be effective in postoperative pain control. **Aim:** The purpose of this study was to evaluate the effect of dexametasonone and magnesium sulphate on postoperative pain management in patients undergoing abdominal surgery (open cholecystectomy). **Methods:** Seventy eight patients scheduled for elective surgery (open cholecystectomy) were included in this study. This was the prospective cohort randomized placebo-controlled study. A total of 78 patients were randomized into three groups. Each group had twenty six patients. The group D, received dexametasonone 0.1 mg/kg iv 30 minutes before surgery. The group M received magnesium sulphate 3 mg/kg iv 30 minutes before surgery. The third group S was placebo group and patients in this group received saline in the same volume for each patient. For pain control after surgery all patients received tramadol 0.9–1.2 mg/kg and diklophenac 1.76 mg/kg. When necessary (VAS \geq 7), morphine sulphate in dose 0.15 mg/kg was administred subcutaneously.

For treatment of emetic episodes metoclopramid 10 mg iv. was used. The patients were observed for intensity of pain measured VAS 0–10, pain relief and satisfaction with therapy, sedation, adverse events, emetic episodes and hemodynamic parameters. **Results:** There was no difference between groups regarding demographic data (age, gender, body weight), ASA score, comorbidity, duration of surgery and anesthesia and amount of fentanyl received during surgery. In group D 11.54% of patients received additional analgesia (morphine sulphate 0.15 mg/kg sc) in the first 4 hours and 27% of patients in the first 24 hours postoperatively. In group M 38.45% of patients received additional analgesia in the first 4 hours and total of 53.8% of patients in the first 24 hours. In placebo group only 2 patients did not require additional analgesia. There was significant statistic difference between groups in morphine consumption in the first 24 hours postoperatively ($p < 0.01$). There was no side effects. **Conclusion:** Dexametasonone and magnesium sulphate given intravenously in preoperative period (30 minutes before surgery) improved pain control in first 24 hour postoperatively. Dexametasonone administered alone provided faster onset and better pain relief including prevention PONV compare with magnesium sulphate iv. There was no side effect of this therapy.

Key words: magnesium; dexametasonone; postoperative pain management

Introduction

Previous published clinical research results have shown that administration of additive substances may have an important role in acute and chronic pain management. Magnesium sulfate is used in neuropathic pain treatment, to reduce opioid tolerance risk and improve morphine substances effect¹. It is believed that analgesic mechanism of magnesium sulfate implies the NMDA receptor's antagonism and calcium ion channel's influence^{2,3}. Dexametasonone as additive substance in pain therapy implies

an inhibitory effect on prostaglandin synthesis with central mechanism, enlarge number of serotonin receptors on cell membrane, change in blood CSF barrier permselectivity to serum protein^{4,5}. Regarding this mechanism of analgesic activity, dexametasonone improves postoperative recovery of patient by providing both, analgesic and antiemetic effect.

Methods

The study was conducted with the approval of ethic committee and all patients gave informed consent. It was a prospective cohort randomized

placebo-controlled study which involved all patients undergoing abdominal surgery (open cholecystectomy) during period of three months. We enrolled 78 patients admitted in hospital for elective cholecystectomy as previously defined. They were adults between 18–60 years old, ASA status I–II and normal mini mental score. We excluded patients with peptic ulcer, malignant hypertension, ischemic coronary disease or arrhythmias, convulsions, recently cerebral insult, neuromuscular disease or history of prolonged neuromuscular block and allergic reaction to medication. After standard preoperative examination all patients received the same premedication: midazolam 0.5 mg/kg iv. and underwent surgery in general anesthesia. On admission to the operating room, before anesthesia induction, patients were randomized into 3 groups. Group D received 0.1mg/kg of dexametasone iv. 30 minutes before anesthesia. Group M received 3mg/kg of magnesium sulphate iv. 30 minutes before anesthesia. The placebo group, group S received sodium chloride iv. in the same volume 30 minutes before anesthesia. Anesthesia induction and maintenance of anesthesia was same for all patients: 3 mg/kg thiopental-sodium, 1.5 mcg/kg fentanyl, 0.15 mg/kg pancuronium and air-oxygen-isoflurane (0.8–1.5%) gases mixture. After reversal of neuromuscular

