# Comparing Different Modalities of Opioid Free Anesthesia for Laparoscopic Cholecystectomy

**Omnia Mohammed Tawfik Ahmed[a*], Gad Sayed Gad[a], Ahmed Fathy Abd El-Lateef[a]**
[a]Anaesthesia &ICU Department, Faculty of Medicine, South Valley University, Qena, Egypt.

**Abstract**

**Background:** Laparoscopic cholecystectomy, though less invasive, can still cause significant postoperative pain. Opioids were traditionally used for pain management but have adverse effects and addiction risks. There's a growing interest in opioid-free approaches, like intraperitoneal lidocaine and magnesium sulfate infusion, to reduce pain and opioid use in laparoscopic cholecystectomy.

**Objectives:** This study aimed to compare intraperitoneal lidocaine and magnesium sulfate infusion as opioid-free anesthesia methods for laparoscopic cholecystectomy patients.

**Patients and methods:** This is prospective clinical-trial at Qena University Hospital involved fifty adult patients divided into Group I (intraperitoneal lidocaine) and Group II (lidocaine with magnesium sulfate infusion). Both groups received anesthesia and postoperative pain assessment using the Visual Analogue Scale (VAS). Intra and post operative hemodynamics monitoring was done.

**Results:** Intra-operative heart rate in Group I was significantly higher in the first 70 min. ($p < 0.05$) and systolic BP was higher at 20, 30, 40 mins ($p < 0.001$). Group I had higher SBP, DBP and HR almost for the all 60 mins ($p < 0.00001$) in PACU. However, in Follow-up SBP was higher for the first 4 hours ($p < 0.01$) and DBP was higher at 6, 12, 18, 24 hours for Group II ($p < 0.05$). Follow up VAS pain score was significantly lower in group I for all 24 hours. No complications were recorded in both groups.

**Conclusion:** Magnesium sulfate infusion showed better hemodynamic stability and less disturbance, while intraperitoneal lidocaine provided better pain control although with more hemodynamic instability.

**Keywords:** Lidocaine; Magnesium sulfate infusion; Opioid-Free Anesthesia; Laparoscopic Cholecystectomy

***Correspondence**: Omniamohammed67@g.mail.com

**DOI: 10.21608/SVUIJM.2023.234019.1680**
**Received**: 9 September, 2023.
**Revised**: 10 September, 2023.
**Accepted**: 16 September, 2023.
**Published**: 24 May, 2024
**Cite this** article as: Omnia Mohammed Tawfik Ahmed, Gad Sayed Gad, Ahmed Fathy Abd El-Lateef.(2024). Comparing Different Modalities of Opioid Free Anesthesia for Laparoscopic Cholecystectomy. *SVU-International Journal of Medical Sciences*. Vol.7, Issue 1, pp: 919-938.

## Introduction

Laparoscopic cholecystectomy is a commonly performed surgical procedure for gallbladder disease due to its benefits, including reduced postoperative pain, shorter hospital stays, and quicker recovery compared to open cholecystectomy **(El Nakeeb et al., 2017; Vindal et al., 2021).** LC also results in minimal scarring and higher patient satisfaction **(Ahuja et al., 2022).**

Laparoscopic cholecystectomy is less intrusive than open surgery, although patients may still endure substantial postoperative discomfort. This discomfort might affect patient recovery and happiness. After surgery, opioid analgesics were used to manage pain. Opioids may cause respiratory depression, nausea, vomiting, and constipation. Chronic opioid use may lead to addiction and dependence **(Bedson et al., 2019; Daoust, 2020).**

Thus, non-opioid anesthetic techniques are being developed to reduce postoperative discomfort in laparoscopic cholecystectomy patients **(Beloeil, 2019; Chia et al., 2020; Forget, 2019).** Lidocaine intraperitoneally (IP) and magnesium sulfate infusion have been found to reduce postoperative pain and opioid usage in numerous surgical procedures. The success of these techniques in laparoscopic cholecystectomy patients is seldom documented **(Chu et al., 2020; Soleimanpour, 2022).**

Lidocaine, a local anesthetic, blocks nerve impulses at the injection site. Lidocaine in the peritoneal cavity blocks pain signals from the belly to the brain, relieving pain temporarily. This method reduces surgery and postoperative discomfort. In surgeries such laparoscopic gastric bypass, intraperitoneal injection reduces postoperative pain and narcotic use **(Gudin & Nalamachu, 2020).**

Postoperative pain and opiate consumption may be reduced with magnesium sulfate. Magnesium is essential for muscular relaxation and pain regulation. Due to its muscle-relaxant characteristics, magnesium sulfate intravenously may reduce pain and opioid use. Limited research exists on intraperitoneal delivery and magnesium sulfate infusion in laparoscopic cholecystectomy patients. Thus, these opioid-free anesthetic methods must be tested in this patient group **(El Mourad & Arafa, 2019; Soleimanpour et al., 2022).**

The aim of this prospective comparative study is to compare different modalities of opioid free anaesthesia in the form of intraperitonial lidocaine (IP) administration and magnesium sulfate infusion in laparoscopic cholecystectomy patients.

## Patients and Methods

The study was a prospective comparative clinical randomized trial carried out at the Anesthesia, Intensive Care Unit, and Pain Management Department of Qena University Hospital. The research included fifty adult patients undergoing laparoscopic cholecystectomy under general anesthesia, divided into two groups: Group I (25 patients) received intraperitoneal lidocaine (IP), while Group II (25 patients) received magnesium sulfate infusion. Randomization was performed using closed envelopes.

The eligibility criteria for inclusion encompassed adult patients aged 18 to 60 years undergoing elective laparoscopic cholecystectomy under general anesthesia, categorized as ASA I or II according to American Society of Anesthesiologists physical status classification **(Daabiss, 2011).** Exclusion criteria comprised hypersensitivity to study medications, history of alcohol or drug abuse, severe systemic diseases, recent opioid analgesic use, specific medication usage, cognitive

impairment, and ASA III or IV classification.

**Patient Preparation:** Informed consent was obtained from all patients. Complete medical history, including personal, medical, surgical, and family history, was recorded. A thorough physical examination, including vital signs (blood pressure, temperature, heart rate, respiratory rate), was conducted.

**Anesthesia Induction:** Patients received specific medications as follows: 1000 mg paracetamol or dexamethasone 0.1 mg/kg, lidocaine 1 mg/kg, and ketamine 0.5 mg/kg intravenously **(Toleska et al., 2022).**

**Treatment Groups:** Group I received a 200 ml saline solution containing 200 mg 2% lidocaine immediately after abdominal CO2 insufflation. The solution was sprayed on the upper liver surface and around the cholecystectomy site **(Gad and Ali, 2022)**. Group II received a continuous infusion of lidocaine at a rate of 2 mg/kg/hr and magnesium sulfate at 1.5 g/hr throughout the surgery **(Farran et al., 2020).**

**Surgical Procedure:** Laparoscopic cholecystectomy was performed with specific steps, including insufflation of the abdomen to 15 mmHg using carbon dioxide, trocar placement, gallbladder retraction and dissection, and careful clipping and transection of the cystic duct and cystic artery. The gallbladder was then separated from the liver bed, hemostasis was achieved, and the gallbladder was removed. We followed instructions of **(Haribhakti & Mistry, 2015; Gaillard et al., 2015).**

**Anesthesia and Ventilation:** Patients were intubated and mechanically ventilated with volume-controlled mechanical ventilation. Anesthetics included propofol 1% at 2 mg/kg and atracurium at 0.5 mg/kg. Anesthesia was maintained with isoflurane in oxygen (FiO2 = 1). Local anesthesia with 1% lidocaine was applied to the incision site. Atracurium besylate doses of 0.1 mg/kg every 20 minutes was used for maintenance of neuromuscular block (**Brown, 1986**).

**Reversal of Neuromuscular Blockade:** Neuromuscular blockade was reversed using neostigmine (0.04 mg/kg) and atropine (0.02 mg/kg) **(Kitajima et al., 1996).**

**Pain Assessment:** Postoperatively, pain was assessed using the Visual Analogue Scale (VAS) **(Begum & Hossain, 2019),** a measure of pain intensity ranging from 0 to 100 mm. Patients marked their pain level on the scale, with higher scores indicating greater pain intensity. Pain was categorized as no pain (0-4 mm), mild pain (5-44 mm), moderate pain (45-74 mm), or severe pain (75-100 mm).

**Postoperative Monitoring:** Pain levels were recorded at 0, 1, 2, 4, 6, 12, 18, and 24 hours postoperatively using the VAS. Hemodynamic parameters (heart rate, blood pressure) were assessed every 5 minutes in the post-anesthesia care unit (PACU). Complications related to both drugs were also monitored.

The primary outcome was to evaluate the impact of intraperitoneal lidocaine (IP) administration and magnesium sulfate infusion on patients, assessed through the Visual Analogue Scale (VAS) to gauge pain perception. Secondary measures encompassed the assessment of patient hemodynamics, including heart rate (HR) and blood pressure (BP), as well as the monitoring of any associated complications arising from the interventions.

***Ethical code of the study*: SVU-MED-AIP029-1-22-9-455**

**Statistical analysis**

Data is depicted through either the utilization of mean and standard deviation (qualitative data representation) or numerical values and percentages (quantitative data representation). Group comparisons were conducted using the Chi-

Square test or Ficher exact test for quantitative data, the Mann-Whitney U test for continuous data that did not adhere to normal distribution, and the Student's t-test for continuous data that adhered to normal distribution. Statistical significance was established at a significance level of less than 0.05.

