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INNOVATIVE APPROACHES TO ANAESTHESIA: EVALUATING MULTIMODAL TECHNIQUES FOR POSTOPERATIVE NAUSEA MANAGEMENT IN LAPAROSCOPIC CHOLECYSTECTOMY

Anaesthesiology

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ABSTRACT

Background : Multimodal anesthesia represents an innovative and strategic approach aimed at optimizing pain management while concurrently minimizing the risk of opioid-related adverse effects, particularly postoperative nausea. By employing a diverse array of medications throughout the surgical procedure, this technique significantly reduces dependence on opioids. Patients undergoing laparoscopic cholecystectomy are especially vulnerable to postoperative nausea, a condition exacerbated by the administration of high doses of opioids.In our study, we sought to meticulously examine the incidence of postoperative nausea across three distinct patient groups, each receiving a combination of lidocaine, ketamine, or magnesium sulfate along with fentanyl during their surgical intervention. Additionally, we aimed to evaluate any subsequent occurrences of nausea within these groups and to quantify the total amount of fentanyl administered throughout the procedure. Through this comprehensive analysis, we aimed to illuminate the effectiveness of multimodal anesthesia in enhancing patient outcomes and reducing the burden of postoperative nausea. **Materials And Methods:** In this randomized prospective study, 60 patients aged 15 to 65 years with American Society of Anesthesiologists (ASA) physical status 1 and 2 were enrolled for laparoscopic cholecystectomy. Participants were randomly assigned to one of three groups based on their analgesic regimen: Group 1 (Lidocaine Group, LG) received an intravenous bolus of lidocaine at 1 mg/kg during induction, followed by a continuous infusion at 2 mg/kg/h post-intubation; Group 2 (Ketamine Group, KG) was administered ketamine at 0.5 mg/kg during induction; and Group 3 (Magnesium Group, MG) received a continuous infusion of magnesium sulfate at 1.5 g/h after intubation. All groups also received bolus doses of fentanyl as part of standard care. The primary objective was to assess the incidence of postoperative nausea at 1, 4, 8, 12, and 24 hours postoperatively. In cases of vomiting, patients were treated with 10 mg of metoclopramide. The frequency and severity of subsequent nausea and vomiting episodes were recorded as secondary endpoints. Additionally, the total fentanyl dosage administered during the intraoperative period was quantified to evaluate the opioid-sparing effects of the interventions. This study aims to elucidate the comparative efficacy of lidocaine, ketamine, and magnesium sulfate in reducing postoperative nausea, thereby enhancing postoperative recovery and patient comfort. **Results:** Patients assigned to the Lidocaine Group exhibited a significantly lower incidence of postoperative nausea and required a reduced total dosage of fentanyl compared to those in the Ketamine and Magnesium Groups. Conversely, the Ketamine Group demonstrated a higher prevalence of nausea relative to the other groups, while the Magnesium Group experienced a greater incidence of vomiting and necessitated a higher total fentanyl dosage during the surgical procedure.In terms of additional episodes of nausea and vomiting recorded across the five monitoring intervals, two patients in the Lidocaine Group, one patient in the Ketamine Group, and two patients in the Magnesium Group reported such occurrences. Quantitatively, the Magnesium Group received the highest average fentanyl dosage during the intraoperative period, calculated at 319.50 ± 120.6 µg, followed by the Ketamine Group at 274.50 ± 70.5 µg, and the Lidocaine Group at 246.65 ± 70.6 µg. However, it is important to note that the differences in fentanyl dosages among the three groups did not achieve statistical significance, indicating that while trends were observed, they may not reflect clinically meaningful distinctions. **Conclusion:** Multimodal anesthesia effectively reduces postoperative nausea within 24 hours following laparoscopic cholecystectomy while also decreasing intraoperative opioid requirements. By utilizing a combination of analgesic agents, such as lidocaine, ketamine, and magnesium sulfate, this approach enhances pain management and promotes smoother recovery. These findings highlight the advantages of multimodal strategies in optimizing anesthesia practices, leading to improved patient outcomes and satisfaction. Further research is needed to refine these protocols and explore their applicability across a wider range of surgical procedures.

