

**OPIOID-FREE VERSUS OPIOID BASED ANAESTHESIA
FOR LAPAROSCOPIC CHOLECYSTECTOMY-
A RANDOMIZED CLINICAL TRIAL.**

By

DR. THASKIN

Dissertation submitted to the

B.L.D.E. (DEEMED TO BE UNIVERSITY),

VIJAYAPURA, KARNATAKA.



In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

Under the guidance of

DR. BASAVARAJ PATIL MD

ASSOCIATE PROFESSOR

DEPARTMENT OF ANAESTHESIOLOGY

B.L.D.E.(DEEMED TO BE UNIVERSITY) SHRI

B.M. PATIL MEDICAL COLLEGE HOSPITAL &

RESEARCH CENTRE, VIJAYAPURA.

DECLARATION BY THE CANDIDATE.

I declare that this dissertation entitled “**OPIOID-FREE VERSUS OPIOID BASED ANAESTHESIA FOR LAPAROSCOPIC CHOLECYSTECTOMY- A RANDOMIZED CLINICAL TRIAL**”, is a Bonafide and genuine research work carried out by me under the guidance of DR. BASAVARAJ PATIL, Associate Professor, Department of Anesthesiology, Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura.

DATE:

PLACE: VIJAYAPURA



DR. THASKIN

DEPARTMENT OF ANESTHESIOLOGY
B.L.D.E (DEEMED TO BE) UNIVERSITY
SHRI B. M. PATIL MEDICAL COLLEGE
HOSPITAL AND RESEARCH CENTRE,
VIJAYAPUR, KARNATAKA.

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled “**OPIOID-FREE VERSUS OPIOID BASED ANAESTHESIA FOR LAPAROSCOPIC CHOLECYSTECTOMY- A RANDOMIZED CLINICAL TRIAL**” is a Bonafide research work done by DR. THASKIN in partial fulfilment of the requirement for the degree of M.D. in ANAESTHESIOLOGY.



DATE:

PLACE: VIJAYAPURA

DR. BASAVARAJ PATIL

ASSOCIATE PROFESSOR

DEPARTMENT OF ANESTHESIOLOGY

B.L.D.E (DEEMED TO BE) UNIVERSITY, SHRI

B. M. PATIL MEDICAL COLLEGE HOSPITAL

AND RESEARCH CENTRE, VIJAYAPUR,

KARNATAKA.

ENDORSEMENT BY THE HEAD OF DEPARTMENT

This is to certify that the dissertation entitled “**OPIOID-FREE VERSUS OPIOID BASED ANAESTHESIA FOR LAPAROSCOPIC CHOLECYSTECTOMY- A RANDOMIZED CLINICAL TRIAL**” is a Bonafide research work done by Dr. THASKIN under the guidance of DR. BASAVARAJ PATIL, Associate Professor, Department of Anesthesiology, Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura.



DATE:

PLACE: VIJAYAPURA

DR. RENUKA HOLYACHI

HEAD OF THE DEPARTMENT.

DEPARTMENT OF ANESTHESIOLOGY

B.L.D.E (DEEMED TO BE) UNIVERSITY, SHRI

B. M. PATIL MEDICAL COLLEGE HOSPITAL

AND RESEARCH CENTRE, VIJAYAPUR,

KARNATAKA

ENDORSEMENT BY THE PRINCIPAL

This is to certify that the dissertation entitled “**OPIOID-FREE VERSUS OPIOID BASED ANAESTHESIA FOR LAPAROSCOPIC CHOLECYSTECTOMY- A RANDOMIZED CLINICAL TRIAL**” is a Bonafide research work done by Dr. THASKIN under the guidance of Dr. BASAVARAJ PATIL, Associate Professor, Department of Anesthesiology, Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura.



DATE:

DR. ARAVIND PATIL

PLACE: VIJAYAPURA

PRINCIPAL.

B.L.D.E (DEEMED TO BE UNIVERSITY), SHRI
B. M. PATIL MEDICAL COLLEGE HOSPITAL
AND RESEARCH CENTRE, VIJAYAPURA,
KARNATAKA.

B.L.D.E. (DEEMED TO BE UNIVERSITY) SHRI B. M. PATIL MEDICAL COLLEGE,
HOSPITAL & RESEARCH CENTRE, VIJAYAPURA.

(COPYRIGHT)

DECLARATION BY THE CANDIDATE

I hereby declare that the B. L. D. E. (DEEMED TO BE UNIVERSITY), SHRI B. M. PATIL medical college and hospital research Centre, Vijayapura -Karnataka shall have the rights to preserve, use and disseminate this dissertation/thesis in print or electronic format for academic / research purpose.

DATE:

PLACE: VIJAYAPURA



DR. THASKIN.

B.L.D.E (DEEMED TO BE UNIVERSITY), SHRI
B.M. PATIL MEDICAL COLLEGE HOSPITAL
AND RESEARCH CENTRE, VIJAYAPURA,
KARNATAKA.

ACKNOWLEDGEMENT

First and foremost, I would like to express my deepest gratitude to Almighty God for providing me with the strength, wisdom, and perseverance necessary to complete this thesis.

I owe a special debt of gratitude to my finest mentor and my guide advisor, Dr. Basavaraj Patil, whose guidance and constructive feedback have been crucial in the successful completion of this work.

I convey my earnest gratitude and regards to my professor and head of the department of Anesthesiology, Dr Renuka Holyachi.

I am profoundly thankful to my teachers, Dr Vijaykumar T. K, Dr Vidya Patil, Dr. Sridevi M, Dr Nirmala, Dr Shivanand L K, Dr Vijay Katti, Dr Pratibha, Dr Santosh K, Dr Mala, Dr Anusha, Dr Santosh A, Dr Rizwana, Dr Nayana and Dr Sai Krishna whose expertise, encouragement, and invaluable insights have been instrumental in shaping my academic pursuits. Your unwavering dedication to my growth and development has been a source of immense inspiration. I am forever indebted to my statistician Dr Vijaya, for her constant guidance.

My heartfelt appreciation goes to my parents, Mr. Valiyakath Majeed and Mrs. Sabira Majeed whose unconditional love and support have been the foundation of my achievements. Thank you for always being there for me.

To my husband Dr Ashar and to my dearest son Zeeshan, I am incredibly grateful for your unwavering support, patience, and understanding throughout this journey.

Lastly, to my friends, Dr Arya, Dr Sandra, Dr Sankar, Dr Mourya, Dr Radhika, Dr Prabhu, Dr Samatha, Dr Suman, Dr Sesha Sai, Dr. Vaishnavi, Dr Priya, Dr Devendra thank you for your companionship, encouragement, and the countless moments of joy and laughter that have lightened this journey. Your support has been invaluable, and I cherish each one of you.

This thesis is a testament to the collective efforts, love, and support of all of you.

Thank you from the bottom of my heart.

With sincere gratitude,

DR. THASKIN

ABBREVIATIONS

- OFA – Opioid-free anesthesia
- OA- opioid-based anesthesia.
- LC- Laparoscopic cholecystectomy
- HR- Heart rate
- PONV-Postoperative nausea and vomiting.
- MAP- Mean arterial pressure
- SBP-Systolic blood pressure
- DBP-Diastolic blood pressure
- VAS- Visual analogue scale.
- Bpm -Beats per minute.
- Hr.- Hour
- Min- Minutes.
- ERAS-Enhanced Recovery After Surgery
- LA-Local anesthesia.
- ASA- American Society of Anesthesiologists.
- Mg- Magnesium
- IV- Intravenous.
- SD- standard Deviation.

ABSTRACT

- **AIM**

To compare the effect of Opioid-free multimodal analgesic regimen over conventional general anesthesia with opioids for post operative pain relief in patients posted for laparoscopic cholecystectomy.

- **BACKGROUND**

Laparoscopic cholecystectomy is the standard surgical procedure for cholelithiasis and Gall stone diseases. Although this procedure is thought to be generally painless and require a shorter hospital stay, they can nonetheless result in significant Pain, particularly in the first four hours after procedure. Opioids have been the primary mode of analgesia in the perioperative period with a number of associated side effects like delirium, constipation, nausea, vomiting, sedation, physical dependence, muscle rigidity, tolerance, respiratory depression etc. The preference of Multimodal opioid-free analgesia over opioids have been seen to be associated with intraoperative hemodynamical stability, early return of the bowel function, earlier mobilization of the patient, reduced length of hospital stay along with reduce in the severity of postoperative pain thereby reducing risk of chronic postoperative pain.

- **METHODOLOGY**

Informed consent was taken before the surgery. Patients kept nil by mouth 6 hours prior surgery.

All the patients were educated on Visual Analogue Scale and its scoring system. They were evaluated with a detailed history, general and systemic examinations in the preoperative room. Airway assessment and systemic examinations were done. Randomization was done and patients in the study were assigned into two Groups viz., Group A- Opioid free Anaesthesia and Group B- Conventional opioid group.

