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# Effect of two different dose regimens of magnesium sulphate on postoperative pain relief after elective inguinal hernioplasty: A randomized controlled study

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***Abstract*---Background:** Postoperative pain following hernia repair is most severe the day following surgeries, with two-thirds experiencing moderate to severe pain throughout activity, and one-third still reporting pain after one week. About 10% continue to have pain after 4 weeks. The aim of this work was to contrast the impact of two dose regimens of magnesium on post-operative pain relief in inguinal hernia surgery. **Methods:** This prospective randomized-blinded work involved 60 individuals (21-50 years old) scheduled for hernioplasty under general anesthesia. Participants had been allocated into three groups: Group A received a magnesium sulfate ($MgSO_4$) bolus (40 mg/kg) and infusion (10 mg/kg/hour) before skin incision; Group B received a $MgSO_4$bolus (40 mg / kg) diluted in 50 ml normal saline 10 mins before induction followed by equal volume of normal saline infusion started before skin incision, Group C received normal saline bolus and infusion before skin incision. **Results:** The time of first and total dose of nalbuphine and total amount of atracurium revealed a substantial reduction in group A and the other two groups. The mean


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heart rate (HR) and mean arterial pressure (MAP) had been significantly lower in group A than group B and C before intubation, one, 15, 30, 45, 60, 75, 90, 105, 120 minutes, after extubation and all postoperative period (P<0.001). A significant decrease between group A than two groups in visual analogue scale immediately after recovery, I, 3, 4, 8, 16, 20 and after 24 hours. No detected postoperative side effects observed. **Conclusions:** Peri-operative administration of $MgSO_4$ significantly reduces MAP and HR during inguinal hernia repair surgery and the 1st 24 hrs. post-operatively. Peri-operative $MgSO_4$ infusion significantly reduces the consumption of narcotics (nalbuphine) during the 1st 24 hrs.

***Keywords*---**Magnesium, Analgesia, Pain Relief, Inguinal Hernia Repair.

## Introduction

The predominant definition of pain is "An unpleasant sensory and emotional experience resulting from actual or potential tissue damage or expressed in relation to such damage." Though, later debated and many more arraying definitions were posed, yet fortunately there is a general agreement, that pain bears physical, psychosocial & psychological distress, to the unfortunate victim [1].

Acute pain usually resolves by drugs that are prescribed by the treating physician, while chronic pain needs an interdisciplinary approach conducted by a team that work together not only to relieve the pain but to enhance the quality of life for those experiencing pain. The standard pain treatment team comprises medical practitioners, physiotherapists, clinical psychologists, occupational therapists, and nurse practitioners [2].

Unmanaged postoperative pain might lead to clinical and psychological alterations that elevate fatalities and morbidity, raise expenditures, and diminish quality of life. Adverse clinical outcomes stemming from inadequate postoperative management of pain including coronary ischemia, pneumonia, myocardial infarction, impaired wound healing, pulmonary embolism, deep vein thrombosis, and insomnia. These difficulties are linked to economic and medical consequences, including prolonged hospital stays, readmissions, and patient dissatisfaction with healthcare. [3].

The therapy for symptomatic inguinal hernias is surgical intervention. The primary indication for mending is to avert the occurrence of imprisonment. This transpires when the intestine gets ensnared inside the hernia defect and could get strangulated, so obstructing blood supply to the intestinal segment. This may result in necrosis if not mitigated within a certain timeframe. [4]

Pain following hernia repair is more significant throughout movement or coughing compared to rest, and younger individuals appear to have more discomfort than older patients. Postoperative pain diminishes with time, peaking the day following

surgery, when two-thirds of patients have moderate to severe pain throughout activity. One-third continues to report moderate to severe pain following one week, and about 10% still experience such pain after four weeks. Postoperative pain is optimally managed with a combination of local analgesia and peripherally acting medicines (like paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) or their combination), whereas the consumption of opioids ought to be minimized owing to adverse effects, namely nausea and drowsiness [5]

Magnesium is the fourth most prevalent cation in the body and the second most abundant intracellular cation behind potassium, serving as a crucial regulator of intracellular biochemistry [6]. The aim of this work was to contrast the impact of two dose regimens of magnesium sulphate on post-operative pain relief in inguinal hernia surgery.