**Results**

The mean age for Group I is 37.12 ± 3.14 years, while Group II is 37.24 ± 7.46 years. The p-value for age comparison is 0.94123. Group I has 60% females, Group II has 48%, with a p-value of 0.3946. Rural residents are 40% in Group I, 44% in Group II, with a p-value of 0.77447. There was no significant difference between both groups regarding demographic data. (**Table .1, Fig.1).**

**Table 1. Demographic data of included subjects in both groups.**

| Variables | Group I (N = 25) | Group II (N = 25) | P. Value |
|---|---|---|---|
| **Age (Years)** | 37.12 ± 3.14 | 37.24 ± 7.46 | 0.94123 |
| **Sex** | | | |
| • **Female** | 15 (60%) | 12 (48%) | 0.3946 |
| • **Male** | 10 (40%) | 13 (52%) | |
| **Residence** | | | |
| • **Rural** | 10 (40%) | 11 (44%) | 0.77447 |
| • **Urban** | 15 (60%) | 14 (56%) | |

*P<0.05 Statistically significant | Data represented as Mean ± SD or number (Percentage)

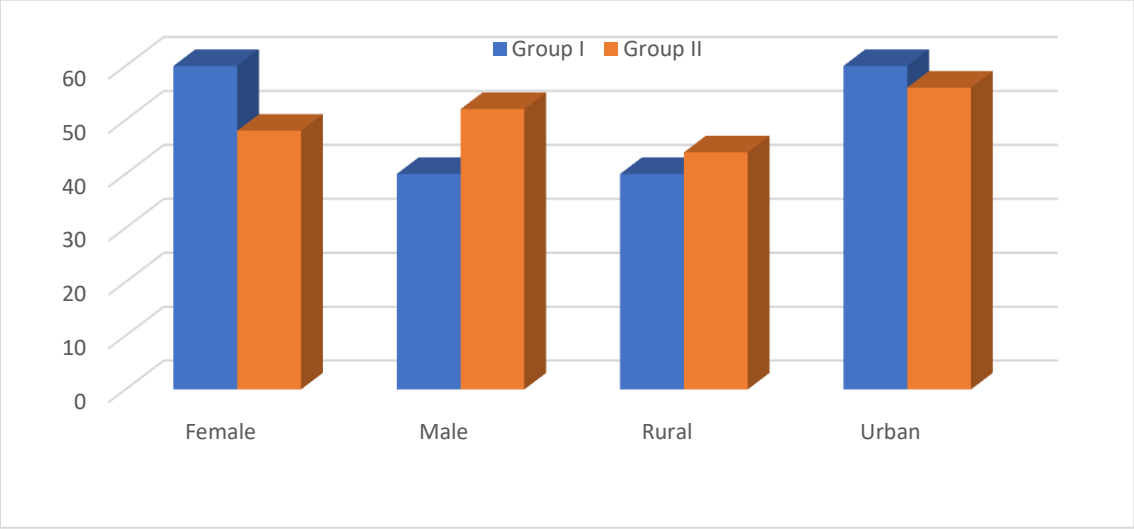


**Fig.1.Sex distribution and residence in both study groups.**

For blood pressure, systolic (mmHg) is 126.24 ± 12.68 in Group I and 123 ± 12.61 in Group II, with a p-value of 0.36938. Diastolic (mmHg) is 75.36 ± 7.3 in Group I and 70.84 ± 10.59 in Group II, with a p-value of 0.08538. Temperature (ºC) is 36.94 ± 0.1 in Group I and 36.97 ± 0.08 in Group II, with a p-value of 0.20491. Heart Rate (Beat/min.) is 92.08 ± 4.47 in Group I and 89.04 ± 7.87 in Group II, with a p-value of 0.09964. Respiratory Rate (Cycle/min.) is 14.56 ± 1.12 in Group I and 14.8 ± 0.91 in

Group II, with a p-value of 0.41062. Operation Time (min) is 72.8 ± 13.08 in Group I and 70 ± 9.57 in Group II, with a p-value of 0.39198. There was no significant difference between both groups regarding initial assessment. (**Table.2, Fig.2).**

**Table 2. Initial (Pre-Operative) assessment of included subjects in both groups**

| Variables | Group I (N = 25) | Group II (N = 25) | P. Value |
|---|---|---|---|
| **ASA (I)** | 25 (100%) | 25 (100%) | - |
| **Blood Pressure** | | | |
| • **Systolic (mmHg)** | 126.24 ± 12.68 | 123 ± 12.61 | 0.36938 |
| • **Diastolic (mmHg)** | 75.36 ± 7.3 | 70.84 ± 10.59 | 0.08538 |
| **Temperature ( ºC )** | 36.94 ± 0.1 | 36.97 ± 0.08 | 0.20491 |
| **HR (Beat/min.)** | 92.08 ± 4.47 | 89.04 ± 7.87 | 0.09964 |
| **RR (Cycle/min.)** | 14.56 ± 1.12 | 14.8 ± 0.91 | 0.41062 |
| **Operation Time (min)** | 72.8 ± 13.08 | 70 ± 9.57 | 0.39198 |

*P<0.05 Statistically significant | Data represented as Mean ± SD or number (Percentage)
HR: Heart Rate | RR: Respiratory Rate

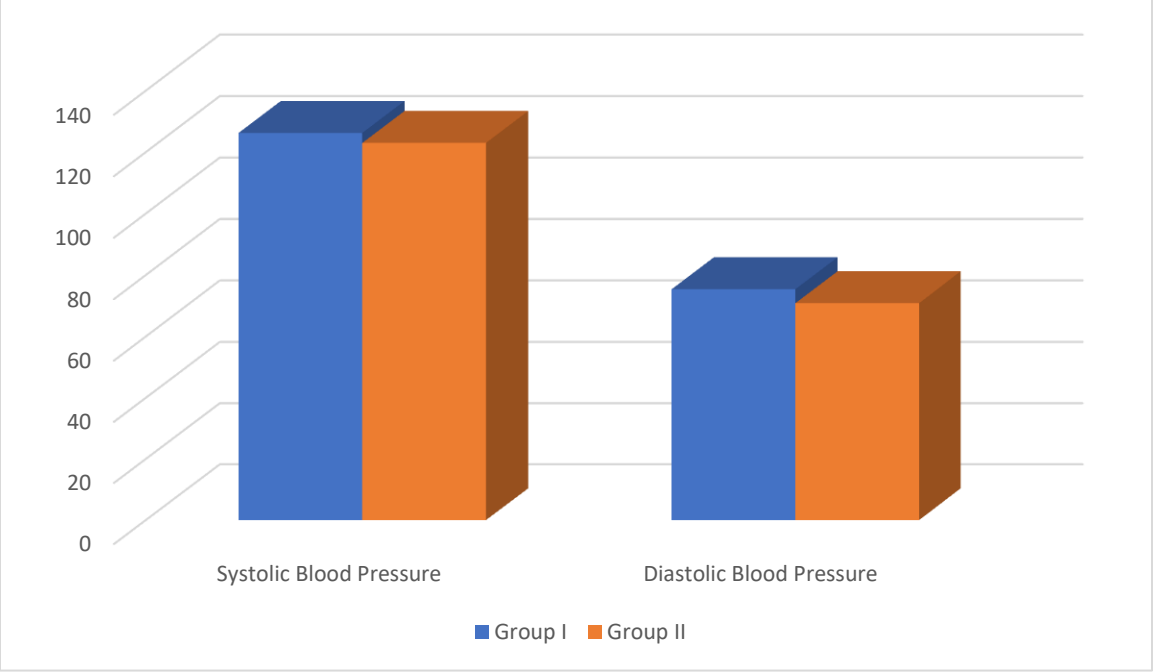


**Fig.2. Pre-operative blood pressure assessment in both study groups.**

During the intra-operative phase, several time points were assessed: at 10 minutes, Group I displayed a significantly elevated heart rate (HR) of 93.6 compared to Group II with 84.44 ($p < 0.0001$), signifying a substantial increase in Group I. At the 20-minute mark, Group I had an HR of 86.32, while Group II had 78.72 ($p = 0.00026$), demonstrating another significant increase in Group I. At 30 minutes, Group I exhibited an HR of 92.52, significantly higher than Group II's 80.24 ($p < 0.0001$). No significant difference was observed at 40 and 80 minutes ($p = 0.59701$ and $p = 0.52676$,

respectively). At 50 minutes, Group I had an HR of 89.52 compared to Group II's 80.5 ($p < 0.0001$), signifying a significant increase in Group I. At the 60-minute mark, Group I showed an HR of 91.24, significantly higher than Group II's 72.96 ($p < 0.0001$), indicating another significant increase in Group I. At 70 minutes, Group I had an HR of 88.69, while Group II had 83.16 ($p = 0.02546$), marking a significant increase in Group I, (**Table.3, Fig. 3).**