KEYWORDS

lidocaine, ketamine, magnesium sulfate, postoperative nausea

INTRODUCTION

Laparoscopic cholecystectomy is widely recognized as the gold standard for the management of symptomatic cholelithiasis, offering numerous advantages over traditional open surgery. This minimally invasive procedure is associated with reduced surgical trauma, smaller incisions that are often more aesthetically pleasing, diminished blood loss, fewer postoperative complications, and shorter durations of hospital stay.(1) Despite these benefits, the incidence of postoperative nausea following laparoscopic cholecystectomy is notably high when compared to other surgical interventions, affecting an estimated 46–75% of patients who do not receive prophylactic antiemetic therapy.(2)

The risk of developing postoperative nausea can be effectively mitigated through the strategic substitution of opioids with non-opioid analgesics and by minimizing opioid consumption during the surgical procedure. Reducing intraoperative opioid administration, especially when integrated into a multimodal analgesia regimen, has been shown to correlate with a decreased incidence of postoperative nausea.(3) Non-opioid agents, including lidocaine, ketamine, and magnesium sulfate, are employed within this multimodal approach and can significantly contribute to the reduction of postoperative nausea by effectively managing postoperative pain.

In our study, we sought to investigate the comparative incidence of postoperative nausea and vomiting among three distinct groups: those receiving lidocaine, those receiving ketamine, and those receiving magnesium sulfate, each administered in conjunction with fentanyl. This comparison served as our primary objective, with assessments conducted at intervals of 1, 4, 8, 12, and 24 hours postoperatively. Our secondary objective was to document any additional occurrences of postoperative nausea within these groups. Furthermore, the third objective involved quantifying the total fentanyl dosage administered during the surgical procedure. Through this comprehensive analysis, we aimed to elucidate the efficacy of these non-opioid agents in reducing PONV and improving overall patient outcomes following laparoscopic cholecystectomy.

MATERIALS AND METHODS

A total of 60 patients participated in this prospective, randomized study, all scheduled for elective laparoscopic cholecystectomy under general anesthesia. Participants ranged in age from 15 to 65 years and were classified as American Society of Anesthesiologists (ASA) physical status 1 and 2. The study received approval from the local ethics committee, and informed consent was obtained from each patient prior to enrollment. Conducted at Madhubani Medical College from January 2024 to June 2024, the study adhered to ethical guidelines throughout its duration.

Exclusion criteria were rigorously defined to ensure participant safety and study integrity. Individuals classified as ASA 3, 4, or 5 were excluded, as were those with known allergies to opioids (specifically fentanyl and tramadol), lidocaine, magnesium, ketamine, paracetamol, and ketoprofen. Additional exclusions included chronic

use of benzodiazepines and opioids, pregnancy, breastfeeding, presence of chronic pain syndromes, heart, renal, or hepatic failure, and psychiatric disorders. Prior to surgery, randomization was conducted, with each patient selecting one of three envelopes containing information about their assigned group before providing informed consent.

All patients underwent induction of general anesthesia utilizing a standardized protocol that included midazolam at 0.04 mg/kg, fentanyl at 0.002 mg/kg, propofol at 2 mg/kg, and rocuronium bromide at 0.6 mg/kg. During the surgical procedure, patients received additional fractionated bolus doses of fentanyl at a range of 0.5 to 1 µg/kg to maintain hemodynamic stability, keeping blood pressure and heart rate within 20% of baseline values.Participants were allocated to one of three intervention groups: in the Lidocaine Group (LG), 20 patients received an intravenous bolus of lidocaine at a dosage of 1 mg/kg during the induction phase, followed by a continuous infusion of lidocaine at 2 mg/kg/h post-intubation, alongside supplemental bolus doses of fentanyl. In the Ketamine Group (KG), 20 patients were administered ketamine at 0.5 mg/kg following propofol induction, also receiving bolus doses of fentanyl throughout the procedure. The Magnesium Group (MG) consisted of 20 patients who received a continuous intravenous infusion of magnesium sulfate at 1.5 g/h after intubation, accompanied by bolus doses of fentanyl.