2nd, 3rd, 4th, 8th, 16th and 24th hour postoperatively. Related data were compared between groups. Postoperative pain management was provided with bolus doses diclofenac 75 bid iv. (1.76 mg/kg) and tramadol 100 mg qd iv. (0.9–1.2 mg/kg) by turn. Analgesia started with diclofenac iv. just before awakening followed with tramadol infusion after 4 hours. If recorded pain intensity score was above 7/10 by VAS both in rest and in regular activities than a rescue dose of 0.15 mg/kg morphine sulfate was administered subcutaneously. Average and total opioid daily dose was calculated in milligram morphine equivalent dose-MED. The quantity of administered morphine indicated the analgesic effect of magnesium, dexametasone and sodium chloride on pain management. Metoclopramid 10 mg tid was administered to prevent emetic episodes. Descriptive statistic methods, mean value, percentage, standard deviation was used to calculate statistic difference as significant ($p < 0.05$) or high significant ($p < 0.01$).

Results

Seventy eight patients were assessed in this study. Average age of patients was 44.46 ± 5.83 years. Regarding gender, there were 44 male and 34 female patients. We had 3 groups of patients:

Table 1: Demographic characteristics of patients among groups

	Gender (n)		Age (year; average)		Body weight (kg; average)	
	male	female	male	female	male	female
Group D	15	11	43.46	45.64	88.73	76.91
Group M	15	11	43.47	44.61	89.53	75.81
Group S	14	12	42.28	47.17	82.93	83.27

block at the end of surgery, the patients were extubated and taken in the ICU. After ICU admission the patients was requested to place a mark corresponding to the intensity of experienced pain on a VAS pain scale 0–10 on which 0 represented no pain and 10 worst possible pain. Also, patient-related data like analgesia consumption, sedation, rescue medication – additional analgesia if it was necessary, blood volume loss, hemodynamic parameters and complications were recorded for each group individually. The data were recorded in 1st,

Group M, Group D and Group S (table 1). Average pain score 8 hours after admission in ICU, was for group D = 2.67/10 by VAS, for group M = 3.78/10 by VAS and for group S = 5.28/10 by VAS. 24 hours postoperatively, mean pain score was for group D = 1.86/10 by VAS, for group M = 2.44/10 by VAS and for group S = 3.78/10 by VAS. Regarding rescue analgesia, in group D, 11.54% of patients (1 male, 2 female) had VAS score 7.29/10 and asked for rescue analgesia in the 3rd hour postoperatively. Eight hour postoperatively in the