**Table 3.HR of included subjects in both groups**

| Variables | Group I (N = 25) | Group II (N = 25) | P. Value |
|---|---|---|---|
| **Intra-Operative** | | | |
| **10 min.** | 93.6 ± 4.34 | 84.44 ± 2.99 | <0.0001* |
| **20 min.** | 86.32 ± 5.7 | 78.72 ± 7.76 | 0.00026* |
| **30 min.** | 92.52 ± 5.47 | 80.24 ± 7.56 | <0.0001* |
| **40 min.** | 87.68 ± 2.29 | 89.2 ± 14.09 | 0.59701 |
| **50 min.** | 89.52 ± 3.47 | 80.5 ± 3.46 | <0.0001* |
| **60 min.** | 91.24 ± 3.36 | 72.96 ± 3.22 | <0.0001* |
| **70 min.** | 88.69 ± 3.59 | 83.16 ± 8.84 | 0.02546* |
| **80 min.** | 88.4 ± 6.06 | 90.75 ± 9.32 | 0.52676 |
| **90 min.** | 78 ± 8 | - | - |
| **100 min.** | 83 ± 3 | - | - |
| **PACU** | | | |
| **5 min.** | 97.2 ± 2.29 | 84.76 ± 6.91 | <0.0001* |
| **10 min.** | 92.8 ± 2.27 | 83 ± 5.17 | <0.0001* |
| **15 min.** | 91.84 ± 1.6 | 79.16 ± 5.84 | <0.0001* |
| **20 min.** | 89.8 ± 1.94 | 80.44 ± 6.06 | <0.0001* |
| **25 min.** | 89.64 ± 0.99 | 77.96 ± 6.52 | <0.0001* |
| **30 min.** | 85.28 ± 0.94 | 81.68 ± 7.2 | 0.01679* |
| **35 min.** | 86.44 ± 1.45 | 77.68 ± 6.52 | <0.0001* |
| **40 min.** | 86.24 ± 2.71 | 76.28 ± 6.49 | <0.0001* |
| **45 min.** | 86.32 ± 2.1 | 78.4 ± 5.01 | <0.0001* |
| **50 min.** | 85.96 ± 2.51 | 77.64 ± 5.14 | <0.0001* |
| **55 min.** | 83.44 ± 2.18 | 79.56 ± 4.21 | 0.00016* |
| **60 min.** | 82.76 ± 2.77 | 80.96 ± 6.23 | 0.19306 |
| **Follow up** | | | |
| **0** | 93.8 ± 2.25 | 85.52 ± 6.42 | <0.0001* |
| **1 h.** | 84.28 ± 3.25 | 78.96 ± 4.96 | 0.00005* |
| **2 h.** | 84.84 ± 1.52 | 75.84 ± 6.55 | <0.0001* |
| **4 h.** | 85.68 ± 1.22 | 82.8 ± 4.34 | 0.00247* |
| **6 h.** | 86.32 ± 3 | 85.24 ± 7.1 | 0.48666 |
| **12 h.** | 84.12 ± 2.76 | 76.56 ± 6.18 | <0.0001* |
| **18 h.** | 80.8 ± 2.9 | 79.4 ± 7.25 | 0.37459 |
| **24 h.** | 79.84 ± 2.27 | 73.52 ± 7.58 | 0.00022* |

*P<0.05 Statistically significant | Data represented as Mean ± SD
P. Value with t.test

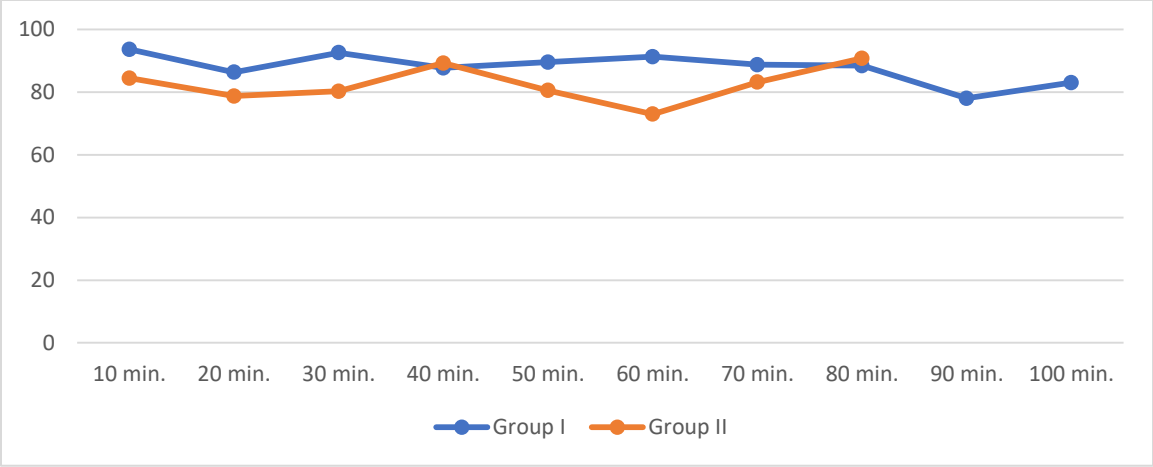


**Fig.3. Intra-Operative HR of included subjects in both groups**

In the Post-Anesthesia Care Unit (PACU), similar trends persisted: at 5 minutes, Group I had an HR of 97.2, significantly higher than Group II's 84.76 ($p < 0.0001$), signifying a significant increase in Group I. At 10 minutes, Group I displayed an HR of 92.8 compared to Group II's 83 ($p < 0.0001$), indicating a significant increase in Group I. At 15 minutes, Group I exhibited an HR of 91.84, significantly higher than Group II's 79.16 ($p < 0.0001$), marking a significant increase in Group I. At 20 minutes, Group I had an HR of 89.8, while Group II had 80.44 ($p < 0.0001$), signifying a significant increase in Group I. At 25 minutes, Group I showed an HR of 89.64 compared to Group II's 77.96 ($p < 0.0001$), indicating a significant increase in Group I. At 30 minutes, Group I had an HR of 85.28, significantly higher than Group II's 81.68 ($p = 0.01679$), signifying a significant increase in Group I. No significant difference was observed at 60 minutes ($p = 0.19306$), (**Table .3, Fig.4).**

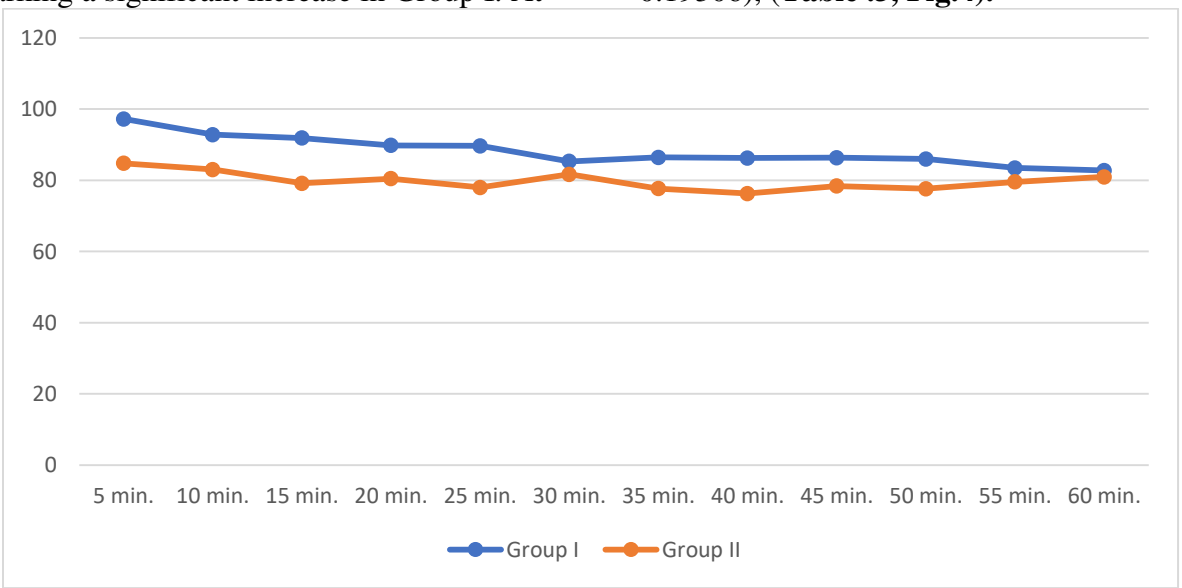


**Fig. 4. PACU – HR of included subjects in both groups**

During the follow-up period, notable trends continued: at 0 hours, Group I displayed an HR of 93.8, significantly higher than Group II's 85.52 ($p < 0.0001$), signifying a significant increase in Group I. At 1 hour, Group I exhibited an HR of 84.28 compared to Group II's 78.96 ($p = 0.00005$), marking a significant increase in Group I. At 2 hours, Group I had an HR of 84.84, significantly higher than Group II's 75.84 ($p < 0.0001$), indicating a significant increase in Group I. At 4 hours, Group I showed an HR of 85.68, while Group II had 82.8 ($p = 0.00247$), signifying a significant increase in Group II. No significant difference was observed at 6 and 18 hours ($p = 0.48666$ and $p = 0.37459$, respectively). At 12 hours, Group I displayed an HR of 84.12, significantly higher than Group II's 76.56 ($p < 0.0001$), marking a significant increase in Group I. Finally, at 24 hours, Group I had an HR of 79.84, significantly higher than Group II's 73.52 ($p = 0.00022$), signifying a significant increase in Group I, **(Table .3, Fig.5).**

