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Original Research Article

Comparison of Intravenous and Intraperitoneal Magnesium Sulfate in Post Operative Analgesia Following Laparoscopic Cholecystectomy

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Abstract: *Laparoscopic cholecystectomy is associated with postoperative pain, primarily due to peritoneal irritation. Magnesium sulfate, an NMDA receptor antagonist, is increasingly being used as an adjuvant for pain relief. This study aimed to compare the analgesic efficacy of intravenous (IV) versus intraperitoneal (IP) magnesium sulfate administration in patients undergoing laparoscopic cholecystectomy in a tertiary care hospital in Pakistan.* ***Methods:*** *This Prospective comparative study was conducted at Aziz Bhatti Shaheed Hospital, Gujrat, from November 2022 to November 2023. A total of 84 patients undergoing elective laparoscopic cholecystectomy were randomized into two equal groups. Group A received 30 mg/kg magnesium sulfate intravenously after induction, while Group B received the same dose intraperitoneally after gallbladder removal. Pain scores were measured using the Visual Analogue Scale (VAS) at 1, 4, 8, 12, and 24 hours postoperatively. Secondary outcomes included time to first rescue analgesia, total tramadol consumption, and adverse events.* ***Results:*** *Demographic variables were comparable between groups. The IP group showed significantly lower VAS pain scores from 4 hours onwards ($p < 0.05$). Mean time to first rescue analgesia was significantly longer in the IP group (138.6 ± 31.2 minutes) versus the IV group (97.4 ± 25.6 minutes) ($p < 0.001$). Total 24-hour tramadol consumption was lower in the IP group (82.1 ± 16.7 mg) compared to the IV group (102.3 ± 18.4 mg) ($p < 0.001$). No significant differences were observed in adverse events between groups.* ***Conclusion:*** *Intraperitoneal administration of magnesium sulfate is more effective than intravenous administration in reducing postoperative pain, delaying the need for rescue analgesia, and lowering total opioid consumption after laparoscopic cholecystectomy. It is also safe and well tolerated.*

Keywords: Magnesium sulfate, intraperitoneal, intravenous, laparoscopic cholecystectomy, postoperative pain

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Introduction

Laparoscopic cholecystectomy (LC) is the gold standard for the treatment of symptomatic gallbladder diseases due to its minimal invasiveness, reduced hospital stay, and faster recovery. However, patients still experience moderate to severe postoperative pain, particularly in the first 24 hours, which may lead to delayed mobilization, increased opioid consumption, and prolonged hospitalization (1, 2). In Pakistan, LC is one of the most frequently performed elective surgeries at tertiary care hospitals, making the optimization of perioperative analgesia a clinical priority (3).

Magnesium sulfate ($MgSO_4$), a non-opioid analgesic adjunct, has gained attention due to its ability to block N-methyl-D-aspartate (NMDA) receptors and calcium channels, both involved in nociceptive transmission and central sensitization (4). Several randomized controlled trials and meta-analyses have evaluated the efficacy of magnesium sulfate in attenuating postoperative pain when administered either intravenously or intraperitoneally, with promising results in terms of reducing visual analogue scale (VAS) scores and total analgesic requirement (5, 6).

A recent study conducted in India demonstrated that intraperitoneal magnesium sulfate significantly reduced pain scores and delayed the need for rescue analgesia in patients undergoing LC (7). Likewise, intravenous magnesium sulfate has also shown comparable benefits, especially when used as a preemptive analgesic (8). However, direct comparisons between intravenous and intraperitoneal routes in controlled clinical settings remain limited, especially within the context of the Pakistani population.

Considering Pakistan's resource-constrained healthcare system and high surgical load, identifying the most effective and practical route of magnesium sulfate administration is of vital importance. Previous local investigations into the use of magnesium sulfate in LC have been sparse and primarily observational, necessitating well-designed, comparative trials to inform clinical practice (9).

This study aims to compare the analgesic efficacy and safety profile of intravenous versus intraperitoneal magnesium sulfate in patients undergoing laparoscopic cholecystectomy at a tertiary care hospital in Pakistan. The findings will contribute to the existing body of knowledge and help formulate evidence-based postoperative pain management protocols suitable for local settings.