In the preoperative room, Preloading was done with IV crystalloids 10ml/kg. IV Dexamethasone 8 mg was administered to all patients. Baseline parameters were monitored and Group A patients were administered IV paracetamol 15 mg/kg preoperatively. Patients in both the groups were pre-oxygenated with 100% O₂ for 3 min and then premedicated. Induction was done using IV propofol 2.5mg/kg until the endpoint of loss of eyelash reflex is obtained, along with Lignocaine 1.5 mg/kg (bolus dose) and 1.5mg/kg of succinyl Choline. Endotracheal intubation was done, Atracurium 0.5 mg/kg was administered as loading dose and then in incremental doses as needed along with Nitrous oxide, oxygen and sevoflurane 1%. Additionally, During the maintenance phase, Group A patients received Lidocaine 1.5mg/kg as slow intravenous infusion for an hour and Magnesium 2 g (bolus dose) over 10-15 minutes. Pre-incisional infiltration using 20 ml of 0.25% Bupivacaine (5 ml in each port) and intraperitoneal instillation of 20 ml of 0.25% Bupivacaine was given in the gall bladder bed, after gall bladder has been taken out.

In the conventional Opioid group, a similar induction protocol was followed, along with 2 mcg/kg bolus dose of Fentanyl was given and later 0.5mcg/kg IV fentanyl to reduce the intraoperative rise of blood pressure. Intra-abdominal pressure was maintained between 12-15 mmHg during

pneumoperitoneum, and end-tidal CO₂ was kept below 35 mmHg. Intraoperative hemodynamic parameters were recorded. Residual neuromuscular blockade was reversed with IV neostigmine 2.5mg and IV Glycopyrrolate 0.5mg and tracheal extubation was done, after meeting the extubation criteria. At the end of surgery, all the patients received 1g paracetamol intravenously. Postoperatively, pain scores were assessed at 0, 2, 4, 6, 12, and 24 hours using the Visual Analogue Scale (VAS). Rescue analgesia with IV paracetamol was provided for VAS >4, and tramadol was administered for severe pain (VAS 8-10). The primary outcomes included postoperative pain scores, total analgesic consumption and the time to first analgesic request.

• RESULTS

Demographic Characteristics:

- The mean age of patients (years) in Group A (OFA) was 46.21 ± 15.497 years, while in conventional opioid group, it was 41.09 ± 13.957 years. The difference was not statistically significant, ensuring comparability between the groups.
- The mean weight of patients in Group A was 68.62 ± 13.298 kg, while in Group B, it was 63.32 ± 12.579 kg. This difference was also not statistically significant ($p = 0.096$).

Intraoperative Hemodynamic Stability:

- The mean systolic blood pressure (SBP) was higher in Group A (123.65 ± 5.672 mmHg) compared to Group B (119.50 ± 5.720 mmHg)

- No significant differences were observed in diastolic blood pressure (DBP), heart rate (HR), or mean arterial pressure (MAP) between the two groups ($p > 0.05$), suggesting comparable intraoperative hemodynamic stability.

Postoperative Pain (VAS Score Comparison):

At 0, 2, 4, and 24 hours postoperatively, the OFA group demonstrated significantly lower pain scores compared to the conventional group ($p < 0.05$), indicating superior early postoperative pain control.

Duration of Analgesia:

The mean duration of analgesia was significantly longer in the OFA group (11.35 ± 7.639 hours) compared to the Opioid group (4.26 ± 2.050 hours) ($p < 0.001$). This indicates prolonged postoperative pain relief in patients receiving opioid-free anesthesia.

Postoperative Analgesic Consumption:

- A higher percentage of patients in the OFA group (24%) did not require postoperative analgesics, whereas all patients in the Opioid group required pain management.
- A greater proportion of patients in the OFA group (71%) required only a single dose of paracetamol, compared to the opioid group.

- None of the patients in the OFA group required combination of paracetamol and tramadol 50 mg, whereas 21% of patients in the conventional group required the additional opioid analgesia for pain relief.

Postoperative Adverse Effects:

- The incidence of nausea and vomiting was higher in the conventional opioid group (n=5) compared to the OFA group (n=0), though this difference did not reach statistical significance ($p = 0.053$).
- Shoulder tip pain, commonly associated with residual carbon dioxide, was significantly more prevalent in the Opioid group than the OFA group. ($p = 0.0115$).
- Other adverse effects, such as generalized pruritus and shivering, were reported only in the conventional opioid anesthesia group but were not statistically significant.

• **CONCLUSION**

Opioid-free anesthesia provided effective postoperative pain relief, reduced analgesic requirements, and lowered adverse effects when compared to the conventional opioid-based anesthesia. This multimodal opioid-free approach may offer a safer alternative for pain management in laparoscopic cholecystectomies.

KEYWORDS: Opioid-free anesthesia, Systolic blood pressure, Visual analogue scale.

TABLE OF CONTENTS

SL No.	TITLE	PAGE No.
1	INTRODUCTION	19
2	AIM AND OBJECTIVES OF THE STUDY	21
3	REVIEW OF LITERATURE	22
4	MATERIALS AND METHODS	49
5	OBSERVATION AND RESULTS	58
6	DISCUSSION	68
7	CONCLUSION	73
9	BIBLIOGRAPHY	74
10	ANNEXURES:	
	SAMPLE INFORMED CONSENT FORM	78
	SCHEME OF CASE TAKING (PROFORMA)	84
	BIODATA OF THE GUIDE	89
	BIODATA OF THE INVESTIGATOR	89
	ETHICAL CLEARANCE CERTIFICATE	90
	MASTER CHART	91
	PLAGIARISM CHECK REPORT	93

LIST OF FIGURES

Figure No.	Figure Name	Page No.
1.	Anatomical location of Gall bladder.	26
2.	Blood supply of Gall bladder	28
3.	Laparoscopic anatomy	29
4.	Visual Analogue Scale facial expressions	32
5.	Chemical structure of Bupivacaine.	33
6.	Bupivacaine Hydrochloride 0.5%.	35
7.	Magnesium sulphate injection	40
8.	Mechanism of action of Lignocaine.	44
9.	Pre-incisional port site infiltration	57
10.	Intraperitoneal instillation of 0.25%Bupivacaine in the gallbladder bed.	58

LIST OF TABLES

Table No.	Table Name	Page No
a.	Mean age of two groups	61
b.	Mean weight (kg) of two groups.	63
c.	Comparison of intraoperative hemodynamics.	64
d.	Postoperative VAS score comparison.	66
e.	Postoperative duration of analgesia	67
f.	Total consumption of analgesics.	68
g.	Post-operative adverse effects.	69

LIST OF GRAPHS

Graph No.	Graph Name	Page No.
1.	COMPARISON OF MEAN AGE	62
2.	COMPARISON OF WEIGHT (Kg)	63
3.	COMPARISON OF INTAOPERATIVE HEMODYNAMICS.	65
4.	COMPARISON OF DURATION OF ANALGESIA.	68

INTRODUCTION

- Laparoscopic cholecystectomy is a minimally invasive surgical technique used for removal of a diseased gallbladder. The open procedure for routine cholecystectomies has been supplanted by this method since the early 1990s.
- In India, the first laparoscopic cholecystectomy was performed in 1990, at JJ hospital, Mumbai. Since then, this surgical procedure has been enjoying ever-increasing popularity and presenting newer anesthetic challenges. Although these procedures are thought to be generally painless and require a shorter hospital stay, they can nonetheless result in significant Pain, particularly in the first four hours after procedure.
- Opioids have been the primary mode of analgesia in the perioperative period with numerous associated side effects like respiratory depression, sedation, pruritis, constipation, delirium, nausea, vomiting, physical dependence, muscle rigidity, tolerance, ileus and addiction. In India, the prevalence of opioid consumption is 0.7% ^[1], while United States rank the highest in average dose of opioid prescriptions for most surgical procedures. Fentanyl is a potent opioid which has been used to control pain, lower the dose of sympathomimetic inhibitors and preserve hemodynamic stability. However, in light of the above known adverse effects, Efforts are made to minimize the usage of opioids intraoperatively. Patients taking higher doses of fentanyl during surgery has been studied to require higher doses of opioids in the post operative period than those

using lower doses.

- The preference of Multimodal opioid-free analgesia over opioids have been seen to be associated with intraoperative hemodynamical stability, early return of the bowel function, earlier mobilization of the patient, reduced length of hospital stay along with reduction in the severity of postoperative pain thereby reducing risk of chronic postoperative pain.
- Therefore, this study was planned to compare an opioid free anesthetic regimen consisting of lidocaine, magnesium and paracetamol in combination with pre-incisional and intraperitoneal infiltration of 0.25% bupivacaine with conventional opioid based techniques. Our primary objective was to assess for the pain scores in post operative period and also to minimize opioid requirement and its associated adverse effects. Secondly, to compare the intraoperative hemodynamic parameters, the length of postoperative analgesia and the total amount of analgesics that was consumed in the first 24 hours post-surgery ^[1]

AIMS AND OBJECTIVES OF THE STUDY

This study aims at comparing the effect of Opioid-free multimodal analgesic regimen over conventional general anesthesia with opioids for post operative pain relief in patients aged between 18-70 years belonging to American Society of Anesthesiologists physical class I and II posted for laparoscopic cholecystectomy.

- **Primary objective**

To compare the Postoperative pain scores using Visual analogue scale (VAS) between opioid free anesthesia and opioid based technique.

- **Secondary objectives**

1. To compare intraoperative Hemodynamic parameters like Heart rate, Systolic, Diastolic Blood pressures and Mean Arterial pressures in both the groups.
2. To compare the Duration of Post operative Analgesia in both the groups.
3. To compare the Total Analgesics consumed in the first 24 hours postoperatively.
4. Any associated adverse effects in the study groups.

REVIEW OF LITERATURE

Historically, opioids have been the first line therapy for surgical pain management, they were considered as the cornerstone of a balanced anesthesia, but recently, concerns about their side effects have been raised, Thus the concept of Opioid free Anesthesia (OFA) was introduced to enhance recovery after surgery. Multiple approaches for analgesia have evolved in due time to provide effective control of early postoperative pain. Many trials have been carried out using non opioid analgesia in recent times which has proved to be safe, shorter hospitalization and early return to normal activity.