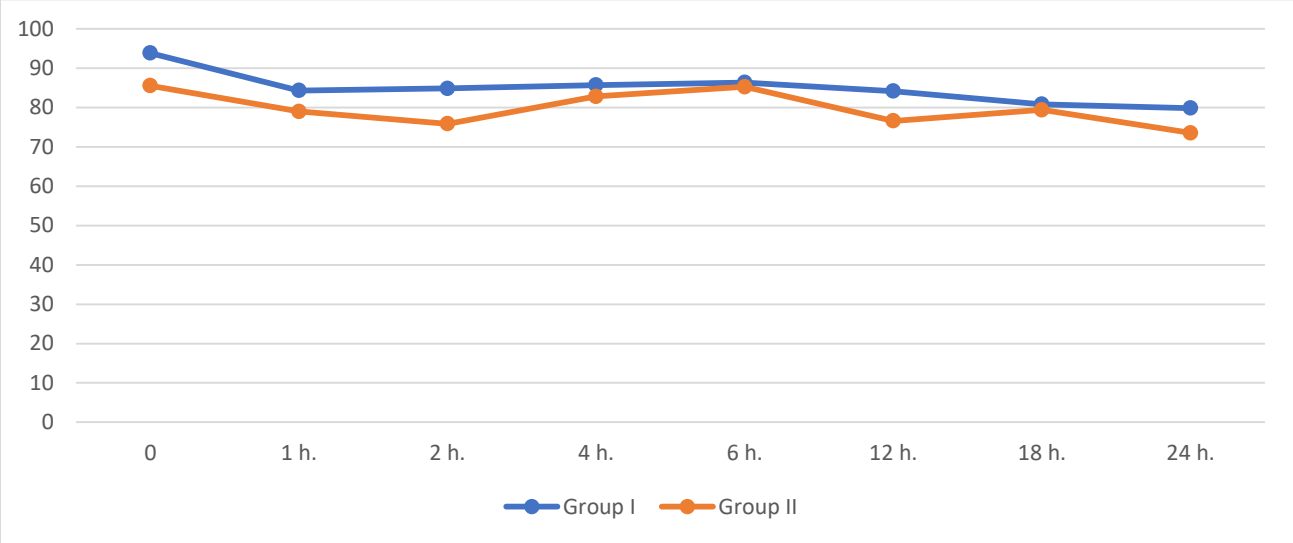


**Fig.5.Follow up HR of included subjects in both groups**

Systolic Blood Pressure (SBP) intra-operatively at 10 minutes was 120.48 ± 10.94 in Group I and 117.08 ± 6.19 in Group II, with no significant difference ($p = 0.18269$). At 20 minutes, Group I had SBP of 127.96 ± 24.16, significantly higher than Group II's 106.76 ± 5.01 ($p = 0.00008$), indicating a significant increase in Group I. At 30 minutes, Group I exhibited SBP of 120.72 ± 14.81, also significantly higher than Group II's 110 ± 5.56 ($p = 0.00141$), marking a significant increase in Group I. At 40 minutes, Group I displayed SBP of 122.44 ± 8.94, significantly higher than Group II's 104.2 ± 11.43 ($p < 0.0001$), indicating a significant increase in Group I. No significant differences were observed at later time points for SBP, **(Table .4, Fig.6) .**

**Table 4. Intra-Operative Blood Pressure of included subjects in both groups.**

| Variables | Group I (N = 25) | Group II (N = 25) | P. Value |
|---|---|---|---|
| **Systolic Blood Pressure** | | | |
| **10 min.** | 120.48 ± 10.94 | 117.08 ± 6.19 | 0.18269 |
| **20 min.** | 127.96 ± 24.16 | 106.76 ± 5.01 | 0.00008* |

| | | | |
|---|---|---|---|
| **30 min.** | 120.72 ± 14.81 | 110 ± 5.56 | 0.00141* |
| **40 min.** | 122.44 ± 8.94 | 104.2 ± 11.43 | <0.0001* |
| **50 min.** | 118.72 ± 8.81 | 118.58 ± 14.24 | 0.96781 |
| **60 min.** | 115.16 ± 11.43 | 119.21 ± 22.09 | 0.42176 |
| **70 min.** | 116.31 ± 4.64 | 123.11 ± 17.58 | 0.14336 |
| **80 min.** | 121.6 ± 13.29 | 131.63 ± 19.15 | 0.20837 |
| **90 min.** | 101.33 ± 12.9 | - | - |
| **100 min.** | 122.33 ± 14.57 | - | - |
| **Diastolic Blood Pressure** | | | |
| **10 min.** | 68.76 ± 5.64 | 71.64 ± 5.05 | 0.06306 |
| **20 min.** | 61.4 ± 19.84 | 59.16 ± 1.82 | 0.57656 |
| **30 min.** | 82.16 ± 15.83 | 69.68 ± 8.2 | 0.00101* |
| **40 min.** | 70.28 ± 12.88 | 67.2 ± 8.22 | 0.31865 |
| **50 min.** | 72.52 ± 15.06 | 71.92 ± 7.97 | 0.86246 |
| **60 min.** | 77.16 ± 7.16 | 75.29 ± 16.3 | 0.60333 |
| **70 min.** | 69.38 ± 9.5 | 68.26 ± 8.96 | 0.72428 |
| **80 min.** | 74.2 ± 4.92 | 74.75 ± 8.14 | 0.86118 |
| **90 min.** | 58.67 ± 1.15 | - | - |
| **100 min.** | 73.33 ± 3.79 | - | - |

*P<0.05 Statistically significant | Data represented as Mean ± SD
P. Value with t.test

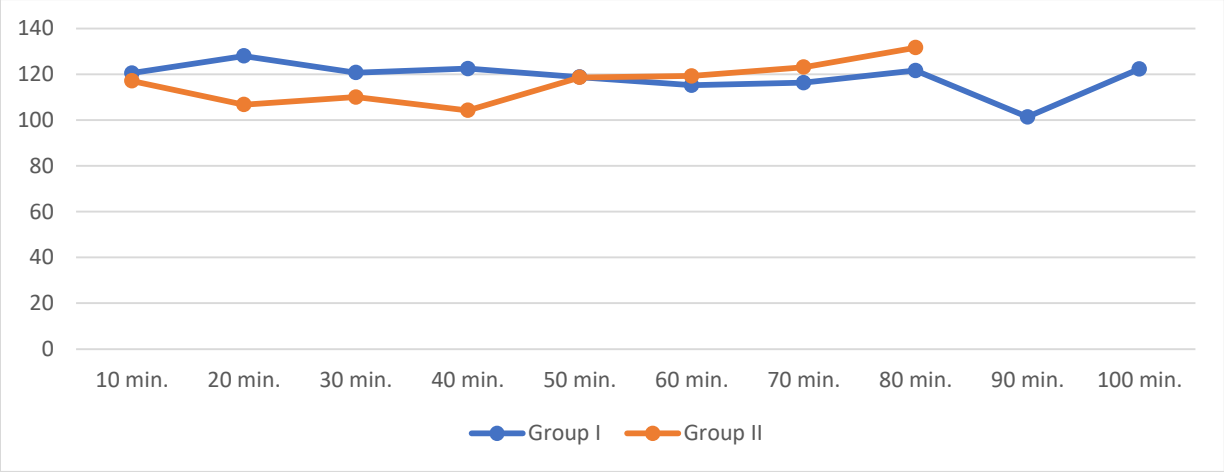


**Fig.6. Intra-Operative SBP of included subjects in both groups**

Regarding Diastolic Blood Pressure (DBP) intra-operatively at 10 minutes, Group I had DBP of 68.76 ± 5.64, while Group II had 71.64 ± 5.05, with no significant difference (p = 0.06306). At 20 minutes, no significant difference was observed (p = 0.57656). However, at 30 minutes, Group I had DBP of 82.16 ± 15.83, significantly higher than Group II's 69.68 ± 8.2 (p = 0.00101), indicating a significant increase in Group I. No significant differences were observed at later time points for DBP, (**Table .4, Fig.7).**

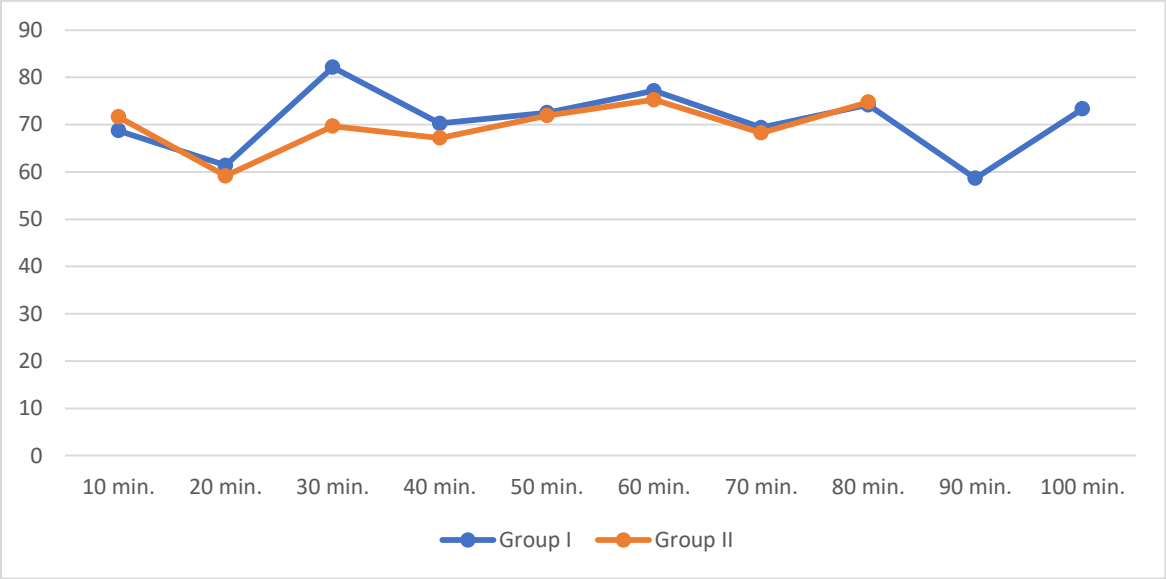


**Fig.7. Intra-Operative DBP of included subjects in both groups**

PACU Systolic Blood Pressure (SBP) at 5 minutes was significantly higher in Group I (133.32 ± 2.53) compared to Group II (117.2 ± 11.46) with a p-value of less than 0.0001, indicating a significant increase in Group I. This trend continued at subsequent time points (10, 15, 20, 25, 30, 35, and 40 minutes), all showing significant increases in SBP in Group I compared to Group II ($p < 0.0001$). At 45 minutes, Group I maintained a significantly higher SBP (124.8 ± 3.38) than Group II (117.88 ± 7.39) with a p-value of 0.0001, signifying a significant increase in Group I. However, at 50 minutes, there was no significant difference ($p = 0.14357$), and at 55 and 60 minutes, Group I exhibited significantly lower SBP ($p = 0.00001$ and $p = 0.00275$, respectively), (**Table.5, Fig.8**).