**Patients and Methods**

This prospective randomized double-blinded controlled work had been conducted on 60 individuals aged from 21 to 50 years old, both genders, American society of anesthesiologists (ASA) I and II physical status, planned for elective inguinal hernioplasty utilizing general anesthesia. The work had been conducted following approval from the Ethics Committee Al-Azhar University Hospitals, Assiut, Egypt; in the duration from Jan.2020 to Oct.2020. Subjects provided well-informed written consent.

Criteria of exclusion were any hypersensitivity to drugs used, myopathies, chronic pain patients, opioid abusers, patients on calcium channel blockers, patients with varying degrees of heart block and recurrent hernia.

**Randomization and blindness**

Patients were randomly categorized by closed envelope method into three groups equally: Group (A): obtained a magnesium sulphate ($MgSO_4$) bolus (40 mg / kg) diluted in 50 ml normal saline 10 mins before induction followed by (10 mg / kg / hour) $MgSO_4$infusion prepared in 100 ml normal saline started before skin incision, group (B): received a $MgSO_4$bolus (40 mg / kg) diluted in 50 ml normal saline 10 mins before induction followed by equal volume of normal saline infusion started before skin incision and group (C): got equal volumes of normal saline . The study medications were administered by an anaesthesiologist blinded to them.

Each participant had been exposed to complete taking of history, physical examinations, laboratory tests [Full blood picture (CBC), prothrombin time (PT), urea, creatinine and random blood sugar] and radiological investigations [Electrocardiogram for patients above 40 years].

Preoperatively, patients were fasting for 6 hours. The usage of the visual analogue scale (VAS) had been explained to participants. On arrival to the operative theatre, an 18 G cannula was inserted, patients were connected to a multichannel monitor (PM-9000 Express-Penlon limited- England) displaying: [Electrocardiograph (lead II) to monitor heart rate (HR) and to detect any

dysrhythmias, peripheral oxygen saturation ($SpO_2$) via pulse oximeter and blood pressure (mmHg)]. Patients had been additionally connected to peripheral nerve stimulator displaying train of four.

Induction of anaesthesia was done with Fentanyl (Fentanyl Hameln – Sunny Pharmaceutical - Egypt) (2μg/kg) and Propofol (Propofol-®Lipuro – B. Braun Melsungen AG - Gremany) (2mg/kg) given as IV bolus. Injection of Atracurium (Atracurium Hameln – Sunny Pharmaceutical - Egypt) as a muscle relaxant in an intubating dose of 0.5 mg/kg. Subjects had been ventilated by 100% oxygen utilising Bain circuit for 2-3 minutes and were intubated using appropriate size endotracheal tube.

For maintenance, patients were connected to anesthesia machine maintaining anesthesia by Isoflurane in 50% oxygen and air. Patients were mechanically ventilated using the following data (Tidal Volume: 6-8 ml/kg, Frequency: 10-12 bpm). Atracurium was given in top up doses (0.1mg/kg) after return of the second twitch in peripheral nerve stimulator in all groups.

Recovery:
Before skin closure patients were given 60 mg of ketorolac (Adolor – Pharco Pharmaceuticals) intravenously. At the end of operation, with recovery of train of four ratio to 0.9, neostigmine (0.04 mg/kg) and atropine (1mg) were given intravenously to reverse neuromuscular blockade.
Subjects who experienced pain rated 40 or more on the VAS received 10 mg nalbuphine (Nalufin – Amoun Pharmaceutical).