In a study conducted by **Ragupathy R et al (2022)** ^[1] comparing Opioid-free anesthesia (OFA) with Opioid-based conventional technique on 60 patients aged between 20 and 70 years in a tertiary care hospital, it was concluded that VAS scores were significantly higher in conventional opioid-based group. Anesthetic doses of lidocaine, paracetamol and magnesium in combination with fascial plane block were administered for the Opioid-free anesthesia group. This study concluded that in comparison to the conventional opioid technique, the OFA along with erector spinae plane block provided better post-operative pain relief. However intraoperative hemodynamic parameters did not reveal a statistically significant difference except for systolic blood pressure which was higher in the

OFA group but was clinically insignificant.

Hao C et al ^[2] in 2023, allocated 80 adult patients to a study which aimed to compare the quality of postoperative recovery between patients undergoing laparoscopic cholecystectomies with opioid-free anesthesia (OFA) and those with opioid-based anesthesia (OA). The study concluded that the quality of recovery of patients receiving OFA was superior to those receiving OA after laparoscopic cholecystectomy.

A prospective randomized clinical trial was conducted on 80 patients aged 20-65 years in 2022 by **Toleska et al (2022)** ^[3] to study Postoperative Nausea and vomiting (PONV) in Opioid-free Anesthesia Versus Opioid-based Anesthesia in laparoscopic Cholecystectomy. PONV is one of the usual complications in patients, post-Laparoscopic cholecystectomy. Minimized use of Opioids have a better effect on patient recovery. This study proved Postoperative nausea and vomiting occurs more often in patients who received opioids during laparoscopic cholecystectomy compared to patients who received opioid free anesthesia, but without statistical significance.

Osama Helal Ahmed et al (2020) ^[4] Conducted a prospective and a randomized clinical study on Opioid Free Anesthesia for patients posted for laparoscopic cholecystectomy. This study aimed to avoid any perioperative opioids and instead used adjuvant anesthetic agents like ketamine, dexmedetomidine and paracetamol along with peri-operative analgesics. Fentanyl was administered as the main anesthetic adjuvant in the conventional opioid group along with peri-operative

analgesics.

The study concluded that the OFA (opioid free anesthesia) group showed a lower need for intraoperative analgesia compared to the opioid group and was as effective as Opioid group in maintaining intraoperative hemodynamic stability.

OFA also showed a significant reduction of incidence of PONV compared to Opioid treated group.

Manan A et al (2020) ^[5]: evaluated the effectiveness of diluted intraperitoneal bupivacaine in post-laparoscopic cholecystectomy pain relief through a randomized controlled trial. A mixture of 20 ml 0.5% bupivacaine in 480 ml normal saline was used to irrigate peritoneal cavity in the study group. The final outcome of the study was to compare the “Pain free duration” in both the groups. They concluded their study proving large volume of diluted bupivacaine when injected intraperitoneally during laparoscopic cholecystectomy gave a long-lasting pain alleviation.

A single blinded randomized study to prove “Opioid-free anesthesia (OFA) is a new Anaesthetic technique”, where the administration of opioids (fentanyl) is avoided in both intra- and post-operative period was conducted by **Toleska M et al (2019)** ^[6].

This approach resulted in a decrease in opioid-related side effects and lower postoperative pain scores among 60 patients undergoing elective laparoscopic cholecystectomy and hence concluded that Opioid-free anesthesia as a part of multimodal analgesia is a safe procedure, where opioid-related negative effects in patients undergoing laparoscopic cholecystectomy are avoided. Furthermore, the study demonstrated that the total opioid consumption during the postoperative period

was markedly higher in the Fentanyl (Opioid) group compared to the OFA group.

Das NT et al (2017)^[7] Conducted a randomized, double blinded, placebo-controlled study to compare the analgesic efficacy of intraperitoneally instilled equipotent concentrations of bupivacaine and ropivacaine versus placebo in relieving postoperative pain after laparoscopic cholecystectomy when used as a part of multimodal analgesia. Study proved that intraperitoneal infiltration of local anesthetics considerably lowered the pain intensity scores in the early postoperative period and helped in improving the postoperative recovery profile and outcome. This makes Laparoscopic cholecystectomies more amenable to day care surgical settings.

CLINICAL ANATOMY^[8,9]

Gallbladder

The gallbladder is a pear-shaped organ that is located in a fossa under the liver. It primarily functions as a reservoir for storage of bile and measures approximately 7-10 cm in length and 4 cm in width. Anatomically, it is located anteriorly on the undersurface of segment IV and V. Its location in respect to the liver might vary, for instance, the so-called "intrahepatic" gallbladder may be fully or partly lodged in the liver parenchyma. This might make dissection more difficult and raise the possibility of liver damage during surgery. Inferiorly the gallbladder has a peritoneal surface. Although it lacks a capsule, some writers describe the extension of the liver capsule, known as Glisson's capsule, to cover the exposed surface of the gallbladder. The fundus of the gallbladder is broad, and its diameter gets smaller as it moves towards the main body.

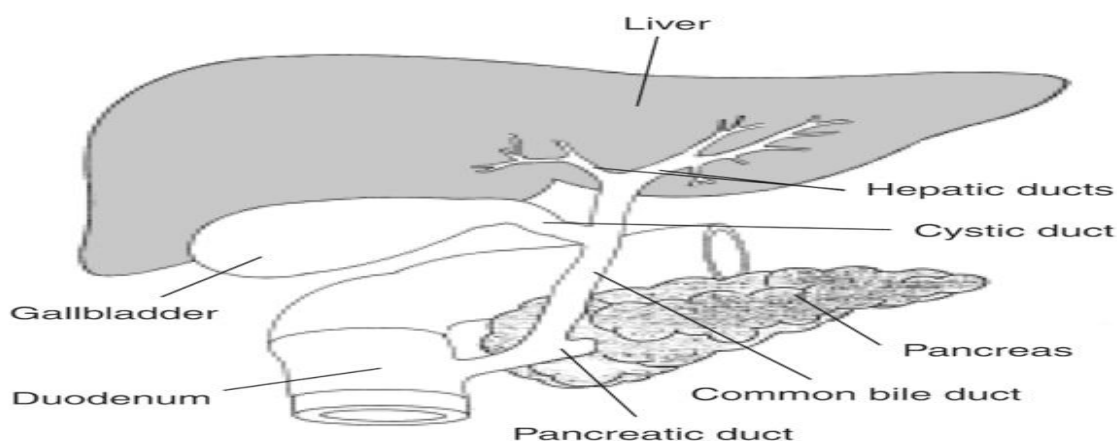


Fig 1. Anatomical location of Gall bladder.

The cystic duct

One of the crucial components that must be correctly identified and divided during a routine cholecystectomy is the cystic duct, which connects the gallbladder to the bile duct. Its length varies from 2- 4 cm, 20% of the cystic ducts being less than 2 cm and hence, there may be a very little space for any ligatures or clips. Typically, the cystic duct has a width of 2-3 mm. When pathology (stones or past stones) is present, it may dilate.

EMBRYOLOGY

The hepatic diverticulum emerges from the growing duodenum towards the end of the fourth week of embryogenesis. Immediately below, a second outpouching called the cystic diverticulum gives rise to the gallbladder, while the hepatic diverticulum becomes the biliary tree. Humans differ greatly in how their biliary trees form, which results in a wide range of biliary system variances.

BLOOD SUPPLY AND LYMPHATICS.

The cystic artery provides the gallbladder with the majority of its blood flow. This artery is a branch of the right hepatic artery and is usually given off in the Calot's triangle. In the gallbladder, it usually gives off an anterior/superior branch and a deep/posterior branch.

It is necessary to ligate the two branches separately if the branching is proximal or the point of dissection is quite close to the gallbladder, as in a laparoscopic cholecystectomy. If the posterior branch is not appreciated, it may result in excessive bleeding during a

posterior dissection. The cystic duct directly receives blood supply from cystic artery; hence these arteries should be divided to obtain the cystic duct.