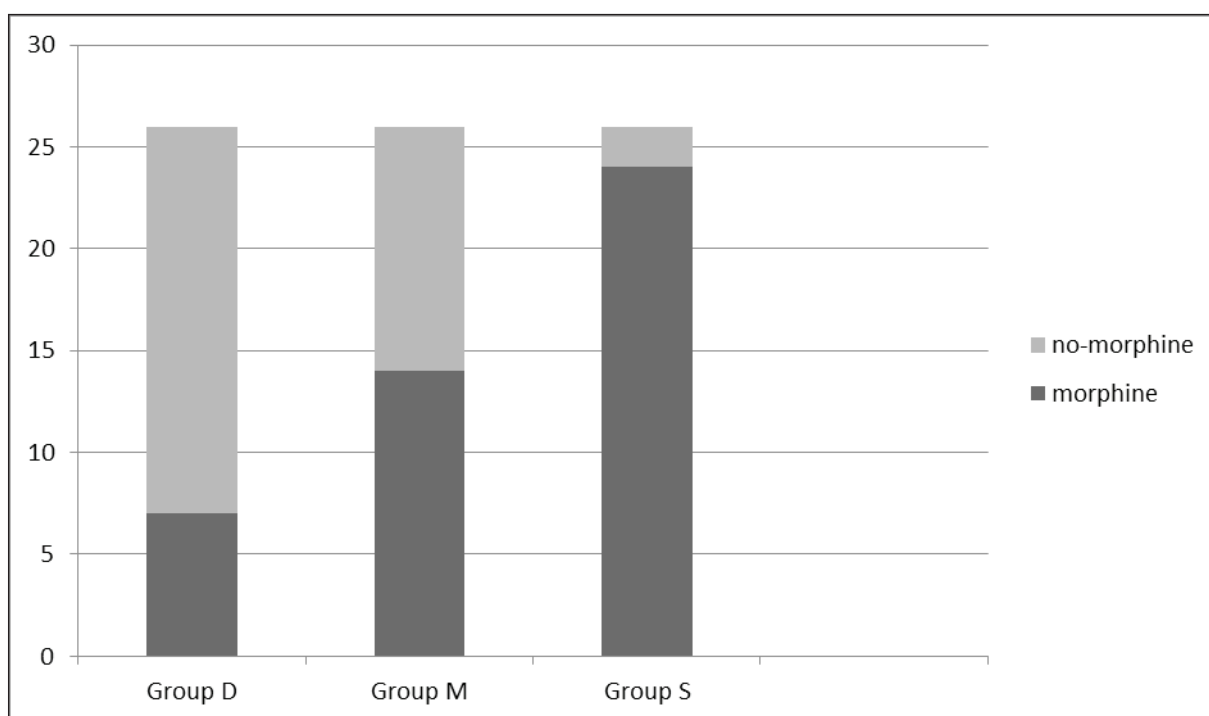
same group, 4 patients (1 male, 3 female) had pain intensity score 7,08/10 and asked for rescue analgesia, additionally. We found a significant difference in morphine (rescue analgesic) consumption regarding gender (13 male vs. 45 female) in this group of patients. Statistical analysis did not show that body weight, age or gender were significant negative predictive factors of pain control. In group M at 1st hour postoperatively average pain intensity measured via VAS was in 10 patients (5 male, 5 female) 7.18/10 and they needed rescue analgesia. Additionally, in the 8th hour postoperatively, 4 patients (3 male, 1 female) had pain score 7.24/10 and asked for rescue analgesia. In total, in group M, 14 patients (53.8%), 8 male and 6 female, asked for rescue analgesia in the first 24 hour. Like in group D, in group M statistical analysis did not confirm that body weight, age or gender were significant negative predictive factors of pain control. In placebo group, 20 patients (92.31%) had average pain score 8.31/10 by VAS and got rescue analgesia, and only 2 patients (7.7%) did not require additional analgesia. Patients in placebo group had significantly higher pain score than in other two groups. Graph 1 shows administration of additional analgesia between groups. Also, group M required rescue analgesia earlier than group D. Group M required rescue analgesia in the 1st hour after admission in ICU while pa-

tients in group D required rescue analgesia in the 3rd hour after ICU admission. Group D patients reached good pain control (VAS \leq 3) faster in the first 8 hour than patients in group M. In group M patients needed more than 8 hours after admission in ICU to reached good pain control (graph 2). Regarding emetic episodes, in group D emetic episodes did not occur, compared with other two groups where emetic episodes occurred in more than 40% of patients.