All patients were intubated with an endotracheal tube and mechanically ventilated utilizing a PVC-VG (Pressure-Controlled Ventilation-Volume Guaranteed) regimen, targeting a tidal volume of 6-8 ml/kg. Ventilation comprised a 50:50 mixture of oxygen and air, with an inspiratory-to-expiratory (I:E) ratio set at 1:2. The respiratory rate was calibrated to maintain end-tidal carbon dioxide ($EtCO_2$) levels between 35 and 45 mmHg, with positive end-expiratory pressure (PEEP) established at 5 cm H_2O. Anesthesia was maintained using sevoflurane at a concentration of 0.7 to 1 MAC, and an orogastric tube was placed for gastric decompression during the procedure. Intra-abdominal pressure during laparoscopy was consistently maintained at 12 mmHg through continuous carbon dioxide (CO_2) insufflation.

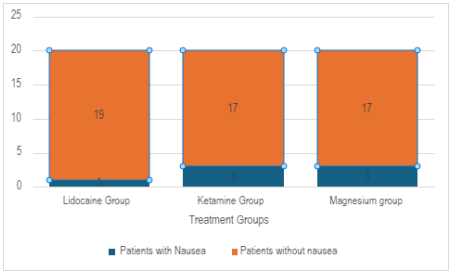
Postoperatively, all patients were transferred to the Post-Anesthesia Care Unit (PACU) for monitoring of postoperative nausea and vomiting. Patients who experienced vomiting were treated with 10 mg of metoclopramide. The first assessment for nausea and vomiting occurred one hour after surgery in the PACU, with subsequent evaluations conducted at 4, 8, 12, and 24 hours postoperatively in the Department of General Surgery. Any additional occurrences of nausea and vomiting were meticulously recorded at these time points. The total fentanyl consumption during the surgical procedure was calculated for all three groups.Postoperative pain intensity was quantified using a Visual Analog Scale (VAS) at rest and during coughing at 1, 4, 8, 12, and 24 hours post-surgery. For patients exhibiting a VAS score exceeding 4, 100 mg of ketamine was administered, while those with a score exceeding 7 received 100 mg of tramadol. Importantly, the examiner conducting follow-up assessments in both the PACU and the surgical department remained blinded to the study group allocations, thus minimizing bias in the evaluation of outcomes.

RESULTS

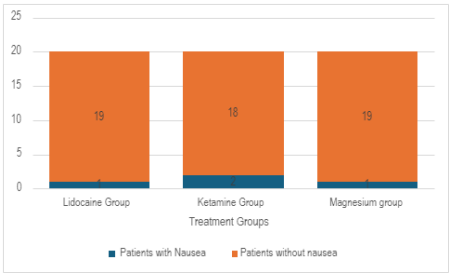
There were no significant differences observed among the groups in terms of age, weight, or sex distribution, with a notable predominance of female patients (44 females and 16 males). Additionally, the duration of both surgery and anesthesia time did not vary appreciably across the groups. For the statistical analysis, we utilized Fisher's exact test, Analysis of Variance (ANOVA), and the Tukey post-hoc test to ensure robust and accurate evaluation of the data.

In the first hour postoperatively, one patient in the Lidocaine Group (LG), three patients in the Ketamine Group (KG), and three patients in the Magnesium Group (MG) reported experiencing nausea (as illustrated in Graph 1). However, the differences in the incidence of vomiting between the groups within this time frame were not statistically significant, indicating that the observed distribution of patients who experienced vomiting did not meet the threshold for clinical significance.