**Measurements:**
-HR and MAP were documented prior to induction (baseline reading), before intubation, one minute after intubation and then every 15 minutes throughout the procedure (MAP was maintained within 20% of the pre-induction value if increased additional bolus of fentanyl 0.5 μg/kg was administered and if decreased isoflurane percentage was decreased), immediately after full recovery and postoperatively every 4 hours for the rest of the first 24 hours.
-Intraoperative Atracurium consumption was recorded.
-Postoperative pain score using VAS was recorded, immediately after recovery and every hour for the first 4 hours then every 4 hours for the rest of the first 24 hours.
Patients who experienced pain rated 40 or more on the VAS received nalbuphine (10 mg).
-Postoperative analgesic utilization and side effects were recorded during the first 24 hours.
The primary outcome was to contrast the impacts of two different dosages of magnesium on post-operative pain relief in inguinal hernia repair surgeries. The secondary outcomes were hemodynamic stability, Intraoperative Atracurium consumption and side effects.

**Statistical analysis:**
Statistical analysis had been conducted utilising SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative parameters had been expressed as mean and standard deviation (SD) and contrasted between the three groups employing ANOVA (F) test

with post hoc test (Tukey). Qualitative parameters had been expressed as frequency and percentage (%) and had been analysed employing the Chi-square test. A two tailed P value < 0.05 was considered statistically significant.

**Results**

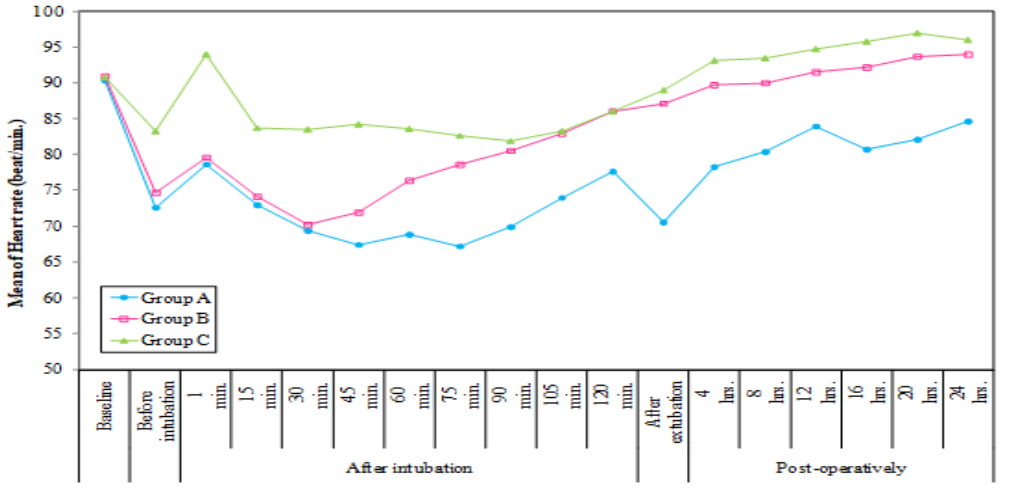
No significant variation existed between the three groups as regard the patients' age and weight. **Table 1**

Table 1: Comparison between the different studied groups according to age and weight