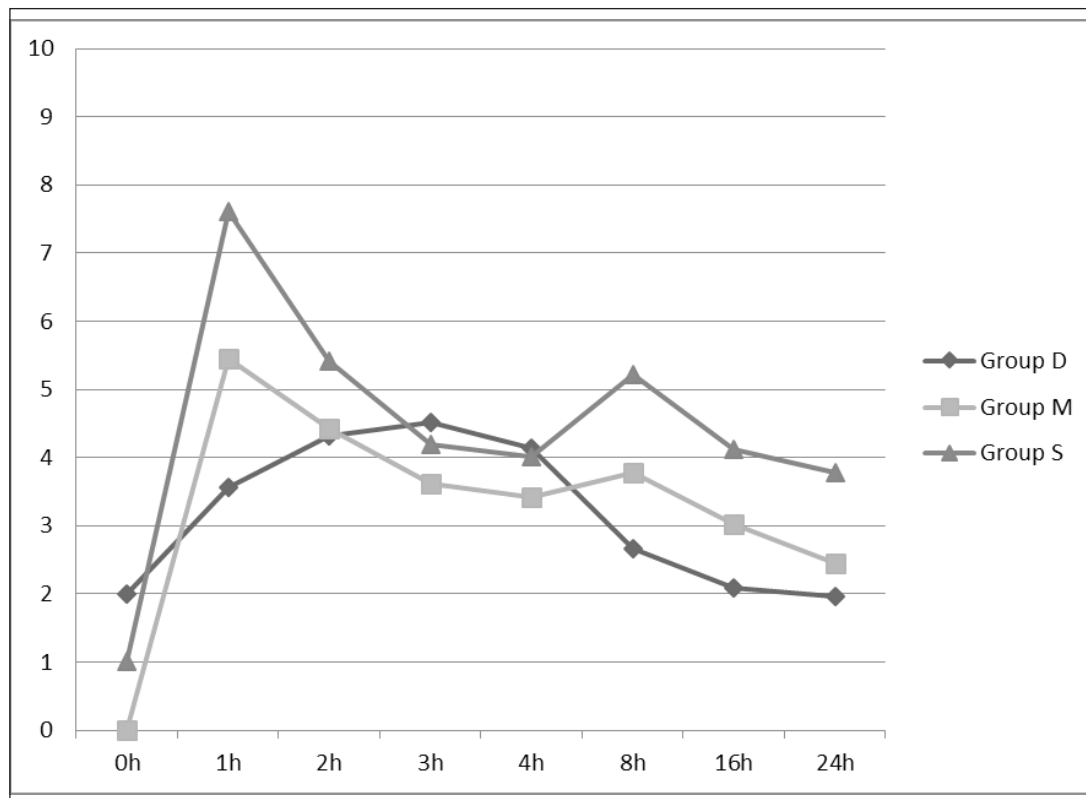
Discussion

Research studies confirmed that administration of additives in the preoperative period may have an impact on acute and chronic pain control. Albrecht et al. showed that difficulties in pain control caused by demographic characteristics were exceeded by administration of additive substances which modulate the main analgesic mechanism¹. As they showed, administration of magnesium in bolus doses in range 3–5 mg/kg followed with infusion of 500 mg provides significantly better pain control. According their opinion, the maximal safe daily dose of magnesium is 2300 mg. During administration of magnesium sulfate the only recorded side effect was bradycardia without hemodynamic consequences. As Mohammadi et al. said administration of magnesium in dose of

Graphic 1: Morphine consumption in different groups (number of patients)



Graphic 2: VAS score dynamic among groups



4 mg/kg followed infusion rate of 10/kg/h significantly improved postoperative pain management by reducing peripheral resistance of blood vessels, lower mean arterial blood pressure and shorter period of recovery bowel⁶. According to our findings, we provided significantly better postoperative pain control by administration of 3 mg/kg of magnesium without side effects compared to the control group. In group M we had high intensity pain score within the 1st hour in 53.8% of patients. After the 1st hour in this group of patients the pain control was good. In group D 0.1 mg/kg of dexametason was administered. However, good pain control onset was reached earlier and remains better compared with group M. In group D, number of patients who required rescue was significantly lower than in group M (27% vs. 53.8%). Quality of postoperative recovery was better in group D compared to group M caused by dexametason antiemetic properties. Liu et al. published recommended antiemetic dose of dexametason in range 0.15–10 mg/kg^{7,8}. Hermens and Gildasio had similar experience. They used dexametason in dose 0.15 mg/kg and 0.5 mg/kg in children, separately. They concluded that administration of different dose had no influence on emetic proph-

ylaxis^{9,10}. According to our research, a dose of 0.1 mg/kg dexametason provided good pain control as well as good emetic prophylaxis. Waldron et al. in meta-analysis about dexametason emphasizes there is no prolonged wound healing but there is reduction of pain score in the first and the second hour postoperatively provided prolonged dose intervals¹¹. We administered analgesics in bolus doses every 4 hour. Patients in group D required rescue in the 3rd hour compared with patients in group M who required rescue in the 1st hour postoperatively.

Conclusion

This study confirmed that administration of magnesium sulphate and dexametason iv. improves pain control compared to placebo group. Preoperative administration of magnesium sulfate and dexametason iv. diminishes postoperative opioid consumption and provides better postoperative pain control without side effects. Dexametason administration provided faster onset and better pain relief including prevention of emetic episodes compared to magnesium group.

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