**Table 5. PACU - BP of included subjects in both groups.**

| Variables | Group I (N = 25) | Group II (N = 25) | P. Value |
|---|---|---|---|
| **Systolic Blood Pressure** | | | |
| **5 min.** | 133.32 ± 2.53 | 117.2 ± 11.46 | <0.0001* |
| **10 min.** | 128.36 ± 2.78 | 115.96 ± 8.47 | <0.0001* |
| **15 min.** | 130.28 ± 1.49 | 114.2 ± 4.43 | <0.0001* |
| **20 min.** | 126.72 ± 1.28 | 110.68 ± 5.97 | <0.0001* |
| **25 min.** | 126.08 ± 0.76 | 115.16 ± 7.01 | <0.0001* |
| **30 min.** | 124.16 ± 3.34 | 117.56 ± 5.16 | <0.0001* |
| **35 min.** | 124.36 ± 2.58 | 118.96 ± 3.06 | <0.0001* |
| **40 min.** | 124.56 ± 0.87 | 116.8 ± 4.87 | <0.0001* |
| **45 min.** | 124.8 ± 3.38 | 117.88 ± 7.39 | 0.0001* |
| **50 min.** | 122.32 ± 4.06 | 119.72 ± 7.74 | 0.14357 |
| **55 min.** | 124.28 ± 1.74 | 115.56 ± 8.65 | 0.00001* |
| **60 min.** | 121.4 ± 2.97 | 116.48 ± 7.2 | 0.00275* |
| **Diastolic Blood Pressure** | | | |

| | | | |
|---|---|---|---|
| **5 min.** | 78.32 ± 5.98 | 67.24 ± 6.05 | <0.0001* |
| **10 min.** | 78.16 ± 1.72 | 79.48 ± 6.27 | 0.31492 |
| **15 min.** | 81.08 ± 0.81 | 74.92 ± 1.98 | <0.0001* |
| **20 min.** | 80.16 ± 3.37 | 71.04 ± 4.19 | <0.0001* |
| **25 min.** | 78.36 ± 1.68 | 73.92 ± 3.53 | <0.0001* |
| **30 min.** | 79.32 ± 4.71 | 82.28 ± 4.28 | 0.02421* |
| **35 min.** | 76.16 ± 0.75 | 74.68 ± 3.96 | 0.07217 |
| **40 min.** | 79.96 ± 1.65 | 72.12 ± 3.17 | <0.0001* |
| **45 min.** | 76.4 ± 1.04 | 74.76 ± 3.37 | 0.02435* |
| **50 min.** | 75.84 ± 1.91 | 75.68 ± 0.48 | 0.68594 |
| **55 min.** | 75.76 ± 1.64 | 78.52 ± 1.33 | <0.0001* |
| **60 min.** | 75.4 ± 3.77 | 74.28 ± 2.95 | 0.2483 |

*P<0.05 Statistically significant | Data represented as Mean ± SD
P. Value with t.test

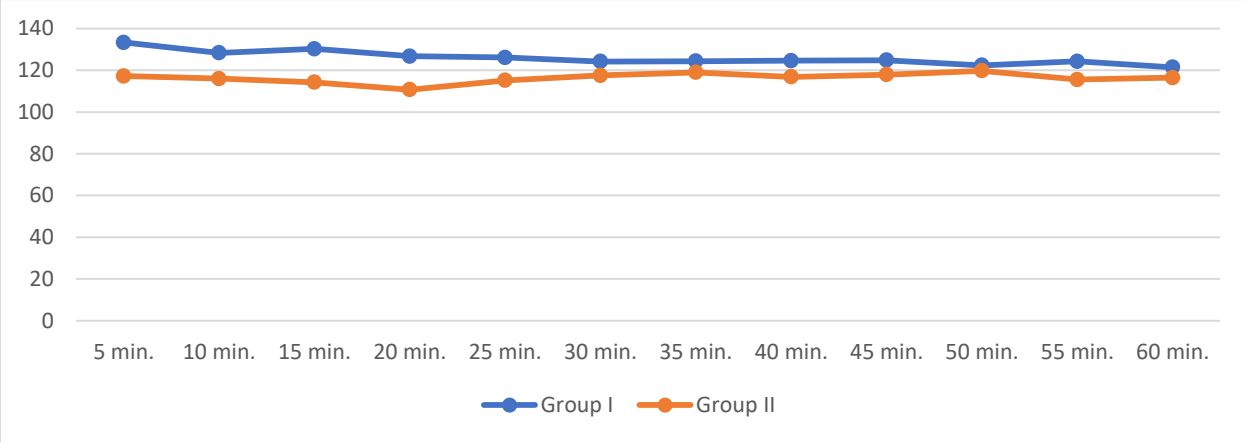


**Fig.8.PACU – SBP of included subjects in both groups**

PACU Diastolic Blood Pressure (SBP) at 5 minutes was significantly higher in Group I (133.32 ± 2.53) compared to Group II (117.2 ± 11.46) with a p-value of less than 0.0001, indicating a significant increase in Group I. This trend continued at subsequent time points (10, 15, 20, 25, 30, 35, and 40 minutes), all showing significant increases in SBP in Group I compared to Group II ($p < 0.0001$). At 45 minutes, Group I maintained a significantly higher SBP (124.8 ± 3.38) than Group II (117.88 ± 7.39) with a p-value of 0.0001, signifying a significant increase in Group I. However, at 50 minutes, there was no significant difference ($p = 0.14357$), and at 55 and 60 minutes, Group I exhibited significantly lower SBP ($p = 0.00001$ and $p = 0.00275$, respectively), (**Table.5, Fig.9**).

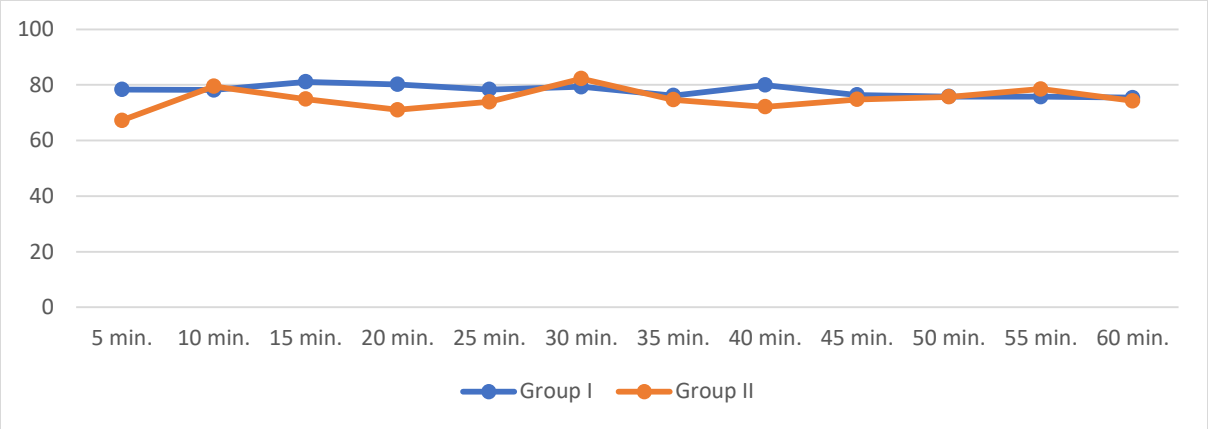


**Fig.9.PACU – DBP of included subjects in both groups**

Regarding VAS score, immediately after surgery Group II had significantly higher scores compared to Group I (2.24 ± 0.78 vs. 1.44 ± 0.51, p = 0.00008*), indicating a substantial initial pain perception difference. At 1 hour, Group II still had higher scores (2.44 ± 0.51 vs. 1.84 ± 0.55, p = 0.00022*), maintaining the pain perception gap. The trend continued at 2 hours (2.36 ± 0.49 vs. 1.8 ± 0.5, p = 0.00022*). Group II's pain perception significantly increased at 4 hours (3.44 ± 1.08 vs. 2.08 ± 0.28, p < 0.0001*). At 6 hours, both groups experienced pain perception elevation, with Group II notably higher (6.6 ± 0.91 vs. 3.12 ± 0.83, p < 0.0001*). A similar pattern persisted at 12 hours (3.04 ± 0.73 vs. 1.64 ± 0.57, p < 0.0001*) and 18 hours (2.52 ± 0.51 vs. 1.28 ± 0.46, p < 0.0001*). At 24 hours, Group II maintained higher scores (2.4 ± 0.5 vs. 1.24 ± 0.44, p < 0.0001*), highlighting consistent and significant pain perception differences favoring Group II throughout the follow-up period, **(Table.6, Fig.10).**

**Table 6. Follow up VAS score of included subjects in both groups**

| Variables | Group I (N = 25) | Group II (N = 25) | P. Value |
|---|---|---|---|
| **0** | 1.44 ± 0.51 | 2.24 ± 0.78 | 0.00008* |
| **1 h.** | 1.84 ± 0.55 | 2.44 ± 0.51 | 0.00022* |
| **2 h.** | 1.8 ± 0.5 | 2.36 ± 0.49 | 0.00022* |
| **4 h.** | 2.08 ± 0.28 | 3.44 ± 1.08 | <0.0001* |
| **6 h.** | 3.12 ± 0.83 | 6.6 ± 0.91 | <0.0001* |
| **12 h.** | 1.64 ± 0.57 | 3.04 ± 0.73 | <0.0001* |
| **18 h.** | 1.28 ± 0.46 | 2.52 ± 0.51 | <0.0001* |
| **24 h.** | 1.24 ± 0.44 | 2.4 ± 0.5 | <0.0001* |