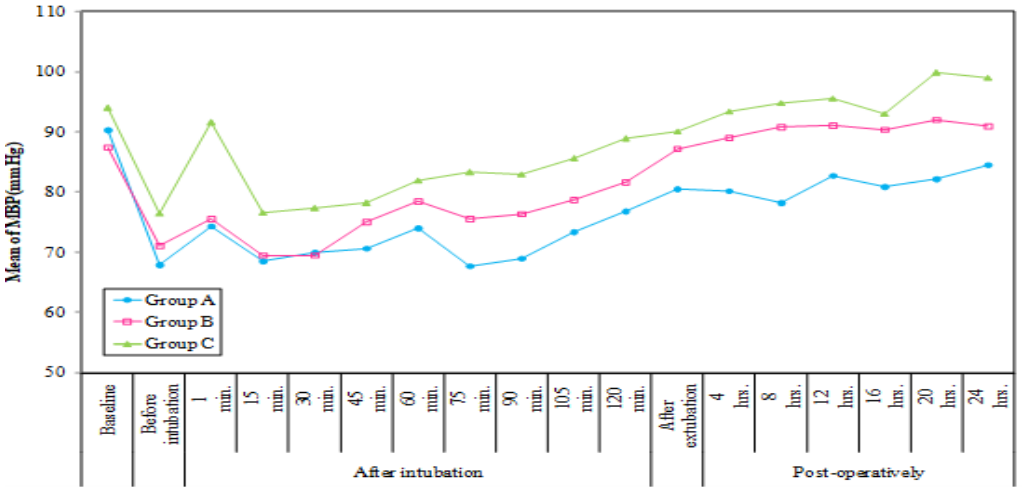
| | Group A (n=20) | Group B (n=20) | Group C (n=20) | F | P |
|---|---|---|---|---|---|
| **Age (years)** | 38.05±10.42 | 36.05±9.16 | 36.50±10.32 | 0.221 | 0.803 |
| **Weight (kg)** | 79.50±12.17 | 72.30±10.91 | 78.80±11.08 | 2.426 | 0.097 |

Data are presented as mean ± SD. F: F test (ANOVA).

Comparing the three groups, the mean HR and MAP value had been substantially reduced in group (A) relative to group (B) and (C) before intubation, one, 15, 30, 45, 60, 75, 90, 105, 120 minutes, after extubation and all through the postoperative period (P<0.001). Comparison between group B and C showed that there were significance decreases in the mean HR in group B during the intraoperative period till at 75 minutes then there was no significant difference from this time and all through the post-operative period. Comparison between group B and C revealed that there were significant decreases in the mean of the MAP in group B throughout the intraoperative period then no significant difference existed during the post-operative period except at 20 hours and 24 hours there were significant increases in group C. **Figure 1**




**(A)**




**(B)**

Figure 1: Comparison between the different studied groups according to (A) heart rate and (B)mean arterial blood pressure

In group A, B and C, immediately after recovery (zero point) the pain intensity according to VAS score was significant increased to reaching its maximum after 12 hours. Comparison between the three studied groups (P) showed that statistically significant decrease existed between group (A) and the other two groups in these readings immediately after recovery, I, 3, 4, 8, 16, 20 and after 24 hours. Comparison between group (A) and group (B) showed substantial decreases in these readings 1, 3, 8, 16, 20 and 24 hours. Comparison between group (A) and group (C) showed substantial decreases in these readings immediately after recovery, 1, 4, 8, 16, 20 and 24 hours. Comparison between group (B) and group (C) showed substantial decreases in these readings immediately after recovery, 3 hours and 24 hours. **Figure 2**

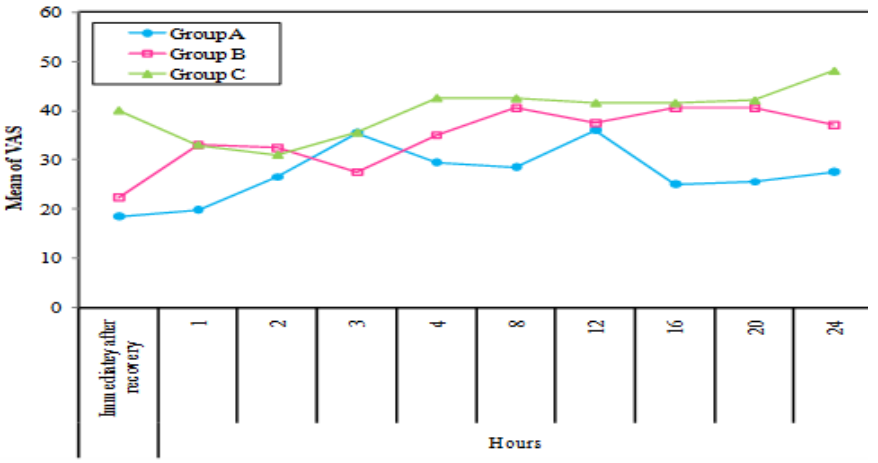



Figure 2: Comparison between the different studied groups according to visual analogue scale