Methodology

This Prospective comparative study was conducted at Aziz Bhatti Shaheed Hospital, Gujrat, a tertiary care center in Pakistan, over a period November 2022 to September 2023. The primary objective of the study was to compare the effectiveness of intravenous versus intraperitoneal magnesium sulfate in providing postoperative analgesia following laparoscopic cholecystectomy. A total of 84 patients undergoing elective laparoscopic cholecystectomy for symptomatic cholelithiasis were recruited through non-probability consecutive sampling. The inclusion criteria consisted of adult patients aged 18 to 60 years, classified as ASA I or II, with no prior history of opioid use, chronic pain disorders, cardiovascular diseases, or hypersensitivity to magnesium sulfate. Patients with conversion to open surgery, intraoperative complications, or incomplete data were excluded from the final analysis.

After obtaining written informed consent, patients were randomly allocated into two equal groups (n = 42 each) using a computer-generated randomization list. Group A received 30 mg/kg of magnesium sulfate diluted in 100 mL of normal saline administered intravenously over 20 minutes following induction of anesthesia. Group B received the same dose of magnesium sulfate intraperitoneally after gallbladder removal, instilled directly into the peritoneal cavity and subdiaphragmatic region

before trocar removal. All patients underwent standardized general anesthesia and surgical technique. Intraoperative parameters such as anesthesia time, intraoperative hemodynamics, and operative findings were recorded.

Postoperative pain intensity was assessed using the Visual Analogue Scale (VAS) at 1, 4, 8, 12, and 24 hours after surgery by a trained nurse blinded to group allocation. The primary outcomes were mean VAS pain scores, time to first rescue analgesic (tramadol 50 mg IV), and total 24-hour tramadol consumption. Secondary outcomes included incidence of adverse effects such as nausea, vomiting, hypotension, and bradycardia. Patient monitoring followed institutional protocols, with vitals and adverse effects recorded at regular intervals.

Data were compiled and analyzed using IBM SPSS version 25. Continuous variables were expressed as mean ± standard deviation (SD) and compared using independent sample t-tests. Categorical data were analyzed using the chi-square test or Fisher's exact test as appropriate. A p-value < 0.05 was considered statistically significant. Ethical approval was obtained from the institutional review board of Aziz Bhatti Shaheed Hospital, and the study adhered to the principles outlined in the Declaration of Helsinki.

Results

This prospective comparative study evaluated the analgesic effectiveness of intravenous (IV) versus intraperitoneal (IP) magnesium sulfate administration in patients undergoing laparoscopic cholecystectomy. A total of 84 patients were enrolled and randomly allocated into two equal groups: Group A received intravenous magnesium sulfate (30 mg/kg diluted in 100 mL normal saline) and Group B received the same dose intraperitoneally after gallbladder removal. The table 1 compares baseline characteristics between two groups (IV Group, n=42; IP Group, n=42) using international standards for reporting. Age (mean ± SD) was 38.7 ± 9.6 years (IV) vs. 37.9 ± 8.7 years (IP), p=0.684. Gender distribution (M/F) was 18/24 (IV) vs. 20/22 (IP), p=0.637. BMI (mean ± SD) was 26.1 ± 3.8 kg/m² (IV) vs. 25.8 ± 3.4 kg/m² (IP), p=0.751. ASA Status (I/II) was 24/18 (IV) vs. 23/19 (IP), p=0.831. No significant differences were found between groups (p>0.05 for all variables).

