



# Comparing the Efficacy of Intraperitoneal Bupivacaine-Tramadol and Bupivacaine-Magnesium Sulfate for Pain Management After Laparoscopic Cholecystectomy

Vibhavari Shivajirao Patil (Junior Resident)<sup>1</sup> and Naseema Vijay Kanase (Professor)<sup>1</sup>

<sup>1</sup>Department of Anaesthesiology, Krishna Institute of Medical Sciences, Karad, Krishna Vishwa Vidyapeeth (Deemed to be University) Karad, Maharashtra, India.

Corresponding author: Vibhavari Shivajirao Patil (Junior Resident)

Department of Anaesthesiology, Krishna Institute of Medical Sciences, Karad, Krishna Vishwa Vidyapeeth (Deemed to be University) Karad, Maharashtra, India.

(Received: 07 October 2023

Revised: 12 November

Accepted: 06 December)

## KEYWORDS

Bupivacaine,  
Cholecystectomy,  
Intraperitoneal,  
Magnesium  
Sulphate, Tramadol

**Abstract:** Background: The use of local anesthetics, administered intraperitoneally, either alone or in combination with other medications, after laparoscopic cholecystectomy has gained popularity as a method to reduce postoperative pain. This approach involves introducing local anesthetic agents into the peritoneal cavity during the surgery to provide pain relief in the postoperative period. Methods: In a prospective, randomised, double-blind study, we enrolled 100 patients aged between 20 to 45 years who were scheduled for laparoscopic cholecystectomy and had ASA grade 1 or 2. These patients were randomly allocated into two groups, Group BT and Group BM. Group BT received 0.25% bupivacaine 30 ml along with 100 mg tramadol, while Group BM received 0.25% bupivacaine 30 ml combined with 50 mg of MgSO<sub>4</sub>. We assessed and compared various parameters, including the analgesic efficacy, duration of pain relief, and any associated side effects. Results: In our study, we observed a higher number of female participants than male participants, although this gender difference was not statistically significant ( $P > 0.05$ ). Regarding the duration of anesthesia, we did not identify any statistically significant difference between the two groups ( $P > 0.05$ ). However, when assessing postoperative pain relief, we noted that the BM group experienced 1 to 2 hours more relief compared to the BT group, and this difference was statistically significant. In terms of side effects, we observed no significant occurrences in either group except for nausea and vomiting in two patients from the BT group. Nonetheless, this difference was not statistically significant ( $P > 0.05$ ). Conclusion: The intraperitoneal instillation of a Bupivacaine-MgSO<sub>4</sub> combination appears to offer effective analgesia during the first 24 hours after surgery. It provides a longer pain-free period when compared to the Bupivacaine-Tramadol combination. This suggests that the Bupivacaine- MgSO<sub>4</sub> combination may be a more suitable option for postoperative pain management in patients undergoing laparoscopic cholecystectomy.

## I. INTRODUCTION

Intraperitoneal instillation of local anesthetics and opioids is gaining recognition for postoperative pain management, especially in laparoscopic surgeries [1]. The nature and intensity of pain vary significantly between laparoscopic cholecystectomy and laparotomy. After laparotomy, the pain is primarily parietal, originating from the abdominal wall, whereas after laparoscopic cholecystectomy, it tends to be more visceral in nature. The pain experienced after laparoscopic cholecystectomy is often unpredictable in both intensity and duration. This variability necessitates tailored approaches to pain management for optimal outcomes and patient comfort. Magnesium Sulphate (MgSO<sub>4</sub>) is known for its antinociceptive (pain-relieving) properties, which are utilized by anesthesiologists to manage post-operative pain. It can help regulate the duration and intensity of pain experienced after surgery.

Tramadol, on the other hand, has demonstrated local pain-relieving effects when administered intraperitoneally after laparoscopic surgery [2], [3]. Both MgSO<sub>4</sub> and tramadol are valuable components of multimodal pain management strategies in surgical settings. Indeed, there has been ongoing research to determine the effectiveness of local anesthetics, especially when administered intraperitoneally during laparoscopic cholecystectomy. However, the optimal dose, concentration, site, and method of administration have not yet been standardized, and this remains an area of active investigation and debate in the medical community. The choice of specific techniques and agents often depends on the preferences of the surgical team and the available evidence regarding safety and efficacy. study aimed to compare the quality and duration of postoperative analgesia in patients who underwent laparoscopic cholecystectomy. Specifically, you evaluated the effectiveness of intraperitoneal Bupivacaine plus Tramadol (BT) versus Bupivacaine plus



Magnesium sulfate (BM) in providing post-operative pain relief. This research is essential for improving pain management and enhancing the recovery process for patients undergoing this surgical procedure [4], [5].