The time of first and total dose of nalbuphine and total amount of atracurium showed a significant decrease in group A and the other two groups. Time of first dose of nalbuphine showed no substantial change between group B and group C. Total dose of nalbuphine showed significant decrease in group A more than group B &C. intraoperative total amount of atracurium (mg) were significantly decrease in group A more than group B & C and significant decrease in group B more than group C. **Table 2**

Table 2: Comparison between the different studied groups according to first and total dose nalbuphine and total amount of atracurium

| | | Group A (n=20) | Group B (n=20) | Group C (n=20) | Test | P |
|---|---|---|---|---|---|---|
| **First dose nalbuphine (hours)** | **1st** | 0(0.0%) | 8(40.0%) | 17(85.0%) | **$x^2$= 43.592*** | **MCp <0.001*** |
| | **2nd** | 4(20.0%) | 9(45.0%) | 3(15.0%) | | |
| | **3rd** | 9(45.0%) | 2(10.0%) | 0(0.0%) | | |
| | **4th** | 7(35.0%) | 1(5.0%) | 0(0.0%) | | |
| | | **P1<0.001*, P2<0.001*, P3=0.014*** | | | | |
| **Total dose nalbuphine (mg)** | | 15.0±4.10 | 25.0±5.71 | 35.50±8.13 | F= **128.932*** | **<0.001*** |
| | | **P1<0.001*, P2<0.001*, P3<0.001*** | | | | |
| **Total amount of atracurium (mg)** | | 45.75±5.25 | 54.50±6.51 | 65.25±6.74 | F= **109.093*** | **<0.001*** |
| | | **P1<0.001*, P2<0.001*, P3<0.001*** | | | | |

Data are presented as mean ± SD or frequency (%). * Statistically significant at $p \leq 0.05$, $P_1$: p value for comparing between group A and group B, $P_2$: p value for comparing between group A and group C, $P_3$: p value for comparing between group B and group C, F: F test (ANOVA), $\chi^2$: Chi square test, MC: Monte Carlo for Chi square test.

There were no detected postoperative side effects e.g. hypotension, nausea and vomiting.

**Discussion**

Pain is an anticipated aspect of the postoperative condition; nonetheless, insufficient pain management is prevalent and may have significant consequences. Unmanaged postoperative pain might lead to clinical and psychological alterations that elevate morbidity and mortality rates, in addition to incur expenditures that diminish quality of life [3].

Comparing the three groups, the mean HR and MAP values had been substantially decrease in group A relative to group B and C before intubation, one, 15, 30, 45, 60, 75, 90, 105, 120 minutes, after extubation and all through the postoperative period. Comparison between group B and C revealed that a substantial decreases in the mean HR in group B during the intraoperative period till at 75 minutes then there was no significant difference from this time and all through the post-operative period. Comparison between group B and C revealed that significant decreases in the mean of the MAP existed in group B throughout the intraoperative period then no significant difference existed during the post-operative period except at 20 hours and 24 hours there were significant increases in group C. In line with the findings of the current work, Seyhan TO et al. [7]

found that the decrease in MAP in the control group ranged from 7-14% while the magnesium groups ranged from 7-17% and that the HR was decreased in magnesium groups and 20 mg/ kg / h infusion group observed the lowest values. Three participants in the magnesium group who got magnesium sulphate infusion at a rate of 20 mg/kg/h demonstrated bradycardia (HR <40 beats/min) that was successfully treated by atropine injection. Also, Jee D et al. [8] documented that magnesium administration before pneumoperitoneum with $CO_2$ effectively attenuated arterial blood pressure increase in patients having laparoscopic cholecystectomy. Meanwhile, Kalra NK et al. [9] found that both magnesium and clonidine can attenuate hemodynamic responses to pneumoperitoneum and that both magnesium and clonidine individuals revealed significantly better hemodynamic control than the control group patients where there was significantly higher systolic blood pressure. In contrary to the results of the present work, Kara H et al. [10] revealed that intravenous magnesium showed no significant difference in MAP.