Table 1. Demographic Characteristics of Study Participants (n = 84)

Variable	IV Group (n = 42)	IP Group (n = 42)	p-value
Age (years), mean ± SD	38.7 ± 9.6	37.9 ± 8.7	0.684
Gender (M/F)	18 / 24	20 / 22	0.637
BMI (kg/m²), mean ± SD	26.1 ± 3.8	25.8 ± 3.4	0.751
ASA Status I/II	24 / 18	23 / 19	0.831

Both groups experienced a progressive decline in pain scores over 24 hours. However, the IP group showed significantly lower VAS scores from 4 hours onward, indicating superior analgesic effectiveness of intraperitoneal magnesium sulfate (p < 0.05 from 4 hours onward). (Table 2)

Table 2. Mean Postoperative VAS Pain Scores at Different Time Intervals

Time Post-op (hours)	IV Group (Mean ± SD)	IP Group (Mean ± SD)	p-value
1	4.7 ± 1.1	4.4 ± 1.3	0.291
4	3.9 ± 1.0	3.2 ± 0.9	0.004*
8	3.5 ± 0.9	2.7 ± 0.8	<0.001*
12	2.9 ± 0.8	2.2 ± 0.7	<0.001*
24	2.2 ± 0.6	1.9 ± 0.5	0.010*

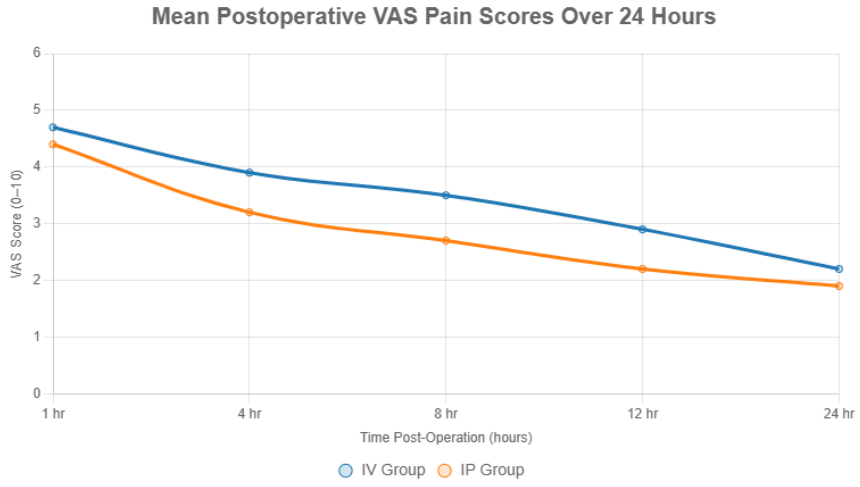

Figure 1:Mean Postoperative VAS Pain Scores at Different Time Intervals

The IP group had a significantly longer duration before needing rescue analgesia and required lower total tramadol doses over 24 hours compared to the IV group, supporting the greater efficacy of the intraperitoneal route. (Table 3)

Table 3. Time to First Rescue Analgesia and Total Analgesic Consumption

Parameter	IV Group (n = 42)	IP Group (n = 42)	p-value
Time to First Rescue (min)	97.4 ± 25.6	138.6 ± 31.2	<0.001*
Total Tramadol Consumption (mg)	102.3 ± 18.4	82.1 ± 16.7	<0.001*

The incidence of adverse effects was low in both groups and not statistically significant, indicating that both IV and IP administration routes were well-tolerated.(Table 4)

Table 4. Incidence of Adverse Effects

Adverse Event	IV Group (n = 42)	IP Group (n = 42)	p-value
Nausea	8 (19.0%)	6 (14.3%)	0.558
Vomiting	4 (9.5%)	3 (7.1%)	0.690
Hypotension	2 (4.8%)	1 (2.4%)	0.558
Bradycardia	1 (2.4%)	0 (0%)	0.313