*P<0.05 Statistically significant | Data represented as Mean ± SD
P. Value with t.test

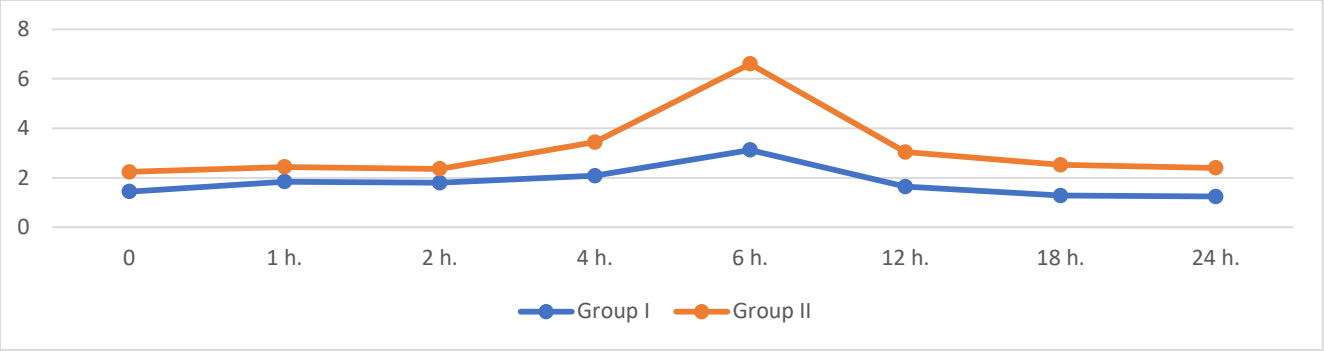


**Fig.10. Follow up VAS score of included subjects in both groups**

Immediately after surgery Group I had a significantly higher systolic blood pressure (131.6 ± 3) compared to Group II (118.28 ± 11.91), indicating a significant decrease in systolic BP in Group II ($p < 0.0001$*). At 1 hour, Group I still had higher systolic BP (122.68 ± 2.78) compared to Group II (117.2 ± 5.58), with a significant decrease observed in Group II ($p = 0.00006$*). This trend continued at 2 hours ($p = 0.00571$*) and 4 hours ($p = 0.00001$*) with significant decreases in Group II. However, at 6 hours and beyond, no significant differences were observed**, (Table .7, Fig.11).**

**Table 7. Follow up BP of included subjects in both groups**

| | **Group I (N = 25)** | **Group II (N = 25)** | **P. Value** |
|---|---|---|---|
| **Systolic Blood Pressure** | | | |
| **0** | 131.6 ± 3 | 118.28 ± 11.91 | <0.0001* |
| **1 h.** | 122.68 ± 2.78 | 117.2 ± 5.58 | 0.00006* |
| **2 h.** | 122.16 ± 2.36 | 118.04 ± 6.72 | 0.00571* |
| **4 h.** | 126.04 ± 2.01 | 121.4 ± 4.1 | 0.00001* |
| **6 h.** | 128.64 ± 4.3 | 127.84 ± 4 | 0.49891 |
| **12 h.** | 125.72 ± 2.39 | 123 ± 2.31 | 0.00016* |
| **18 h.** | 119.84 ± 2.15 | 120.32 ± 2.15 | 0.43475 |
| **24 h.** | 115 ± 3.94 | 116.24 ± 5.15 | 0.34365 |
| **Diastolic Blood Pressure** | | | |
| **0** | 74.72 ± 2.91 | 65.84 ± 6.3 | <0.0001* |
| **1 h.** | 76.24 ± 3.1 | 73.84 ± 2.95 | 0.00729* |
| **2 h.** | 76.44 ± 1.42 | 81.04 ± 2.94 | <0.0001* |
| **4 h.** | 77.64 ± 1.73 | 78.48 ± 2.24 | 0.1441 |
| **6 h.** | 79.4 ± 3.29 | 78.16 ± 7.46 | 0.45099 |
| **12 h.** | 77.68 ± 2.85 | 77.4 ± 5.43 | 0.82047 |
| **18 h.** | 76.28 ± 3.76 | 76.68 ± 8.51 | 0.83067 |
| **24 h.** | 72.48 ± 3.62 | 72.92 ± 2.77 | 0.63135 |

*P<0.05 Statistically significant | Data represented as Mean ± SD
P. Value with t.test

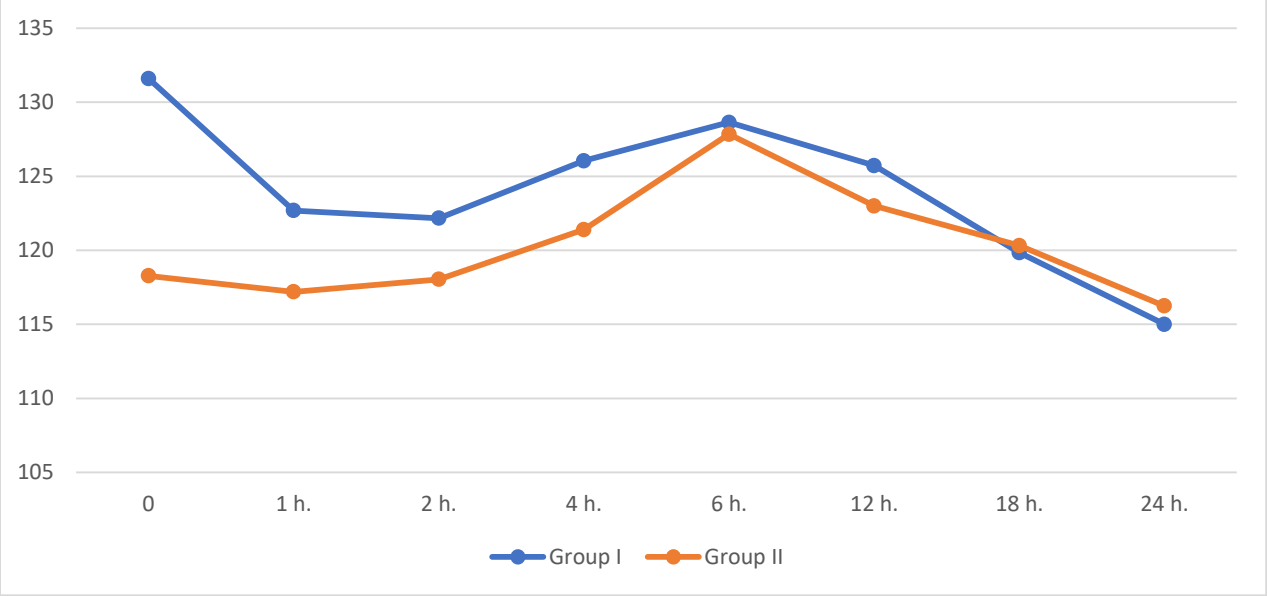


**Fig.11. Follow up SBP of included subjects in both groups**

In terms of diastolic BP, immediately after surgery Group I had a significantly higher value (74.72 ± 2.91) compared to Group II (65.84 ± 6.3), signifying a significant decrease in diastolic BP in Group II ($p < 0.0001$*). At 1 hour, Group I still had a higher diastolic BP (76.24 ± 3.1) compared to Group II (73.84 ± 2.95), with a significant decrease in Group II ($p = 0.00729$*). The diastolic BP difference persisted at 2 hours ($p < 0.0001$*) but became non-significant at later time points, indicating a sustained decrease in diastolic BP in Group II during the early hours of observation, (**Table.7, Fig.12).**There were no recorded complications in both groups.

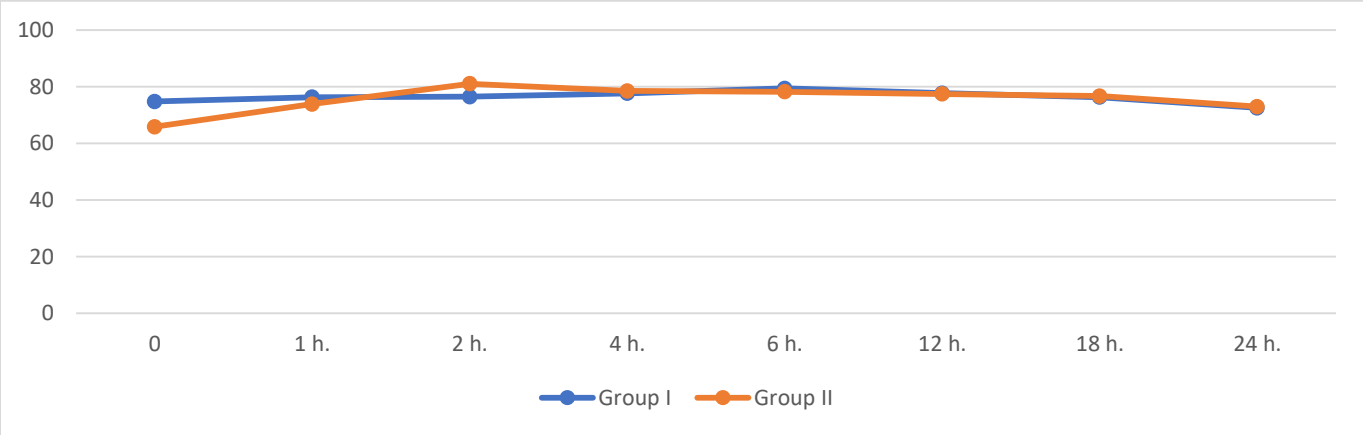


**Fig.12.Follow up DBP of included subjects in both groups**

## Discussion

Laparoscopic cholecystectomy, a common gallbladder surgery, causes significant postoperative discomfort, reducing patient recovery and satisfaction. Opioid analgesics, which may cause respiratory depression and addiction, are used to treat the surgery's discomfort despite its minimally invasive nature. Thus, new pain treatment methods are evolving. Intraperitoneal lidocaine

intercepts pain signals and reduces discomfort and opioid intake in various procedures **(Gudin & Nalamachu, 2020; Yu et al., 2019).**

Another option is to infuse magnesium sulfate, which relaxes muscles and reduces opiate use. Both methods show promise, but further research is needed to determine their efficacy and safety in laparoscopic cholecystectomy patients **(El Mourad & Arafa, 2019; Soleimanpour et al., 2022).**

In our Study Magnesium sulfate infusion substantially reduced heart rate, mean systolic blood pressure, and diastolic blood pressure compared to intraperitoneal lidocaine. During surgery and at the PACU. Magnesium sulfate had a considerably lower follow-up heart rate and systolic blood pressure than intraperitoneal lidocaine for much of the first day postoperative. In the first two hours, diastolic blood pressure differed across groups, but this difference faded afterwards. Magnesium sulfate infusion reduces postoperative heart rate and systolic blood pressure longer than intraperitoneal lidocaine.