Regarding Efficacy of postoperative analgesia, postoperative analgesia was evaluated in the present study using the VAS, the time of the first rescue analgesics and the total opioid use in the first 24-hr postoperative period. The contrast among the examined groups showed that VAS was less in group A compared to the other two groups in these readings immediately after recovery, I, 3, 4, 8, 16, 20 and 24 hours. Comparison among group A and group B showed substantial lower VAS in these readings 1, 3, 8, 16, 20 and 24 hours postoperatively. Comparison among group A and group C showed statistically substantial lower VAS in these readings immediately after recovery, 1, 4, 8, 16, 20 and 24 hours postoperatively. Comparison among group B and group C showed statistically substantial lower VAS in these readings immediately after recovery, 3 and 24 hours postoperatively.

The time of first and total dose of nalbuphine and total amount of atracurium showed a significant decrease in group A and the other two groups. Time of first dose of nalbuphine showed no substantial change between group B and group C. Total dose of nalbuphine and total amount of atracurium had been substantially decreased in group B more than group C. In line with the present study, Kiran S et al. [11] observed that preoperative magnesium sulfate infusion reduces postoperative pain and the need for rescue analgesia. Seyhan TO et al. [7] determined that a bolus of magnesium sulfate at 40 mg/kg, then by a continuous infusion of 10 mg/kg/h, significantly reduces postoperative morphine use. Augmenting magnesium dose had no benefits but resulted in hemodynamic effects (Hypotension). In another study, Ryu JH et al. Ryu, 2009 #14} concluded that IV magnesium sulfate used throughout TIVA enhanced the quality of postoperative analgesics. Levaux C et al. [12] discovered that cumulative piritramide intake over the 24-hour research period had been decreased in the Mg group contrasted to the C group. Postoperative opioid use and pain assessments had been decreased in the magnesium cohort. Conversely, the findings of the current investigation differ with those of Ko SH et al. [13], who determined that perioperative intravenous injection of MgSO4 did not influence postoperative pain. Consistent with the current investigation, Seyhan TO et al. [7] observed that administering magnesium sulfate at a bolus dosage of 40 mg/kg, then by infusions of 10 and 20 mg/kg/h, resulted in substantial decreases in atracurium

consumption. Ryu JH et al. [14] discovered that IV magnesium sulfate throughout TIVA decreased the required for rocuronium.

There were no detected postoperative side effects. Ryu JH et al. [14] found that magnesium sulphate was correlated with a more favorable course throughout the immediate postoperative period regarding analgesics and decreasing the incidence of shivering and post-operative vomiting and nausea. Limitations of the study included that the sample size was relatively small. The work had been in a single center.

## Conclusions

Peri-operative administration of $MgSO_4$ significantly reduces MAP and HR during inguinal hernia repair surgery and the 1st 24 hrs. post-operatively. Peri-operative $MgSO_4$ infusion significantly reduces the consumption of narcotics (nalbuphine) during the 1st 24 hrs. post-operatively. Peri-operative $MgSO_4$ administration in regimen of (40 mg/kg bolus IV followed by 10 mg/kg/hr. continuous IV infusion during surgery) more effective than just IV bolus of 40 mg/kg preoperatively in inguinal hernia surgery. Peri-operative $MgSO_4$ infusion significantly potentiates the effect of non-depolarizing muscle relaxants (atracurium) intraoperatively.

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**Conflict of Interest:** Nil

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