## II. MATERIAL AND METHODS

A randomized, double-blind study was planned and approval from the institutional ethics committee before proceeding was taken. A total of 100 patients, ranging in age from 20 to 45 years, who were undergoing laparoscopic cholecystectomy and had ASA grades 1 and 2 were enrolled. To ensure ethical standards were met, all patients were provided with comprehensive explanations about the study, and written informed consent was obtained from each of them. Subsequently, these patients were randomly allocated into two groups, with 50 individuals in each group. This rigorous methodology helps ensure the credibility and reliability of your study's results [6]. 1. Group BT: This group received a combination of 0.25% bupivacaine (30 ml) and 100 mg tramadol. 2. Group BM: The patients in this group were administered a combination of 0.25% bupivacaine (30 ml) and 50 mg magnesium sulfate ( $\text{MgSO}_4$ ). This division allowed to compare the effectiveness of these two different combinations in providing post-operative pain relief. In this prospective study, a systematic approach was undertaken to assess the analgesic efficacy and duration of pain relief in patients undergoing laparoscopic cholecystectomy. The study was conducted with the highest standards of scientific rigor. To maintain a double-blind design, one anaesthesiologist, not involved in the anesthesia process, administered the study drugs intraperitoneally, while another anaesthesiologist handled data collection and subsequent analysis [7]. The patients were educated about the use of the visual analogue scale (VAS) to assess pain levels, which was a scale from 0 to 10. Throughout the study, hemodynamic variables and any side effects were diligently monitored and documented. The primary focus of this investigation was to compare the effectiveness of post-operative analgesia and the duration of pain relief between the two groups, aiming to contribute to the understanding of pain management in laparoscopic cholecystectomy. In this study, specific criteria were established to determine the eligibility of participants. The inclusion criteria encompassed patients who were scheduled for laparoscopic cholecystectomy, falling within the American Society of Anesthesiologists (ASA) grade 1 and 2 classification, and were aged between 20 and 45 years. These criteria were crucial for ensuring that the study focused on a particular patient population undergoing the same surgical

Parameter	Group BT (n=50)	Group BM (n=50)	P value
Age in years	37.64 $\pm$ 6.32	38.49 $\pm$ 6.45	0.6400
Sex (Males/Females)	12/13	11/14	>0.05
Duration of Surgery (minutes)	52.61 $\pm$ 5.48	51.98 $\pm$ 7.13	0.3693
Duration of Anaesthesia (minutes)	72.68 $\pm$ 4.09	73.57 $\pm$ 5.07	0.6527

**TABLE 1.** Demographic profile, duration of surgery and anaesthesia in two groups

procedure [8]. On the other hand, the exclusion criteria were applied to exclude patients with certain characteristics or conditions that might interfere with the study or put them at risk. Patients with known allergies to the study drugs ( $\text{MgSO}_4$ , bupivacaine, and tramadol) were excluded to prevent adverse reactions. Additionally, individuals with a history of chronic alcoholism, pre-existing heart block, renal failure, or those who required peritoneal drain post-surgery were also not included in the study. These criteria were vital in maintaining the safety and integrity of the research.

## III. RESULTS

The analysis of demographics revealed that there was no statistically significant difference between the two groups (Group BT and Group BM) in terms of various factors. These factors included age, gender, weight, height, and the duration of anesthesia [9]. The distribution of age and gender was fairly balanced among the two groups. Specifically, while there were more female patients than males in the study, this difference was not statistically significant, indicating that both groups had a similar gender distribution. Moreover, the duration of anesthesia also did not exhibit a statistically significant difference between the two groups. These findings suggest that the two groups were comparable in terms of the selected demographic factors, ensuring a balanced and unbiased comparison of the analgesic interventions.

The study also assessed the diastolic blood pressure (DBP) at 5-minute intervals in both groups, and these DBP values were compared with the baseline DBP. The analysis showed that the differences in DBP during the observation period compared to the baseline DBP were not statistically significant ( $P > 0.05$ ). This indicates that the changes in diastolic blood pressure observed during the post-operative period did not significantly vary from the baseline values, further supporting the safety of the analgesic interventions in both groups.