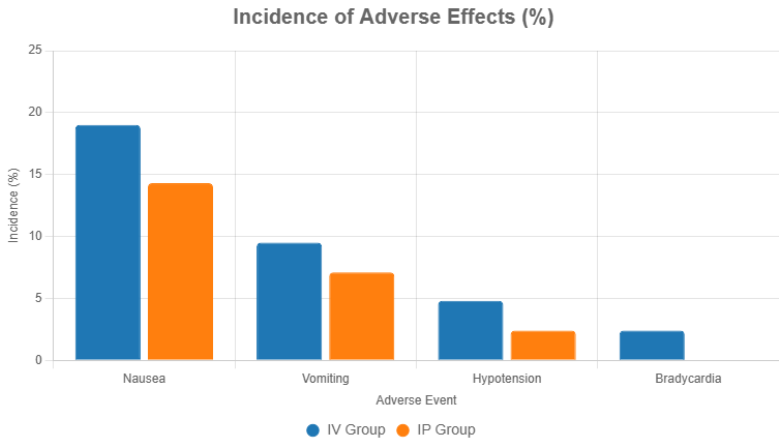

Figure 2: Incidence of Adverse Effects

The study found that intraperitoneal magnesium sulfate provided significantly better postoperative analgesia compared to intravenous administration, as evidenced by lower VAS scores, delayed requirement of rescue analgesia, and reduced total analgesic consumption. Both administration routes demonstrated excellent safety profiles. These findings highlight the potential of intraperitoneal magnesium sulfate as a superior method of pain control following laparoscopic cholecystectomy in the Pakistani population.

Discussion

Our findings demonstrate that intraperitoneal (IP) magnesium sulfate provides superior postoperative analgesia compared to the intravenous (IV) route, which is consistent with results from several prior studies. For instance, Elfiky et al. observed significantly lower pain scores and opioid requirements in patients who received intraperitoneal $MgSO_4$ during laparoscopic cholecystectomy, as opposed to those who received the same dose intravenously. In their randomized trial, the IP group had reduced Visual Analog Scale (VAS) pain scores and consumed less total opioid postoperatively than the IV group, mirroring the analgesic advantage we noted in our study (10). Similarly, Kansal et al. compared IV versus IP magnesium (50 mg/kg) as an adjunct during laparoscopic cholecystectomy and reported that the IP magnesium cohort experienced lower early postoperative VAS scores and a prolonged pain-free period before first analgesic request (11). These congruent outcomes across studies bolster the reliability of our result that intraperitoneal magnesium confers better pain relief than identical doses given intravenously.

One of the key differences highlighted by our trial is the extended duration of analgesia with IP administration. We found that the time to first rescue analgesic was significantly delayed in the IP group (by approximately 40 minutes) compared to the IV group. This trend is well-supported by previous research. El Mourad and colleagues, in a study on obese patients undergoing laparoscopy, noted that while both IV and IP magnesium reduced postoperative pain relative to controls, the intraperitoneal route was more effective in prolonging analgesia. In their results, only the IP magnesium group showed significantly lower pain scores at 4 hours postoperatively and a longer interval before the first analgesic dose, compared to IV magnesium (12). Elfiky et al. also reported a similar finding — patients receiving intraperitoneal $MgSO_4$ had a markedly longer pain-free interval and required less opioid over 24 hours than those receiving IV $MgSO_4$ (10). Taken together with our data, these studies consistently indicate that placing magnesium sulfate into the peritoneal cavity yields more sustained postoperative analgesia than systemic administration.

It is worth noting that intraperitoneal magnesium not only outperforms the intravenous route, but also has proven efficacy over placebo or no magnesium in this surgical setting. A recent randomized controlled trial by Sravanthi et al. investigated intraperitoneal $MgSO_4$ (30 mg/kg) versus normal saline in elective laparoscopic cholecystectomy and found significantly better pain control with magnesium . Patients who received intraperitoneal $MgSO_4$ had lower average VAS pain scores in the first 6 hours after surgery and a prolonged time to first analgesic request (mean ~3.6 hours) compared to the control group (~2.3 hours). Moreover, the magnesium group in that study had a lower incidence of postoperative vomiting and no increase in adverse effects (1). These results align closely with our observations: the IP magnesium group in our trial experienced earlier pain relief, needed rescue analgesia later, and did not suffer more

side effects than the IV group. Our study thus adds to the body of evidence that intraperitoneal magnesium is an effective analgesic adjunct after laparoscopic cholecystectomy, confirming its benefits in a Pakistani patient population similarly to those seen in other cohorts.