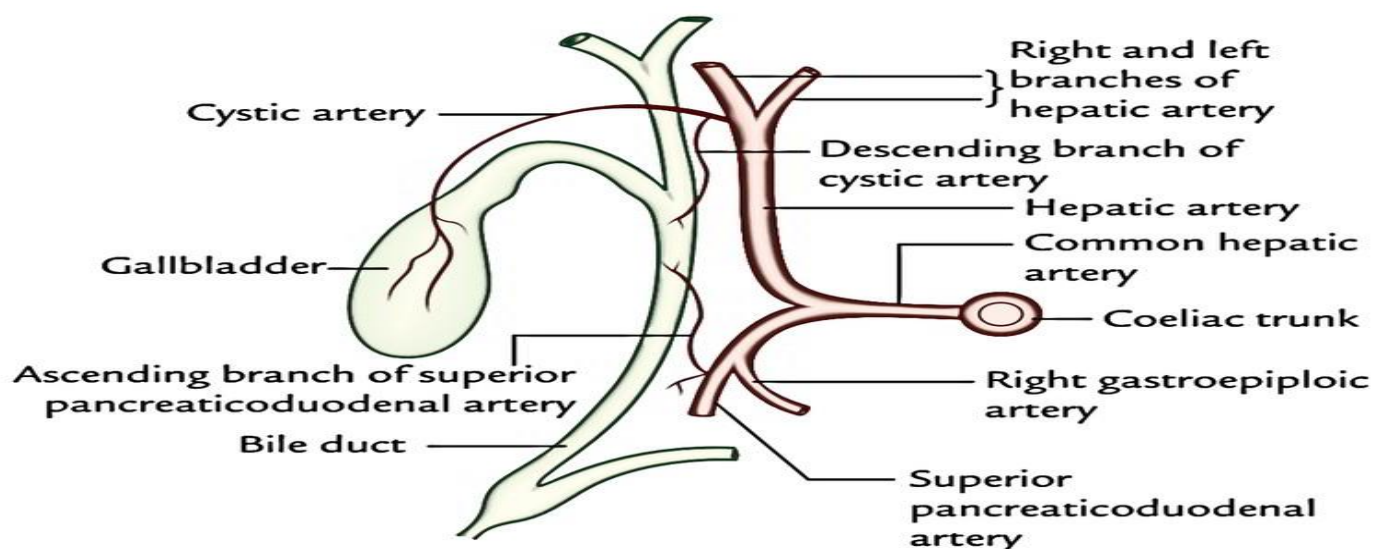


Fig 2: Blood supply of Gall bladder

Venous drainage occurs via the small cystic veins, which accounts for the drainage of the neck and cystic duct. The venous drainage of the fundus and the body of the gallbladder is directly into the visceral surface of the liver and through the hepatic sinusoids. Lymph drains into the cystic lymph nodes which then empty into the hepatic or celiac lymph nodes.

NERVE SUPPLY

Three nerves innervate the gallbladder and cystic duct: The hepatic branch of the right vagus nerve, the right phrenic nerve and the coeliac plexus. Many gastric surgeries de-innervate the gallbladder, causing dysfunction of the pear-shaped organ leading to

gallstone formations and cholecystitis and hence requiring the need for prophylactic cholecystectomy.

LAPAROSCOPIC ANATOMY

The emergence and widespread acceptance of laparoscopic cholecystectomy has provided a novel perspective on biliary anatomy, particularly on Calot's triangle, and the phrase 'laparoscopic anatomy' has been included into anatomical literature. The Laparoscopic retraction approach flattens the Calot's triangle rather than opening it. The popular "reverse" dissection of the Calot's triangle during a laparoscopic cholecystectomy provides an alternative perspective of the region and may result in additional anatomical distortion when the gallbladder is flipped over.^[8]

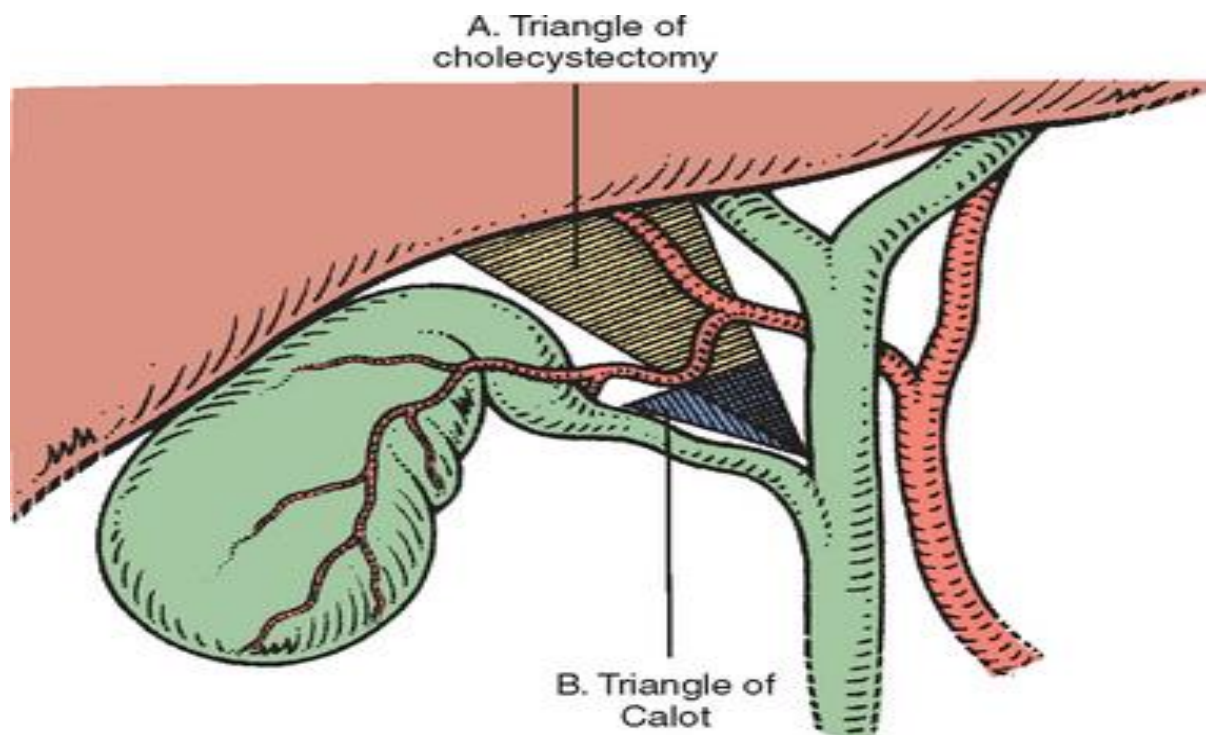


Fig 3: Laparoscopic anatomy.

PAIN AFTER LAPAROSCOPIC CHOLECYSTECTOMY

Laparoscopic cholecystectomy is considered as a first choice of treatment for gallbladder diseases, as this technique provides less operative pain, shorter hospitalization and a better cosmetic result compared to the open technique.

Despite the fact that the patients believe laparoscopic surgeries have brought about a painless era, patients still report more of visceral pain than parietal pain after a laparoscopic surgery when compared to open technique. Large inter-individual variance in early postoperative pain following laparoscopic cholecystectomy has been highlighted by many small-scale studies, highlighting the need for better analgesic treatment postoperatively.

Although there is a dearth of documentation from large-scale studies, prior small-scale studies have found that the overall pain after a laparoscopic cholecystectomy has been due to the following 3 main components: Incisional pain, visceral pain and shoulder pain. Abdominal distension, port-site incisions, trauma related to gallbladder surgery, phrenic nerve irritation from CO₂ insufflation into the peritoneal cavity, socioeconomic status, and individual factors are some of the elements that contribute to the development of this discomfort.

Pain after laparoscopic cholecystectomy is typically considered “visceral”^[10] with its maximum intensity during the first hour and is exacerbated by respiration, coughing and mobilization. Compared to somatic pain, this pain is clearly distinct. The enteric nervous

system, a huge network of unique and functionally different neuronal subtypes, is the mechanism through which visceral signaling takes place. Through afferents in the vagus nerve, viscera like the gallbladder and its overlying peritoneum, transmits unpleasant sensations and autonomic responses to injury.

PAIN ASSESSMENT

Assessment of pain is a necessary component to achieve adequate pain control in the post operative period. Few of the pain evaluation scales are used in an attempt to assess pain. Most of these scales can be used by the patients themselves to evaluate pain when the patient can express and communicate what pain feels like.

VISUAL ANALOGUE SCALE (VAS): Visual analogue scale is one of the pain rating scales introduced in 1921 by Hayes and Patterson^[11]. It was used in psychology to measure mood disorder in the earlier days. It has become a standard and a popular tool for pain assessment. Scores are recorded by making a handwritten mark on a 10-cm line that represents a continuum between “no pain” and “worst pain.”^[11]. The distance in millimeters between the patient's mark and the left endpoint is measured after the patient creates a mark that represents their perception.

Visual Analogue Scale facial expressions: It is a pictorial self-assessment tool which includes six faces. Each face conveys different emotions which range from a face with a cheerful smile to a face with a crying one. It is popular among the population such as

younger patients, elderly patients or patients with disorientation or even in patients who cannot comprehend local language or any sort of difficulty in communication.