In the four hours following the surgery, we observed that one patient in the Lidocaine Group (LG), two patients in the Ketamine Group (KG), and one patient in the Magnesium Group (MG) reported experiencing nausea, as shown in Graph 2. However, the differences in the number of patients who experienced nausea among the three groups were not statistically significant.

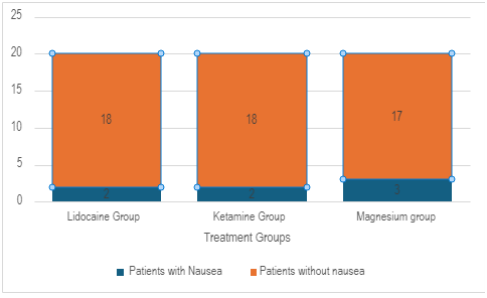


Graph 1. Occurrence of vomiting at 1 hour after surgery in the lidocaine, ketamine and magnesium groups



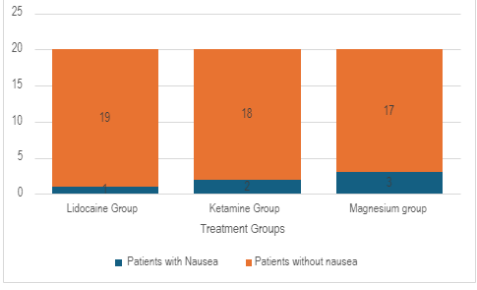
Graph 2. Occurrence of vomiting at 4 hour after surgery in the lidocaine, ketamine and magnesium groups

Eight hours after the surgery, we found that two patients in the Lidocaine Group (LG), two patients in the Ketamine Group (KG), and three patients in the Magnesium Group (MG) reported experiencing nausea, as illustrated in Graph 3. However, the differences in nausea rates between the groups were not statistically significant.



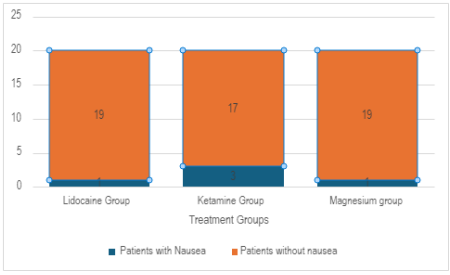
Graph 3. Occurrence of vomiting at 8 hour after surgery in the lidocaine, ketamine and magnesium groups

Twelve hours after the surgery, we found that one patient in the Lidocaine Group (LG), two patients in the Ketamine Group (KG), and three patients in the Magnesium Group (MG) reported feeling nauseous, as shown in Graph 4. However, the difference in nausea rates between the ketamine group and the other groups was not statistically significant.



Graph 4. Occurrence of vomiting at 12 hour after surgery in the lidocaine, ketamine and magnesium groups

In the twenty four hour post-operation, 1 patients in the lidocaine group (LG), 3 in the ketamine group (KG), and 1 in the magnesium group (MG) experienced nausea (Graph 5).



Graph 5. Occurrence of vomiting at 24 hour after surgery in the lidocaine, ketamine and magnesium groups

Throughout the five control time points, additional nausea and vomiting were reported in 2 patients in the lidocaine group (LG), 2 in the ketamine group (KG), and 3 in the magnesium group (MG).

Additional episodes of nausea and vomiting were reported at various times. In the lidocaine group (LG), one patient experienced nausea and vomiting 2 hours post-surgery, another at 15 hours, and a third at 21 hours. In the ketamine group (KG), one patient had symptoms 6 hours after surgery, while another experienced them at 7 hours. In the magnesium group (MG), nausea and vomiting were noted in one patient immediately after surgery, in another 10 hours later, and in a third patient at 16 hours.