Several mechanisms may explain magnesium sulfate infusion's persistent postoperative heart rate and systolic blood pressure reduction. Magnesium sulfate directly dilates blood arteries, lowering blood pressure. Magnesium blocks calcium channels in blood vessel smooth muscle cells, relaxing and dilation them. This impact may persist, which may explain the magnesium sulfate group's extended blood pressure drop. Second, magnesium sulfate slows the heart rate by lowering sinoatrial node depolarization. This impact may explain the magnesium sulfate group's extended heart rate drop **(Abd-Eldayem et al., 2022; Nahar, 2022; Thakur, 2022).**

However, intraperitoneal lidocaine is mostly used as a local anesthetic to relieve pain rather than to lower heart rate and blood pressure. Lidocaine may lower blood pressure locally, but it is unlikely to have the same persistent effects on blood pressure and heart rate as magnesium sulfate. Intraperitoneal lidocaine may not have the same systemic absorption as intravenous magnesium sulfate infusion, which may restrict its heart rate and blood pressure-lowering effects **(Rutherford et al., 2021).**

Compared to intraperitoneal lidocaine, magnesium sulfate infusion substantially reduced heart rate, mean systolic blood pressure, and diastolic blood pressure throughout intra-operative and post-anesthesia care unit periods. The magnesium sulfate group also had persistent heart rate and systolic blood pressure decreases for much of the first postoperative day. This persistent effect of magnesium sulfate on heart rate and blood pressure may be due to its direct vasodilatory action on blood vessels and its capacity to reduce heart rate by preventing sinoatrial node depolarization. These physiological processes explain the magnesium sulfate group's longer blood pressure and heart rate drop **(Abd-Eldayem in 2022; Nahar in 2022; Thakur in 2022).**

Intraperitoneal lidocaine relieves local discomfort rather than controlling heart rate and blood pressure. Lidocaine may cause local vasodilation, whereas magnesium sulfate has prolonged and systemic effects. Localized delivery and less effective systemic absorption than intravenous magnesium sulfate infusion may decrease intraperitoneal lidocaine's ability to reduce heart rate and blood pressure **(Rutherford et al., 2021).**

Along with our study, **Ali et al. (2015)** found that intraperitoneal magnesium sulphate (MgSO4) reduced pneumoperitoneum-induced hemodynamic stress in laparoscopic cholecystectomy patients.

Our research found that intraperitoneal lidocaine reduced the Follow-up Visual Analog Scale (VAS) score in group I compared to group II on the first postoperative day, suggesting better pain management. Lidocaine's sensorineural suppression of nociceptive signals, systemic absorption, and anti-inflammatory actions may explain this. In contrast, magnesium sulfate infusion blocks NMDA receptors and calcium channels, relieving neuropathic pain and relaxing muscles. Unlike lidocaine, magnesium sulfate has systemic effects but lacks site-specificity **(Abu-Zaid et al., 2021; Perniola, 2014; Lee, 2009; Noland, 2019).**

Our findings match earlier studies as, **Roberts et al. (2011)** found that subperitoneal diaphragm local anesthetic injections reduced postoperative discomfort and recovery room stays after laparoscopic cholecystectomy. **Morsy et al. (2014)** found that intraperitoneal nalbuphine and lidocaine reduced pain intensity and VAS ratings during recovery. In LC patients, intraperitoneal lidocaine improved postoperative pain, according to **Yang et al. (2014)** and **Khan et al. (2012).** Open operations may cause more tissue stress, hence **Ali et al. (2015)** found intraperitoneal local anesthetics less effective than laparoscopy. **Aasim et al. (2017)** and **IGIMS et al. (2022)** also found magnesium sulfate infusion increased analgesia.

Intraperitoneal lidocaine and magnesium sulfate infusion help laparoscopic cholecystectomy patients manage discomfort. Although there is little evidence comparing these opioid-free anesthetic methods, **Saadawy et al. (2010)** found that lidocaine reduced pain more than magnesium. The magnesium sulfate infusion group needed rescue analgesia 32% of the time, whereas the intraperitoneal lidocaine group did not. This difference was statistically significant, suggesting lidocaine's focused pain reduction impact may reduce rescue analgesia($p=0.004$).

However Contrary to our findings, **Lysakowski et al. (2007)** stated that evidence is still lacking to support the claim that perioperative magnesium has favorable effects on post-operative pain intensity and analgesic requirements. They recommended further studies to investigate the role of magnesium as a supplement to post-operative analgesia because the biological basis for its potential anti-nociceptive effects is promising.

Our findings align with **Saadawy et al. (2010),** showing that Lidocaine and magnesium reduced anesthetic needs ($P<0.01$) and morphine usage ($P<0.001$) compared to controls. Specifically, Lidocaine significantly decreased morphine consumption at 2 hours ($P<0.05$). Both Lidocaine and magnesium groups exhibited lower morphine consumption than the placebo group at 2 and 24 hours ($P<0.001$). Notably, group L had significantly lower morphine requirements than group M at 2 hours ($P<0.05$). Also, **Morsy et al. (2014)** showed intraperitoneal lidocaine significantly decreased postoperative analgesic usage. In the present investigation, intraperitoneal lidocaine and magnesium sulfate infusion did not cause postoperative problems in laparoscopic cholecystectomy patients. Also, **Li et al. (2018)** who found decreased incidence of postoperative complications with lidocaine as the overall incidence of nausea and vomiting was 31/178 in the lidocaine groups compared 58/176 in control groups ($P < .05$).

Contrary to our findings, **Morsy et al. (2014)** reported a higher complication rate in the lidocaine group compared to our results. Among the patients in the lidocaine group (Group L), six out of the total experienced PONV. This accounted for 22.2% of the patients within the lidocaine group.

Similarly, the outcomes in **Safavi et al. (2015)** study diverged from our results. This study similarly involved two groups: Group M, which received Magnesium sulfate, and Group L, administered with Lidocaine. The study's focus revolved around examining various variables, notably the occurrence of distinct skin reactions. The results demonstrated that within Group M, 2 cases (4.4%) displayed erythema (skin redness), 4 cases (8.9%) experienced edema (swelling), and 4 cases (8.9%) exhibited allergic reactions. For Group L, 1 case (2.2%) showcased erythema, 1 case (2.2%) had edema, and 8 cases (17.8%) manifested allergic reactions. Importantly, it was observed that Lidocaine (Group L) appeared to exhibit a slightly decreased occurrence of erythema and edema when compared to Magnesium sulfate (Group M), but conversely displayed a heightened frequency of allergic reactions.

## Conclusion

Both intraperitoneal lidocaine (IP) administration and magnesium sulfate infusion are effective methods for reducing pain and improving recovery in patients undergoing laparoscopic cholecystectomy. Our study found that magnesium sulfate infusion was associated with lower heart rate and blood pressure values during and after the surgery, while intraperitoneal lidocaine provided better overall pain control and had a lower incidence of patients requiring rescue analgesia. Importantly, neither intervention was associated with any postoperative complications, indicating that both are safe to use in laparoscopic cholecystectomy patients.

## References


- **Aasim SA, Kumar KA, Suram GA (2017).** Comparison of Intraperitoneal Instilllation of Bupivacaine-Tramadol with Bupivacaine-Magnesium Sulphate for Pain Relief after Laparoscopic Cholecystectomy, 5(9): 28015-28020.
- **Abd-Eldayem OT, Ali Amy, Mohamed AAE, Ahmed MAE (2022).** Effect of Magnesium Sulphate on Perioperative Hemodynamic Responses in Hypertensive Patients Undergoing Laparoscopic Cholecystectomy. A Randomized Controlled Double Blinded Trial. The Medical Journal of Cairo University, 90(3): 647-656.
- **Abu-Zaid A, Baradwan S, Himayda S, Badghish E, Alshahrani MS, Miski NT et al (2021).** Intraperitoneal lidocaine instillation during abdominal hysterectomy: A systematic review and meta-analysis of randomized placebo-controlled trials. Journal of Gynecology Obstetrics and Human Reproduction, 50(10): e102226.
- **Ahuja V (2022).** Significance of Robotic Cholecystectomy over Laparoscopic Cholecystectomy in The Management of Cholecystitis: A Case Study of Factors Influencing Patients'decision at a Hospital In Texas, USA. AU eJournal of Interdisciplinary Research (ISSN: 2408-1906), 7(2): 62-80.
- **Ali, R. M., Rabie, A. H., Elshalakany, N. A., & El Gindy, T. M. (2015).** Effect of intraperitoneal magnesium sulfate on hemodynamic changes and its analgesic and antiemetic effect in laparoscopic cholecystectomy. Ain-Shams Journal of Anaesthesiology, 8(2): 153-159.
- **Bedson J, Chen Y, Ashworth J, Hayward RA, Dunn KM, Jordan KP (2019).** Risk of adverse events in patients prescribed long-term opioids: a cohort study in the UK clinical practice research Datalink. European Journal of Pain, 23(5): 908-922.
- **Begum, M. R., & Hossain, M. A. (2019).** Validity and reliability of visual analogue scale (VAS) for pain measurement. Journal of Medical Case Reports and Reviews, 2(11): 394-402.