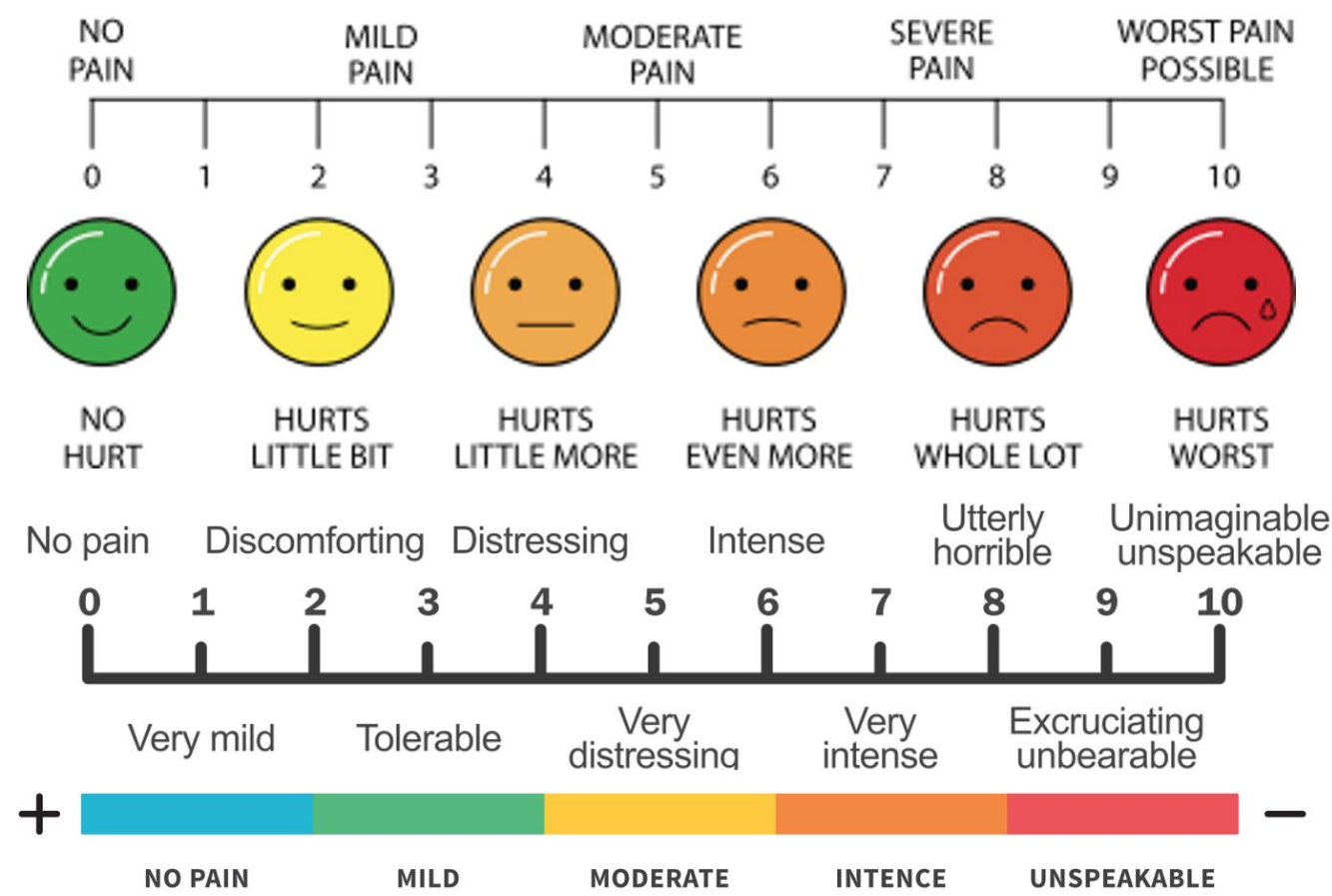


Fig 4: Visual Analogue Scale facial expressions

BUPIVACAINE ^[12,13,14,15]

Local anesthetics have a wide range of applications in day -to-day anesthesia practice. They are used in regional anesthesia, spinal anesthesia, epidural anesthesia, and analgesia, local infiltration all of which aim at achieving perioperative analgesia and postoperative comfort. Bupivacaine is a local anesthetic which belongs to the amide group. It was first developed in 1957 by Ekenstam and clinically used for the first time in 1963 by L.J. Telivuo. It is a water-soluble hydrochloride salt of lipid soluble bases.

Structure:

A local anesthetic contains a tertiary amine attached to aromatic ring linked together by an intermediate chain which can either be an ester or an amide. Based on the intermediate chain local anesthetics can be divided into 2 groups namely, esters (e.g.: Procaine) and amides (e.g.: bupivacaine).

It is tertiary amine which is a relatively hydrophilic basic end while the aromatic ring attached to it by an amide linkage imparts a lipophilic property.

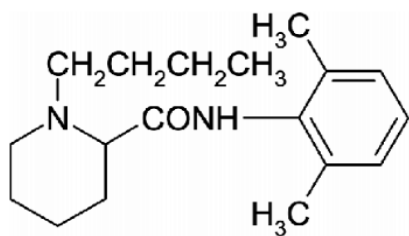


Fig 5: CHEMICAL STRUCTURE OF BUPIVACAINE.

Chemical properties:

- Molecular weights of the base: 288
- Molecular weight of chloride: 324
- Protein binding capacity: 96%.
- pKa = 8.2 at 25 degrees
- specific gravity – 1.035 – 1.040

Mechanism of action:

The resting membrane potential of all living cells is -60 to -70mV and is usually due to potassium efflux since the membrane is generally leaky to potassium. Neurons and cardiac muscle cells have a unique ability to generate action potentials. Local anesthetics act by preventing the generation of action potentials in these cells.

Voltage gated sodium channels present in the membrane play an important role in initiation and transmission of the of action potential in neurons and muscle cells. These voltage gated sodium channels have one large α subunit with four domains and 6 loops and one or two smaller β subunit.

They usually exist in one of the three conformational states: Resting state, Active state or Inactive state.

Resting and inactive states are non-conducting while active state is conducting. When the membrane depolarizes, sodium channels change their conformation and allow the sodium influx hence generating an action potential.

Local anesthetics in their ionized bind to the larger α subunit of the sodium channel. They selectively inhibit the sodium channels in active state and blocks the sodium influx which

results in prevention of generation and propagation of action potential by increasing the firing threshold, essentially ceasing the nerve transmission. This results in reversible nerve conduction inhibition ensuing sensory loss in the affected area. Higher the concentration of the local anesthetic, higher fraction of the sodium channels are inhibited. Factors that influence the nerve fibre sensitivity to local anesthetics are diameter of axons, myelination of nerve fibres and conduction velocity.

- Slow conducting and small nerve fibres are more sensitive. E.g.: C fibres
- Fast conducting and large fibres are less sensitive. E.g.: A- δ fibre
- Myelinated fibres are more sensitive compared to unmyelinated fibres.

The sequence of blockade of nerve function by local anaesthetic administration is as follows: Autonomic $\rightarrow$ sensory (pain $\rightarrow$ temperature $\rightarrow$ touch $\rightarrow$ proprioception) $\rightarrow$ motor.



Fig 6: Bupivacaine Hydrochloride 0.5%.

Bupivacaine is available in the concentrations of 0.25%, 0.5% and 0.75% preparations.

ADJUVANTS

Adding adjuvants to bupivacaine prolongs the duration of action. The drugs used as adjuvants with proven benefit are α -2 agonists, Dexamethasone, Ketamine, Fentanyl, Magnesium etc.

USES:

1. Infiltration Anesthesia

Bupivacaine is employed for local infiltration to ensure extended post-surgical pain relief. It is commonly used in surgeries such as cesarean sections, hernia repairs, and breast surgeries to manage postoperative discomfort effectively.

2. Regional Anesthesia

Bupivacaine is commonly utilized in several regional anesthesia techniques, including:

- **Epidural Anesthesia:** Frequently used for labor pain relief and postoperative analgesia, offering efficient sensory blockade while maintaining motor function at lower doses.
- **Spinal Anesthesia:** Often administered for lower abdominal, pelvic, and lower extremity surgeries due to its quick onset and sustained effects.
- **Peripheral Nerve Blocks:** Applied in orthopedic and other surgical procedures to provide localized pain relief, reducing the necessity for systemic opioid use.

3. Continuous Infusion for Postoperative Pain Control

For postoperative management, continuous infusion of bupivacaine via epidural or peripheral nerve catheters offers prolonged analgesia, minimizing opioid consumption and related adverse effects. This method is frequently incorporated into Enhanced Recovery After Surgery (ERAS) protocols.

4. Management of Chronic Pain

Bupivacaine is also beneficial in chronic pain treatment, including:

- **Intrathecal Administration:** Provides long-term pain relief in chronic illnesses such as cancer-related pain.
- **Sympathetic Nerve Blocks:** Used in conditions like complex regional pain syndrome (CRPS) to alleviate sympathetically mediated pain.

5. Obstetric Anesthesia

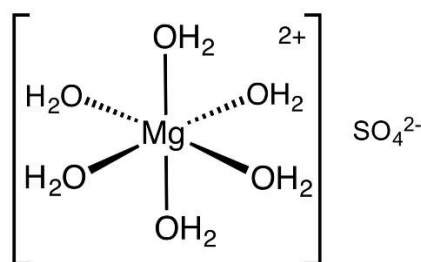
Bupivacaine is widely used for labor analgesia because it gives efficient pain relief with minimal motor impairment. It is often used together with opioids to improve analgesia while allowing for lower local anesthetic doses.

5. Cardiac and Thoracic Surgery Applications

For patients undergoing cardiac or thoracic procedures, bupivacaine is employed in epidural anesthesia to ensure superior pain control and reduce surgical stress responses.

Bupivacaine remains a fundamental element in modern anesthesia due to its ability to provide prolonged analgesia across various surgical and pain management applications. Its application in regional and neuraxial anesthesia, postoperative analgesia, and chronic pain treatment underscores its essential role in improving patient outcomes and minimizing opioid dependency.

MAGNESIUM SULPHATE ^[16,17,18,19,20,21,22,23]



Magnesium sulfate (MgSO_4), a substance called Epsom salt, has gained importance in several medical fields because of its numerous uses and therapeutic benefits. In the realm of general anesthesia, magnesium sulfate (MgSO_4) has emerged as a beneficial adjunct because it provides a range of benefits that enhances and optimizes the conventional anesthetic procedures.

Mechanism of action.

Magnesium suppresses the release of acetylcholine from motor endplates and blocks calcium channels at presynaptic nerve terminals. This decreases the amplitude of endplate potential and the excitability of muscle fibres, increasing the efficacy of neuromuscular blockade with non-depolarizing neuromuscular blockers. This characteristic of the medication reduces the requirement for a muscle relaxant. Furthermore, its ability to potentially reduce the overall amount of primary anesthetic agents required emphasizes its value in optimizing anesthesia dose, ensuring adequate depth while potentially minimizing undesirable effects associated with greater dosages.