Table 1: Mean amount of fentanyl that was given intravenously to patients in all three groups during surgery

Groups	Fentanyl given i.v during surgery		P value
	Mean ±SD	range	
Lidocaine	246.65 ± 70.6	150-400	0.0000
Ketamine	274.50 ± 70.5	150-400	0.0001
Magnesium	319.50 ± 120.6	150-1000	0.0001

Patients in the magnesium group received the highest average dose of fentanyl during surgery (319.50 ± 120.6), followed by those in the ketamine group (274.50 ± 70.5), while patients in the lidocaine group received the lowest dose (246.65 ± 70.6). However, the differences in fentanyl doses among the three groups were statistically significant.

DISCUSSION

Nausea and vomiting are most commonly observed within the first two hours following recovery from anesthesia. The administration of high doses of opioids during surgical procedures significantly increases the risk of developing postoperative nausea. Moreover, the continued use of opioids in the postoperative period exacerbates this risk.(4) In the context of laparoscopic cholecystectomy, additional factors contributing to postoperative nausea may include the physiological effects of intraperitoneal carbon dioxide insufflation, which can lead to residual distension and irritation of the peritoneal lining. The duration of the surgical procedure itself is also a relevant factor, as prolonged surgery has been associated with an increased likelihood of postoperative nausea and vomiting.(5) These multifactorial influences highlight the complexity of managing postoperative symptoms and the need for comprehensive analgesic strategies to mitigate these adverse effects.

Our study reveals that within the first 24 hours postoperatively, patients in the Ketamine Group reported the highest incidence of nausea, with 12 individuals affected. This was closely followed by the Magnesium Group, which recorded 11 patients experiencing nausea, while the Lidocaine Group reported the lowest incidence, with only 6 patients displaying symptoms across the five postoperative assessment time points.

Notably, the Lidocaine Group demonstrated significantly lower levels of both nausea and vomiting compared to the other two groups. This difference is likely attributable to the smaller doses of fentanyl administered during the surgical procedure. Conversely, the Magnesium Group, which received the highest cumulative fentanyl dosage, exhibited an increased incidence of vomiting in the postoperative period. Additionally, the Ketamine Group's heightened reports of nausea can be attributed to the known emetic properties of ketamine.

These findings underscore the complex interplay between analgesic regimens and postoperative symptoms, highlighting the importance of carefully selecting analgesics to optimize patient outcomes following laparoscopic cholecystectomy.

Lidocaine is classified as an amino-amide local anesthetic with a multifaceted pharmacological profile. Its primary mechanism involves the reversible blockade of impulse transmission through nerve fibers, achieved by binding to sodium channels, thereby facilitating local or regional anesthesia. Additionally, lidocaine possesses antiarrhythmic properties and exhibits anti-inflammatory effects that have been demonstrated to surpass those of non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids.(6) Furthermore, lidocaine displays antibacterial activity and antinociceptive effects.

The intraoperative administration of lidocaine offers several advantages, including effective pain relief, reduced incidence of postoperative nausea and vomiting, decreased likelihood of ileus, diminished opioid requirements, and shorter hospital stays.(7) Additionally, lidocaine infusion accelerates the return of bowel function, as evidenced by a reduction in the time to first flatulence and intestinal motility.

However, a recent meta-analysis of 68 studies involving patients undergoing various open and laparoscopic abdominal surgeries has revealed inconsistencies regarding the effects of perioperative lidocaine infusion on early postoperative pain, gastrointestinal recovery, postoperative nausea, and opioid consumption compared to placebo or no treatment.(8) Notably, patients who received a continuous intravenous lidocaine infusion reported lower levels of postoperative pain at all assessment time points, experienced reduced nausea, required smaller total doses of fentanyl, and expressed greater overall satisfaction. This contrasts sharply with outcomes observed in patients receiving ketorolac, either in bolus doses or as a continuous intravenous infusion. These findings highlight the potential role of lidocaine in enhancing postoperative recovery while emphasizing the need for further investigation to clarify its efficacy relative to other analgesic modalities.