- **Beloeil H (2019).** Opioid-free anesthesia. Best Practice & Research Clinical Anaesthesiology, 33(3): 353-360.
- **Chia PA, Cannesson M, Bui CCM (2020).** Opioid free anesthesia: feasible? Current opinion in anaesthesiology, 33(4): 512-517.
- **Brown EM (1986).** Regional Anesthesia and Clinical Applications. Anesthesia & Analgesia, 65(2): 216-216.
- **Chu R, Umukoro N, Greer T, Roberts J, Adekoya P, Odonkor CA, Hagedorn JM, Olatoye D, Urits I, Orhurhu MS (2020).** Intravenous lidocaine infusion for the management of early postoperative pain: a comprehensive review of controlled trials. Psychopharmacology bulletin, 50(1): 216-259.
- **Daabiss, M. (2011).** American Society of Anaesthesiologists physical status classification. Indian journal of anaesthesia, 55(2): 111-115.
- **Daoust R, Paquet J, Cournoyer A, Piette É, Morris J, Lessard J, Castonguay V, Williamson D, Chauny JM (2020).** Side effects from opioids used for acute pain after emergency department discharge. The American journal of emergency medicine, 38(4): 695-701.
- **El Mourad MB, Arafa SK (2019).** Effect of intravenous versus intraperitoneal magnesium sulfate on hemodynamic parameters and postoperative analgesia during laparoscopic sleeve gastrectomy–A prospective randomized study. Journal of Anaesthesiology, Clinical Pharmacology, 35(2): 242-247.
- **El Nakeeb A, Mahdy Y, Salem A, El Sorogy M, El Rafea AA, El Dosoky M et al (2017).** Open cholecystectomy has a place in the laparoscopic era: a retrospective cohort study. Indian Journal of Surgery, 79(1): 437-443.
- **Farran HA, Soliman S, Alfy MO (2020).** Opioid free anesthesia in patients undergoing three-ports laparoscopic cholecystectomy. Al-Azhar International Medical Journal, 1(2): 160-165.
- **Forget P (2019).** Opioid-free anaesthesia. Why and how? A contextual analysis. Anaesthesia Critical Care & Pain Medicine, 38(2): 169-172.
- **Gad GS, Ali HS (2022).** Rectal indomethacin versus intraperitoneal lidocaine for analgesia after laparoscopic cholecystectomy. SVU-International Journal of Medical Sciences, 5(1): 114-125.
- **Gaillard, M., Tranchart, H., Lainas, P., & Dagher, I. (2015).** New minimally invasive approaches for cholecystectomy: review of literature. World journal of gastrointestinal surgery, 7(10): 243-248.
- **Gudin J, Nalamachu S (2020).** Utility of lidocaine as a topical analgesic and improvements in patch delivery systems. Postgraduate Medicine, 132(1): 28-36.
- **Haribhakti, S. P., & Mistry, J. H. (2015).** Techniques of laparoscopic cholecystectomy: Nomenclature and selection. Journal of minimal access surgery, 11(2): 113-118.
- **IGIMS P, Kumar A (2022).** comparison Of Intravenous Lignocaine With Intravenous Lignocaine And Magnesium Sulfate Combination For Laparoscopic Cholecystectomy. European Journal of Molecular & Clinical Medicine, 9(7): 1790-1794.
- **Khan MR, Raza R, Zafar SN, Shamim F, Raza SA, Pal KMI et al (2012).** Intraperitoneal lignocaine (lidocaine) versus bupivacaine after laparoscopic cholecystectomy: results of a randomized controlled trial. Journal of Surgical Research, 178(2): 662-669.

- **Kitajima T, Ishii K, Ogata H (1996).** Assessment of neuromuscular block at the thumb and great toe using accelography in infants. Anaesthesia, 51(4): 341-343.
- **Lee CH, Wen Z, Chang Y, Huang S, Tang C, Chen W et al (2009).** Intra-articular magnesium sulfate (MgSO4) reduces experimental osteoarthritis and nociception: association with attenuation of N-methyl-D-aspartate (NMDA) receptor subunit 1 phosphorylation and apoptosis in rat chondrocytes. Osteoarthritis and cartilage, 17(11): 1485-1493.
- **Li J, Wang G, Xu W, Ding M, Yu W (2018).** Efficacy of intravenous lidocaine on pain relief in patients undergoing laparoscopic cholecystectomy: a meta-analysis from randomized controlled trials. International Journal of Surgery, 50(1): 137-145.
- **Lysakowski C, Dumont L, Czarnetzki C, & Tramèr MR (2007).** Magnesium as an adjuvant to postoperative analgesia: a systematic review of randomized trials. Anesthesia & Analgesia, 104 (6): 1532-1539.
- **Meistelman C (2017).** Neuromuscular Blocking Drugs: Physiology, Pharmacology and Clinical Aspects. Total Intravenous Anesthesia and Target Controlled Infusions: A Comprehensive Global Anthology, 267-297.
- **Morsy KM, Abdalla EEM (2014).** Postoperative pain relief after laparoscopic cholecystectomy: intraperitoneal lidocaine versus nalbuphine. Ain-Shams Journal of Anaesthesiology, 7(1): 40-44.
- **Nahar A (2022).** A Hospital Based Prospective Study to Compare the Effect of Intravenously Administered Clonidine and Magnesium Sulfate on Hemodynamic Responses During Laparoscopic Surgeries at a Tertiary Care Center. European Journal of Molecular & Clinical Medicine, 9(3): 2232-2239.
- **Noland A (2019).** Intravenous Magnesium Sulfate for Multimodal Analgesia. Anesthesia eJournal, 7(1): 17-18.
- **Perniola A, Fant F, Magnuson A, Axelsson K, Gupta A (2014).** Postoperative pain after abdominal hysterectomy: a randomized, double-blind, controlled trial comparing continuous infusion vs patient-controlled intraperitoneal injection of local anaesthetic. British journal of anaesthesia, 112(2): 328-336.
- **Roberts K, Gilmour J, Pande R, Nightingale P, Tan L, Khan S et al (2011).** Efficacy of intraperitoneal local anaesthetic techniques during laparoscopic cholecystectomy. Surgical endoscopy, 25(1): 3698-3705.
- **Rutherford D, Massie M, Worsley C, Wilson MS (2021).** Intraperitoneal local anaesthetic instillation versus no intraperitoneal local anaesthetic instillation for laparoscopic cholecystectomy. Cochrane Database of Systematic Reviews, 1(10): CD007337.
- **Saadawy I, Kaki A, Abd El Latif A, Abd-Elmaksoud A, Tolba O (2010).** Lidocaine vs. magnesium: effect on analgesia after a laparoscopic cholecystectomy. Acta Anaesthesiologica Scandinavica, 54(5): 549-556.
- **Safavi M, Honarmand A, Sahaf AS, Sahaf SM, Attari M, Payandeh M et al (2015).** Magnesium sulfate versus Lidocaine pretreatment for prevention of pain on etomidate injection: A randomized, double-blinded placebo controlled trial. Journal of research in pharmacy practice, 4(1): 4-8.
- **Soleimanpour H, Imani F, Dolati S, Soleimanpour M, Shahsavarinia K**

**(2022).** Management of pain using magnesium sulphate: A narrative review. Postgraduate Medicine, 134(3): 260-266.

- **Soleimanpour H, Imani F, Dolati S, Soleimanpour M, Shahsavarinia K (2022).** Management of pain using magnesium sulphate: A narrative review. Postgraduate Medicine, 134(3): 260-266.
- **Thakur N, Pula R, Raya R.** Effect of Preoperative Ketamine and Magnesium Sulfate on Intra & Postoperative Analgesia in Laparoscopic Cholecystectomy: A Comparative Randomized Controlled Study. Academia Anesthesiologica International, 4(2): 281-287.
- **Toleska M, Dimitrovski A, Dimitrovska NT (2022).** Postoperative Nausea and Vomiting in Opioid-Free Anesthesia Versus Opioid Based Anesthesia in Laparoscopic Cholecystectomy. Prilozi, 43(3): 101-108.
- **Vindal A, Sarda H, Lal P (2021).** Laparoscopically guided transversus abdominis plane block offers better pain relief after laparoscopic cholecystectomy: results of a triple blind randomized controlled trial. Surgical Endoscopy, 35 (1): 1713-1721.
- **Yang SY, Kang H, Choi GJ, Shin HY, Baek CW, Jung YH et al (2014).** Efficacy of intraperitoneal and intravenous lidocaine on pain relief after laparoscopic cholecystectomy. Journal of International Medical Research, 42(2): 307-319.
- **Yu S, Wang B, Zhang J, Fang K (2019).** The development of local anesthetics and their applications beyond anesthesia. Journal of Clinical and Experimental Medicine, 12(12): 13203-13220.
- **Yu S, Wang B, Zhang J, Fang,K (2019).** The development of local anesthetics and their applications beyond anesthesia. Int J Clin Exp Med, 12(12): 13203-13220.