Optimal muscular relaxation, effective management of discomfort such as nausea and vomiting, and preservation of hemodynamic stability are critical elements of anesthetic care for successful surgical interventions. Because of its well-known analgesic,

vasodilatory, and muscle relaxant properties, MgSO_4 has emerged as a useful addition to enhance these crucial elements of anesthetic care.

Absorption and Distribution:

When administered intravenously (IV), magnesium sulphate rapidly reaches therapeutic levels, peaking in approximately 20-30 minutes. It is widely dispersed throughout the body, including the central nervous system and the muscles. The half-life is usually between 4-6 hours, depending on renal function.



Fig 7: MAGNESIUM SULPHATE

Clinical Uses of Magnesium Sulfate in Anesthesia

1. Analgesia:

Magnesium sulfate is used in anesthesia for pain management and to reduce the need for opioids. By blocking NDMA receptors (N-methyl-D-aspartate), it can decrease central sensitization, which aids in the management of both acute and chronic pain.

2. Muscle Relaxation:

Magnesium sulfate enhances neuromuscular blockade by preventing acetylcholine

release at the neuromuscular junction. This makes it a useful muscle relaxant in surgeries requiring muscle paralysis, such as for intubation or controlled ventilation.

3. Prevention of Eclampsia:

Although not directly related to anesthesia, magnesium sulfate is commonly used to prevent seizures in pregnant women with preeclampsia or eclampsia.

Anesthesiologists often manage patients receiving magnesium for this purpose.

4. Cardiac Protection:

Magnesium has antiarrhythmic properties and is used to treat or prevent arrhythmias, particularly those caused by low magnesium levels, such as torsades de pointes. It stabilizes the myocardial cell membranes, thereby reducing risk of arrhythmias during surgery, especially in patients with a history of cardiac problems.

Dosing and Administration

- Typical Dosage:

Magnesium sulfate is usually administered IV, with a common dose for muscle relaxation being 30-50 mg/kg over 10 minutes, followed by a maintenance dose of 1-2 mg/kg/h. For pain relief, a lower dose, such as 1-2 grams, is often used.

- Special Considerations:

Doses should be adjusted in patients with renal impairment, as primary elimination of magnesium is through the kidneys. Renal dysfunction increases the risk of toxicity, requiring close monitoring.

Contraindications and Precautions.

- Renal Impairment:

Magnesium sulfate should be avoided or used with extreme caution in patients with severe renal dysfunction to prevent toxicity.

- Bradycardia and Heart Block:

It is contraindicated in patients with advanced heart block or bradycardia unless they have a pacemaker.

- Hypermagnesemia:

Consider hypermagnesemia while administering magnesium, as conditions like dehydration or myasthenia gravis might increase the risk of toxicity.

Recent Research and Trends.

- Recent studies have shown that magnesium sulfate can reduce opioid use after surgery, making it a valuable component of opioid-sparing pain management strategies.
- Research is ongoing into magnesium's potential neuroprotective effects, particularly in the brain and spine surgeries, where magnesium may reduce injury due to ischemia.
- New studies continue to refine dosing strategies and explore the optimal timing for magnesium administration in perioperative care.

INTRAVENOUS LIGNOCAINE (LIDOCAINE) IN ANESTHESIA ^[24,25,26,27,28]

Anesthesia is a critical component of modern healthcare, allowing patients to undergo surgeries and medical procedures without pain or distress. The introduction of safe and effective anesthetic agents has revolutionized medical practice, with intravenous (IV) anesthetics playing a crucial role in contemporary anesthesia. Lignocaine, often known as lidocaine, is a versatile drug widely used in both local and intravenous forms. Its quick action and consistent reliability make it a drug of choice for a wide range of anesthetic and pain management procedures both in surgical and emergency settings. The intravenous administration of lignocaine is particularly significant, as it not only provides effective anesthesia but also plays a key role in managing conditions like ventricular arrhythmias. With its proven effectiveness and favorable safety profile, lignocaine remains a critical tool in anesthesia today.

Mechanism of Action:

Lignocaine (or lidocaine) is a widely used antiarrhythmic agent and a local anesthetic. Its main mechanism of action involves blocking voltage-gated sodium channels in excitable cells like neurons and cardiac muscle cells (cardiomyocytes). Lignocaine stabilizes the membrane potential by blocking sodium ions from entering these cells, which makes it more difficult for the cells to cross the threshold required to produce action potentials. As a result, aberrant electrical activity in the heart is suppressed, which aids in the treatment of arrhythmias, and nerve signal transmission is stopped, resulting in local anesthesia.

When given intravenously, lignocaine works systemically to control pain, making it useful during various medical procedures, including surgeries or emergency treatments.

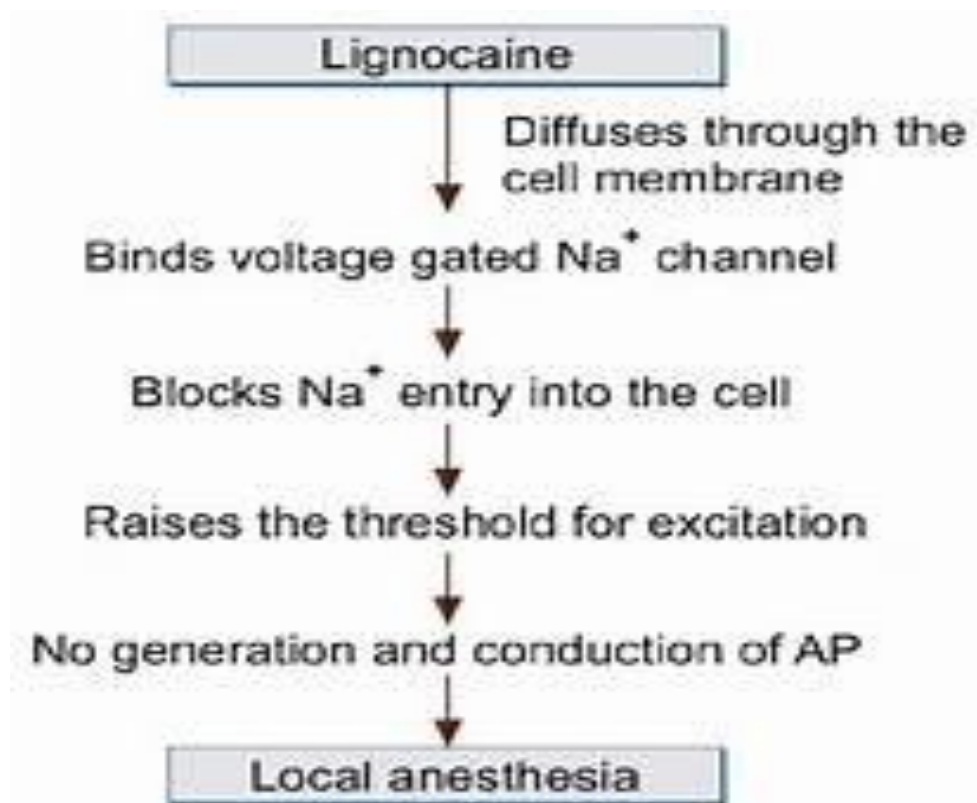


Fig 8: Mechanism of action of Lignocaine.

Pharmacodynamics and Pharmacokinetics ^[29,30]

Lignocaine works by blocking sodium channels in nerve cells, preventing the transmission of nerve impulses, and thereby inhibiting pain sensation. As a class 1b antiarrhythmic drug, it stabilizes the cardiac cell membrane, which helps control abnormal heart rhythms. After intravenous administration, lignocaine rapidly reaches the bloodstream, allowing for swift onset of action.

It is distributed throughout the body, with its highest concentrations found in the liver and kidneys. Lignocaine is metabolized primarily in the liver by cytochrome P450 enzymes, and its metabolites are excreted through the urine. Although the drug's pharmacokinetics can be affected by variables like liver function and cardiac condition, its half-life is typically between 1.5 and 2 hours. Age, health status, and the presence of other medications can all have an impact on lignocaine's bioavailability, which can impact the drug's effectiveness as well as its potential for toxicity. Understanding the pharmacokinetics of lignocaine is essential for determining appropriate dosages and ensuring patient safety, particularly when administered intravenously.

Clinical Applications of IV Lignocaine

Intravenous lignocaine is utilized in a variety of clinical settings, most notably in anesthesia, where it is commonly used for procedural sedation and regional anesthesia. It offers rapid onset and potent analgesic effects, making it ideal for short surgical procedures or in emergency situations. Additionally, IV lignocaine is frequently employed to manage acute pain, particularly in the perioperative period. Beyond its role in anesthesia, lignocaine is also widely used as an antiarrhythmic drug, especially for treating ventricular arrhythmias. It works by stabilizing the electrical activity of the heart, reducing the risk of life-threatening arrhythmic episodes. In some cases, it is used as an adjunct to other anesthetic agents to prolong anesthesia or enhance analgesia.

Lignocaine's ability to both control pain and prevent arrhythmias gives it a unique and versatile role in clinical medicine.