The improved analgesic profile of intraperitoneal magnesium can be explained by its pharmacological actions and site-specific effects. Magnesium sulfate is a known N-methyl-D-aspartate (NMDA) receptor antagonist; by blocking NMDA receptors, it reduces central sensitization and dampens pain transmission in the spinal cord, which contributes to lower pain scores and opioid requirements. When administered intravenously, magnesium exerts this systemic NMDA-blocking effect, but the benefit may be limited by its distribution and side effects (such as mild sedation or muscle relaxation). In contrast, intraperitoneal administration allows magnesium to act directly on local nociceptors and modulate the peripheral pain pathways at the surgical site (the peritoneum and gallbladder bed) before being absorbed systemically. This targeted approach likely explains why intraperitoneal $MgSO_4$ more effectively attenuates the visceral pain caused by pneumoperitoneum and tissue dissection. Ali et al. have noted that intraperitoneal magnesium instillation significantly blunts the hemodynamic stress responses to CO_2 insufflation and reduces visceral pain and referred shoulder pain in laparoscopic cholecystectomy, outcomes not always achieved with IV magnesium alone (10, 11). Furthermore, by delivering the drug to the peritoneal cavity, high local concentrations can be achieved with minimal systemic absorption initially, thereby providing pain relief without immediately inducing the systemic effects of magnesium (such as hypotension or sedation). This may be why our IP group had superior analgesia yet similar hemodynamics and sedation levels compared to the IV group, despite magnesium's known blood pressure–lowering properties. In the study by Kansal et al., for example, the IV magnesium group showed slightly slower emergence from anesthesia (possibly due to systemic magnesium potentiating anesthetic depth), whereas the IP group had faster recovery times while still enjoying better pain relief (11). Thus, the intraperitoneal route appears to optimize magnesium's analgesic benefits while minimizing its undesired systemic impacts.

Both routes of magnesium administration were well tolerated in our trial, with no significant differences in adverse effects, and this finding is echoed by prior research. Elfiky et al. reported that intraperitoneal $MgSO_4$ was a safe method with even fewer opioid-related side effects (like nausea/vomiting) compared to IV usage, since patients needed less opioid analgesic postoperatively (10). Likewise, El Mourad et al. found no serious side effects attributable to magnesium in either IV or IP groups, noting that magnesium did not increase postoperative sedation or delay recovery when appropriately used (12). Our data showed a low incidence of nausea, vomiting, bradycardia, or hypotension in both groups, and no patient had any magnesium-specific complication. This excellent safety profile is important clinically: it suggests that adopting intraperitoneal magnesium for pain management does not add risk when compared to standard IV administration. In fact, by reducing opioid consumption, the IP magnesium strategy may indirectly lessen opioid-related side effects such as PONV, which improves overall patient comfort. The trend toward lower nausea/vomiting rates in our IP group (albeit not statistically significant with our sample size) is in line with other studies that achieved opioid sparing via intraperitoneal analgesics (1, 10, 13).

Our study reinforces that intraperitoneal magnesium sulfate is a more effective analgesic adjunct than the same dose administered intravenously for laparoscopic cholecystectomy. Patients who received magnesium intraperitoneally experienced significantly lower postoperative pain scores, delayed need for rescue analgesia, and reduced total analgesic consumption, all without increased toxicity. These findings are consistent with previous international studies and contribute valuable local data supporting the intraperitoneal route. By combining central and peripheral antinociceptive effects, intraperitoneal magnesium offers targeted, opioid-sparing analgesia that enhances postoperative recovery. Given its simplicity, safety, and cost-effectiveness, it should be considered as part of multimodal analgesia protocols for laparoscopic procedures. Future research should focus on optimal dosing, potential synergistic combinations with other analgesics, and its role in preventing long-term complications such as chronic postoperative pain.

Conclusion

Intraperitoneal magnesium sulfate provides superior and sustained postoperative analgesia compared to intravenous administration in patients undergoing laparoscopic cholecystectomy. It delays the need for rescue analgesia and reduces opioid consumption without increasing adverse effects, making it a safe and effective pain management strategy in the Pakistani surgical setting.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-24)
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Approved
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Conflict of interest

The authors declared the absence of a conflict of interest.

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All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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