Moreover, the study monitored the occurrence of side effects such as nausea, vomiting, loss of tendon reflexes, and hemodynamic abnormalities like hypotension at various intervals during the post-operative period. These intervals included 30 minutes, 40 minutes, 1 hour, 2 hours, 4 hours, and 6 hours after patients were transferred to the recovery room. The findings demonstrated that there were no significant differences in the occurrence of side effects between the two groups. Specifically, nausea and vomiting were reported in only two patients from the BT group, and this difference was not statistically significant ( $P > 0.05$ ). This suggests



VAS	Group BT (n=50)	Group BM (n=50)
1 Hour	3.62±2.75	1.69±1.13
2 Hours	3.82±2.31	2.59±1.25
4 Hours	4.65±2.52	2.14±1.58
6 Hours	2.78±1.41	2.15±1.24
8 Hours	2.55±1.09	1.49±1.54
12 Hours	2.86±1.67	2.04±1.56
24 Hours	2.22±1.12	1.56±1.02

**TABLE 2.** Visual analogue scale pain score at different time intervals in the two groups

that the analgesic interventions in both groups were well-tolerated, with a low incidence of side effects.

#### IV. DISCUSSION

Laparoscopic cholecystectomy offers several advantages over open cholecystectomy, including reduced postoperative pain and the need for postoperative analgesia, as well as shorter hospital stays. To enhance the success rate of outpatient laparoscopic cholecystectomy and improve post-operative analgesia, the use of opioid-sparing regimens has been recommended. This is because both pain and opioid medications can induce nausea, which can be a significant concern for patients. Traditionally, analgesics were administered intravenously or via other parenteral routes. However, recent research has demonstrated that the intraperitoneal instillation of local anesthetics and opioids can provide superior pain relief with minimal side effects. This approach has been gaining popularity among medical professionals, offering a promising alternative to traditional pain management strategies following laparoscopic cholecystectomy. The mechanism underlying the achievement of analgesia through the intraperitoneal instillation of local anesthetics around the operative site is believed to involve the obstruction of conduction from visceral sites. This effectively reduces the intensity of referred pain experienced by the patient. Another factor contributing to analgesia may be the absorption of the local anesthetic agents from the extensive peritoneal surface into the systemic circulation. There is some debate regarding the optimal timing for administering intraperitoneal local anesthetics. Some authors advocate for early instillation during the surgery, as it provides better control of post-operative pain compared to instillation at the end of the procedure. However, other researchers hold a contrasting view and recommend an alternative approach. This indicates that the timing of intraperitoneal local anesthetic administration remains an area of ongoing investigation and discussion in the medical field<sup>10,11</sup>. The mechanism by which magnesium sulfate (MgSO<sub>4</sub>) achieves analgesia is believed to involve the reduction of calcium influx into cells by magnesium. Additionally, magnesium acts as an antagonist to N-methyl-D-aspartate (NMDA) receptors, which play a critical role in neuronal signaling and pain processing in the central

nervous system. This antagonism leads to a reduction in post-operative pain, as both somatic and visceral pain fibers are blocked. In the context of laparoscopic cholecystectomy, MgSO<sub>4</sub> has conventionally been administered through various routes, including intravenous (IV) bolus, continuous infusion, epidural infusion, and into the subarachnoid space. More recently, studies have demonstrated that intraperitoneal administration of local anesthetics alone or in combination with MgSO<sub>4</sub> has the potential to improve post-operative pain management after laparoscopic cholecystectomy. This approach presents a promising alternative for enhancing the quality of post-operative care. In our study, we conducted a comparison of the quality and duration of post-operative analgesia between two groups of patients who underwent laparoscopic cholecystectomy. The first group received intraperitoneal Bupivacaine plus Tramadol (BT), while the second group received intraperitoneal Bupivacaine plus Magnesium sulfate (BM)<sup>12</sup>. Our findings indicated that patients in the BM group experienced reduced post-operative pain during the first 24 hours following surgery and enjoyed a longer pain-free period when compared to patients in the BT group after laparoscopic cholecystectomy. These results align with a study conducted by Maharjan SK and colleagues. They investigated the effects of intraperitoneal instillation of bupivacaine, administered either alone or in combination with MgSO<sub>4</sub> at a dose of 50 mg/kg. Their research demonstrated that patients who received intraperitoneal bupivacaine along with MgSO<sub>4</sub> at the end of the surgery reported better pain relief for a period ranging from 2 to 5 hours, in contrast to patients who received intraperitoneal bupivacaine alone<sup>13</sup>. These findings emphasize the potential benefits of using this combined approach to post-operative pain management. Akinci SB<sup>14</sup> and colleagues conducted a study comparing the efficacy of tramadol administered intravenously (IV) and intraperitoneally to manage post-operative analgesia after laparoscopic cholecystectomy. Their findings indicated that IV tramadol provided superior post-operative analgesia when compared to intraperitoneal tramadol administration. Similarly, Shukla U and colleagues conducted a study to assess the effectiveness of various approaches, including bupivacaine alone, bupivacaine with tramadol, and intraperitoneal bupivacaine combined with dexmedetomidine<sup>15,16</sup>. Their research demonstrated that the intraperitoneal instillation of bupivacaine in combination with dexmedetomidine was more effective in reducing post-operative pain when compared to the other two methods. These studies contribute valuable insights into the optimization of post-operative pain management strategies following laparoscopic cholecystectomy.