Ketamine functions as a non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor and additionally interacts with AMPA receptors and sigma opioid receptors. As a dissociative anesthetic, ketamine presents multiple therapeutic benefits, including analgesic, antihyperalgesic, amnestic, hypnotic, anti-inflammatory, and antidepressant properties, along with bronchodilatory effects and a potential emetic response.(9)

While anesthetic doses of ketamine are known to induce nausea, administration of subanesthetic doses has been associated with a significant reduction in nausea and vomiting, likely due to its opioid-sparing effects. Common gastrointestinal side effects may include nausea, vomiting, anorexia, and abdominal discomfort.Subanesthetic doses of ketamine have been shown to effectively manage postoperative pain, potentially decreasing the requirement for morphine during the first 24 hours following surgery. Furthermore, ketamine has demonstrated utility in reducing postoperative nausea. A meta-analysis examining the effects of adding ketamine to morphine or hydromorphone for patient-controlled analgesia indicated that while the addition of ketamine had a minimal impact on postoperative pain relief, it significantly reduced both postoperative nausea and overall opioid consumption.Moreover, another meta-analysis focused on randomized clinical trials regarding the analgesic efficacy of intravenous ketamine in laparoscopic cholecystectomy highlighted that ketamine significantly decreases postoperative pain levels and reduces opioid usage. These findings underscore the potential role of ketamine as an effective adjunct in multimodal analgesia strategies, enhancing postoperative recovery while minimizing opioid-related adverse effects.Magnesium sulfate is associated with a range of beneficial effects, primarily due to its pharmacological mechanisms, including its role as a non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptors and its ability to block calcium channels.(10) These actions contribute to its analgesic properties, prolongation of neuromuscular blockade, neuroprotective effects, prevention of postoperative shivering, reduction of blood hypercoagulability, and anti-inflammatory effects.A study has demonstrated that the administration of magnesium sulfate significantly enhances the quality of postoperative recovery by effectively reducing pain, minimizing the incidence of postoperative nausea and vomiting, and decreasing opioid requirements in patients

undergoing outpatient segmental mastectomy. Whether administered as a bolus dose or via continuous intravenous infusion, magnesium sulfate has consistently been shown to enhance postoperative analgesia, reduce opioid consumption during the recovery period, mitigate nausea and vomiting, and improve overall pain management outcomes.

These findings highlight the potential role of magnesium sulfate as a valuable adjunct in multimodal analgesic strategies, facilitating improved postoperative recovery profiles while minimizing the adverse effects commonly associated with opioid analgesics.

CONCLUSION

Multimodal anesthesia has emerged as an effective strategy for mitigating postoperative nausea and vomiting (PONV) in patients undergoing laparoscopic cholecystectomy. This approach facilitates a reduction in opioid consumption during the surgical procedure, thereby minimizing the associated adverse effects of fentanyl in the postoperative period.

In our study, patients in the Lidocaine Group reported the lowest incidence of postoperative nausea, which can be attributed to their receiving the least amount of fentanyl during surgery. Conversely, those in the Ketamine Group exhibited the highest rates of nausea. Notably, the incidence of vomiting was similar among both the Lidocaine and Ketamine Groups, suggesting that other factors may also contribute to this symptom. In contrast, the Magnesium Group, which received the highest total fentanyl dose during the intraoperative period, experienced the greatest frequency of vomiting.

These findings underscore the importance of optimizing analgesic regimens to enhance patient outcomes following laparoscopic cholecystectomy, highlighting the potential benefits of multimodal approaches in reducing PONV and improving overall postoperative recovery.

Limitations To This Study

The way we administered medications varied among the groups: one group received both a bolus dose and a continuous infusion, another group received only bolus doses, and the third group received only a continuous infusion. Instead of using a PONV Intensity Scale to measure nausea and vomiting after surgery, we asked patients a few sample questions about their symptoms. Additionally, we did not give dexamethasone as an anti-nausea medication before surgery. We also felt it was inappropriate to wake patients during the night just to ask them if they felt nauseous or had vomited.

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