Advantages over other anesthetic agents:

When compared to other intravenous anesthetic agents like propofol, ketamine, and etomidate, lignocaine presents distinct advantages and drawbacks. Propofol, for instance, is known for its smooth induction and rapid recovery times, but it may not provide the same level of analgesia as lignocaine. Conversely, Ketamine has unique properties in maintaining hemodynamic stability, but it may cause dissociative effects that some patients find unpleasant. Lignocaine offers a balance between anesthetic and analgesic effects, with less pronounced sedative qualities compared to ketamine, making it ideal for cases where pain relief is the primary concern. In terms of safety, lignocaine is considered relatively well-tolerated, although it carries a risk of toxicity, especially in patients with pre-existing cardiovascular conditions. Etomidate, another commonly used anesthetic, is noted for its minimal cardiovascular effects, though it may not provide the same level of analgesia as lignocaine. Overall, lignocaine is often preferred when both local anesthesia and systemic pain relief are necessary, with its wide therapeutic index being a key factor in its continued use.

Recent Research and Innovations

Recent studies on intravenous lignocaine have focused on optimizing its use in both anesthesia and antiarrhythmic therapy. New research is exploring the drug's potential benefits when used in combination with other anesthetic agents, as well as its role in reducing postoperative pain and improving recovery times.

Innovations in drug delivery systems, such as controlled-release formulations, may also help to minimize side effects and improve patient outcomes. Additionally, studies have examined lignocaine's efficacy in treating specific patient populations, such as those with heart failure or renal impairment, where its pharmacokinetics may differ from the general population.

Emerging evidence also suggests that lignocaine may have potential benefits beyond its traditional uses, including in the management of chronic pain conditions.

REASON FOR SELECTION OF THIS TOPIC: [31,32,33,34]

Effective pain management is essential in medical care, particularly in surgical and post-operative settings. Historically, opioids have been the primary option for pain relief; however, their excessive use has resulted in major issues such as addiction, tolerance, and adverse side effects. To address these concerns, multimodal analgesia has emerged as a superior and safer alternative.

Multimodal analgesia is a comprehensive pain management strategy that utilizes multiple analgesic agents and techniques to target different pain pathways. This approach integrates non-opioid medications such as NSAIDs (nonsteroidal anti-inflammatory drugs), acetaminophen and local anesthetics. Additionally, regional anesthesia techniques, including nerve blocks and epidurals, are employed to enhance pain control. By engaging multiple pain mechanisms, multimodal analgesia offers superior pain relief while minimizing opioid dependency.

Drawbacks of Opioid-Based Pain Management

Although opioids are effective in controlling severe pain, their use presents several significant limitations:

1. Risk of Addiction and Dependence – Long-term opioid use can lead to physical dependence and addiction worsening the opioid crisis.
2. Tolerance – Over time, patients require higher doses to achieve the same level of pain relief thereby elevating the risk of overdose.

3. Adverse side effects – Most common opioid-related adverse effects includes nausea, vomiting, respiratory depression, constipation, and sedation, all of which can hinder recovery and overall well-being.
4. Delayed Recovery – Excessive opioid use can impair post-operative recovery due to sedation and cognitive dysfunction, restricting mobility and increasing the likelihood of complications such as blood clots and infections.

Advantages of Multimodal Analgesia

1. Superior Pain Control

By utilizing multiple agents with distinct mechanisms of action, multimodal analgesia delivers more effective pain relief than opioid-only regimens. This method allows for lower doses of individual medications while maximizing overall pain management.

2. Reduction in Opioid Use and Associated Risks

Multimodal analgesia significantly reduces opioid consumption, thereby decreasing the risks of addiction, overdose, and related side effects. Patients experience fewer opioid-associated complications, leading to safer and more efficient pain management.

3. Faster Recovery and Rehabilitation:

Patients receiving multimodal analgesia often recover more quickly due to improved pain control and reduced sedation. Early mobilization is essential in preventing post-operative complications such as pneumonia and deep vein thrombosis.

4. Enhanced Patient Satisfaction and Improved Outcomes

Patients report greater satisfaction with multimodal analgesia due to better pain relief and fewer side effects. This approach aligns with Enhanced Recovery After Surgery (ERAS) protocols, contributing to improved surgical outcomes, reduced hospital stays, and lower healthcare costs.

Implementation of Multimodal Analgesia in Clinical Practice

Multimodal analgesia can be adapted to individual patient needs and specific surgical procedures using various strategies:

- Preoperative administration of NSAIDs or acetaminophen to establish baseline pain control.
- Intraoperative application of regional anesthesia techniques, such as epidurals or nerve blocks, to reduce reliance on systemic analgesics.
- Postoperative continuation of non-opioid analgesics, with minimal opioid use reserved for breakthrough pain.

Multimodal analgesia represents a pivotal advancement in pain management, offering a safer and more effective alternative to opioid-based treatments. By minimizing opioid dependency and improving pain control, multimodal strategies contribute to better patient outcomes, expedited recovery, and reduced opioid-related complications. As healthcare professionals continue prioritizing patient safety and well-being, the integration of

multimodal analgesia into clinical practice should be emphasized to replace traditional opioid-heavy pain management models.

MATERIALS AND METHODS

- **SOURCE OF DATA**

This study was carried out in the Department of Anaesthesiology, BLDE, Shri. B.M. Patil Medical College, Hospital and Research center, Vijayapura from April 2023 to September 2024.

- **METHOD OF COLLECTION OF DATA:**

Study Design: A randomized comparative study.

Study Period: 1.5-year study from April 2023 to September 2024.

- **SAMPLE SIZE:**

Using G*Power ver. 3.1.9.4 software for sample size calculation, the anticipated Mean $\pm$ SD of MAP in Opioid free anesthesia patients 92.53 $\pm$ 8.1 and in Conventional patients 87.22 $\pm$ 7.76 resp. (ref) the required minimum sample size is 34 per group (i.e., a total sample size of 68 assuming equal group sizes) to achieve a power of 80% and a level of significance of 5% (two sided), for detecting a true difference in means between two groups.

- Level of significance= 95%
- Power of the study= 90%
- d = Clinically significant difference between two parameters
- SD = Common standard deviation

STATISTICAL ANALYSIS:

- The data obtained was entered in a Microsoft Excel sheet, and statistical analysis were performed using a statistical package for the social sciences (SPSS) (Version 20). The findings were displayed as graphs, counts and percentage, mean and SD.
- The normally distributed continuous variables between 2 groups were compared using independent sample t test.
- While for the not normally distributed variables, the Mann-Whitney test was used, for example, VAS scores between both the groups. Friedman test was used for repeated measures comparison.
- P value <0.05 was considered statistically significant. All statistics were calculated two-tailed.

RANDOMIZATION: Patients will be divided by computer-generated random number into two study groups A and B; each consisting of 34 patients as follows:

- ✓ **Group A:** (*Opioid free Anaesthesia group*): Patients will receive Anaesthetic doses of Lidocaine, Magnesium and Paracetamol in combination with pre-incisional infiltration and Intra peritoneal 0.25% Bupivacaine Instillations during Laparoscopic Cholecystectomy
- ✓ **Group B:** (*Conventional Opioid group*): Patients will undergo Laparoscopic cholecystectomy under conventional opioid based anaesthesia.

STUDY POPULATION

- This study will be done in 68 patients aged 18-70 years belonging to ASA grade I and II undergoing laparoscopic cholecystectomy under general anaesthesia.

INCLUSION CRITERIA:

- Patients aged between 18-70 years.
- Patients of either sex.
- Patients admitted for laparoscopic cholecystectomy under General Anesthesia with ASA Grade I & II.

EXCLUSION CRITERIA:

- Patients with body mass index $>35\text{kg/m}^2$.
- Patients with known allergy to Study medications.
- Patients having significant cardiopulmonary, hepatic or renal insufficiencies.
- Patients with Obstructive sleep Apnea Syndrome (OSAS)
- Pregnant and Lactating mothers.

This study was started after CTRI Registration (Reg no: **CTRI/2024/02/063345**) and was carried out in the operation theatre complex of Shri B M Patil medical college hospital and research Centre, Vijayapura.

METHODOLOGY:

PRE-ANESTHETIC EVALUATION:

- The Pre-anesthetic evaluation included the following:

HISTORY:

- A detailed history of underlying medical illness, previous history of any surgery, anesthetic exposure, and history of any hospitalizations was elicited. General and physical examinations were carried out. Airway, respiratory and cardiovascular system were assessed.

PHYSICAL EXAMINATION:

- The general condition of the patient.
- Vital signs -heart rate, blood pressure, respiratory rate, MAP, SpO2
- Height and weight, and BMI was calculated.
- Examination of the Gastrointestinal system, respiratory system, cardiovascular system, central nervous system, and vertebral system.
- Airway assessment by Mallampati grading.
- The procedure was explained to the patient and patient attenders.
- Patients were divided into 2 groups – Group A and Group B

INVESTIGATIONS /INTERVENTIONS

- Routine investigations include CBC, RBS, ECG, LFT, Chest X-ray, HIV, HbsAg, and Urine routine.