#### V. CONCLUSION



The study demonstrates that intraperitoneal instillation of a combination of Bupivacaine and Magnesium Sulfate (MgSO<sub>4</sub>) offers effective analgesia in the initial 24 hours following surgery. This approach provides a more extended duration of pain relief when compared to

the use of Bupivacaine in combination with Tramadol. Importantly, both combinations exhibited minimal side effects, making them promising options for post-operative pain management in laparoscopic cholecystectomy procedures.

## REFERENCES

- [1] Yadava A, Rajput SK, Katiyar S, Jain RK. A comparison of intraperitoneal bupivacaine-tramadol with bupivacaine- magnesium sulphate for pain relief after laparoscopic cholecystectomy: A prospective, randomised study. *Indian Journal of Anaesthesia*. 2016;60(10):757-762
- [2] Golubovic S, Golubovic V, Cindric Stanancin M, Tokmadzic VS. Intraperitoneal analgesia for laparoscopic cholecystectomy: Bupivacaine versus bupivacaine with tramadol. *Coll Antropol* 2009;33:299-302.
- [3] Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: A critical assessment of the evidence. *Anesthesiology* 2006;104:835-46.
- [4] Shoeibi G, Sadegi M, Firozian A, Tabas somi F. The additional effect of magnesium sulphate to lidocaine in spinal anaesthesia for caesarean section. *Int J Pharmacol* 2007;3:425-7.
- [5] Upadya M, Pushpavathi SH, Seetharam KR. Comparison of intraperitoneal bupivacaine and intravenous paracetamol for postoperative pain relief after laparoscopic cholecystectomy. *Anesthesia, Essays and Researches*. 2015;9(1):39-43.
- [6] Pasqualucci A, de Angelis V, Contardo R, Colo F, Terrosu G, Donini A, et al. Preemptive analgesia: Intraperitoneal local anesthetic in laparoscopic cholecystectomy. A randomized, double-blind, placebo-controlled study. *Anesthesiology*. 1996;85:11-20.
- [7] Kehlet H, Rung GW, Callesen T. Postoperative opioid analgesia: Time for a reconsideration? *J Clin Anesth*. 1996; 8:441-5.
- [8] Gvozdenovic L, Cvijanovic R, Kolak R, Pjevic M, Gavrilovic S, Veljkovic R et al. Anaesthesiology in current world of laparoscopic surgery. *Med Danas*. 2003;2: 298-301.
- [9] Marks JL, Ata B, Tulandi T. Systematic review and metaanalysis of intraperitoneal instillation of local anesthetics for reduction of pain after gynecologic laparoscopy. *J Minim Invasive Gynecol*. 2012;19:545- 53.
- [10] Paulson J, Mellinger J, Baguley W. The use of intraperitoneal bupivacaine to decrease the length of stay in elective laparoscopic cholecystectomy patients. *Am Surg*. 2003;69:275-8.
- [11] Maharjan SK, Shrestha S. Intraperitoneal magnesium sulphate plus bupivacaine for pain relief after laparoscopic cholecystectomy. *J Kathmandu Med Coll*. 2012; 1:21-5.
- [12] Buyukakilli B, Doruk N, Comelekoglu U, Camdeviren H, Gune S. Do adjuncts (tramadol and magnesium) potentiate impulse inhibition by a local anesthetic in isolated frog sciatic nerves? *Turk J Med Sci*. 2006;36:201-6.
- [13] Akinci SB, Ayhan B, Aycan IO, Tirmaksiz B, Basgul E, Abbasoglu O, et al. The postoperative analgesic efficacy of intraperitoneal tramadol compared to normal saline or intravenous tramadol in laparoscopic cholecystectomy. *Eur J Anaesthesiol*. 2008;25:375-81.
- [14] Shukla U, Prabhakar T, Malhotra K, Srivastava D, Malhotra K. Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol for postoperative analgesia following laparoscopic cholecystectomy: A comparative evaluation. *Indian J Anaesth*. 2015;59:234-9.
- [15] Jee D, Lee D, Yun S, Lee C. Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy. *Br J Anaesth*. 2009;103:484-9.
- [16] Menten O, Harlak A, Yigit T, Balkan A, Balkan M, Cosar A, et al. Effect of intraoperative magnesium sulphate infusion on pain relief after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand*. 2008;52:1353-9.