PROCEDURE:

- Informed written consent was taken before the surgery. Patients kept nil by mouth 6 hours prior surgery. All the patients were educated on Visual Analogue Scale and its scoring system.
- Randomization was be done by computer generated random numbers assigned to each patient in the study, thereafter they were assigned into Two Groups viz., Group A- Opioid free Anaesthesia and Group B-Conventional opioid group.
- After shifting the patient to the preoperative room, Preloading was done with IV crystalloids 10ml/kg. IV Dexamethasone 8 mg was administered to all patients. Baseline parameters such as systolic and diastolic blood pressure, Heart rate, Mean Arterial pressure (MAP), oxygen saturation, Respiratory rate and End-tidal carbon dioxide monitoring was done. Group A patients were administered IV paracetamol 15 mg/kg preoperatively.
- All patients were pre-oxygenated with 100% O2 for 3 min then premedicated

using Midazolam 1 mg IV, Glycopyrrolate 0.2 mg IV and Ondansetron 4 mg IV and then induced with IV propofol 2.5mg/kg until the endpoint of loss of eyelash reflex is obtained, along with Lignocaine 1.5 mg/kg (bolus dose) and 1.5mg/kg of succinyl Choline. Endotracheal intubation was done, Atracurium 0.5 mg/kg was administered as loading dose and then in incremental doses as needed along with Nitrous oxide 0.5L/min, oxygen 0.5L/min, sevoflurane 1%. Pre-incisional infiltration using 20 ml of 0.25% Bupivacaine (5 ml in each port) was done for Group A patients.



Fig 9: Pre-incisional port site infiltration

- During the maintenance phase, Group A- (Opioid-free anaesthesia group) received Lidocaine 1.5mg/kg as slow intravenous infusion for one hour and Magnesium 2 g (bolus dose) over 10-15 minutes. Hemodynamic parameters such as heart rate, systolic and diastolic blood pressure and MAP was monitored just before induction and at 5, 10,15,30,60 mins after induction for all patients. The intraperitoneal instillation of 20 ml of 0.25% Bupivacaine was given in the gall bladder bed, after gall bladder

has been taken out and the peritoneal wash was done.

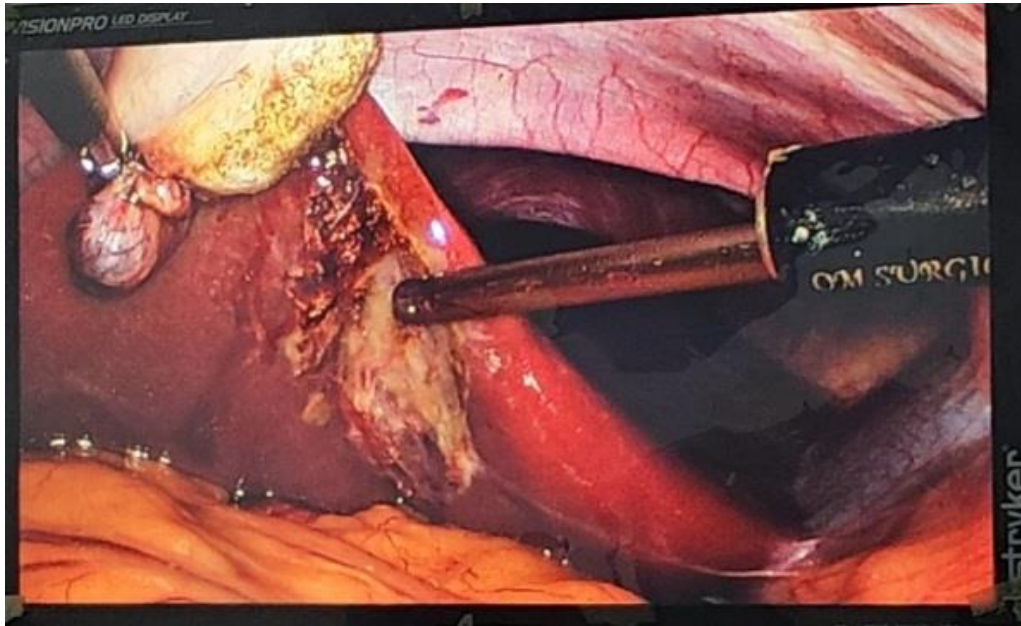


Fig 10: Intraperitoneal instillation of 0.25%Bupivacaine in the gallbladder bed.

- In the conventional Opioid-based anaesthesia group, a similar induction protocol was followed, along with 2 mcg/kg bolus dose of Fentanyl was given and later 0.5mcg/kg IV fentanyl to reduce the intraoperative rise of blood pressure.
- During Pneumoperitoneum, end tidal Carbon dioxide was maintained below 35 mm Hg in both the groups and the intra-abdominal pressure was maintained within 12-15 mm Hg.
- Residual neuromuscular blockade was reversed with IV neostigmine 2.5mg and IV Glycopyrrolate 0.5mg and tracheal extubation was done, when the patient met the extubation criteria. At the end of surgery, both the groups received 1g paracetamol intravenously.

- After extubation, vitals, Pain score and adverse effects was assessed in all patients in the post operative care unit. Postoperatively, follow up VAS scores and monitoring was done at 0,2,4,6,12,24 hours post-surgery and rescue analgesic, IV Paracetamol 1 g was given if the VAS score >4. For patients with severe persistent pain (VAS 8-10) and limiting movements, Tramadol 50 mg was given. The time for first analgesic request and the total analgesic consumption was documented in data collection Proforma.
- Pain Assessment: The scale consists of a line measuring 10 centimeters anchored at one end by a label as “No pain” and at the other extreme by a label such as “the worst pain imaginable” or ‘pain as bad as can be’. The patients will be asked to mark the line to indicate pain intensity in relation to 0 (no pain) to 10 (worst possible pain). The result will be interpreted as a distance in centimeter (cm) between 0 to the point marked by the patient as;
 - ✓ No pain will be considered when the VAS is 0.
 - ✓ Mild pain will be considered when the VAS score is between 1 and 3;
 - ✓ Moderate pain when VAS Score is between 4 and 6
 - ✓ Severe pain will be recorded when the VAS Score is >7
- Mann-Whitney test to be used to compare VAS scores between both the groups. Friedman test was used for repeated measures

comparison. Conversion to open technique and continuation of post operative ventilation was considered as **Drop outs**.

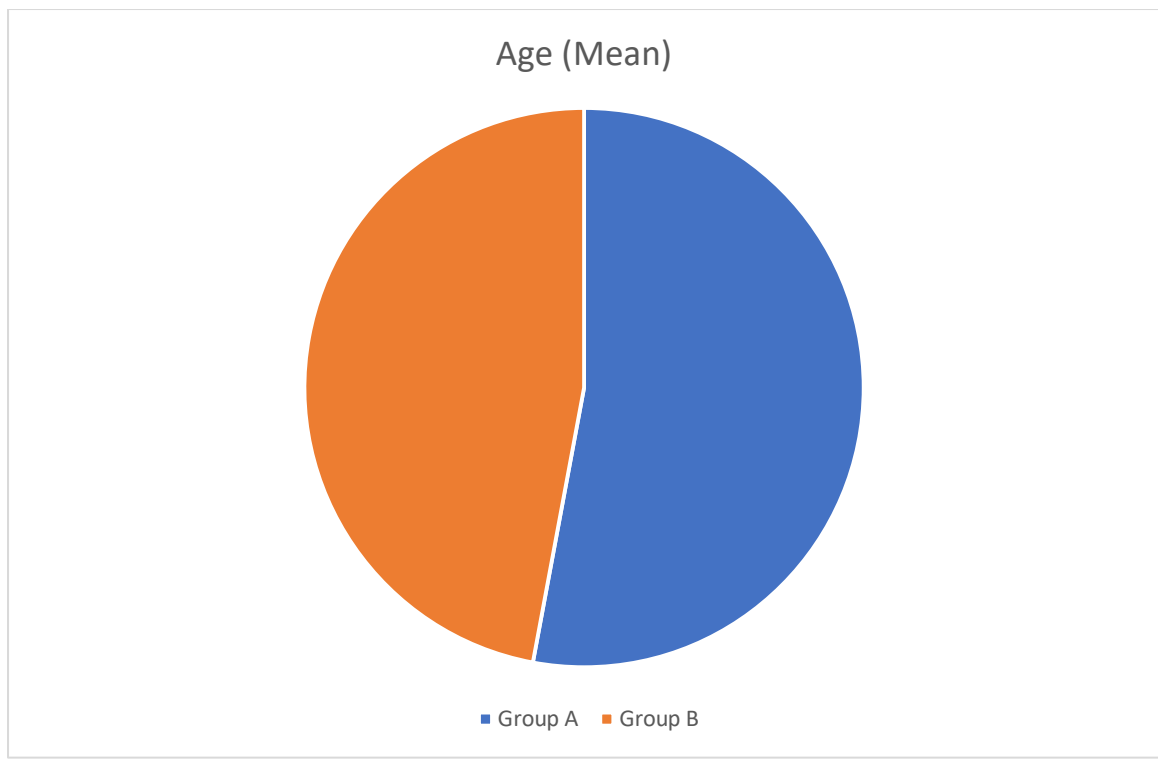
OBSERVATION AND RESULTS.

- The collected data from my study conducted was represented in the master chart. Total sample size is 68 (group A and group B containing 34 patients each who are undergoing laparoscopic cholecystectomies).
- **Group A:** (*Opioid free Anaesthesia group*): Patients received Anaesthetic doses of Lidocaine, Magnesium and Paracetamol in combination with pre-incisional infiltration and Intra peritoneal 0.25% Bupivacaine Instillations.
- **Group B:** (*Conventional Opioid group*): Patients underwent Laparoscopic cholecystectomy under conventional opioid based anaesthesia
- P value less than 0.05 was considered statistically significant.

1. DEMOGRAPHIC VARIABLES:

a) TABLE A – MEAN AGE OF TWO GROUPS.

AGE (Yrs)	Sample size	MEAN $\pm$ SD	P
GROUP A	34	46.21 $\pm$ 15.497	0.157
GROUP B	34	41.09 $\pm$ 13.957	

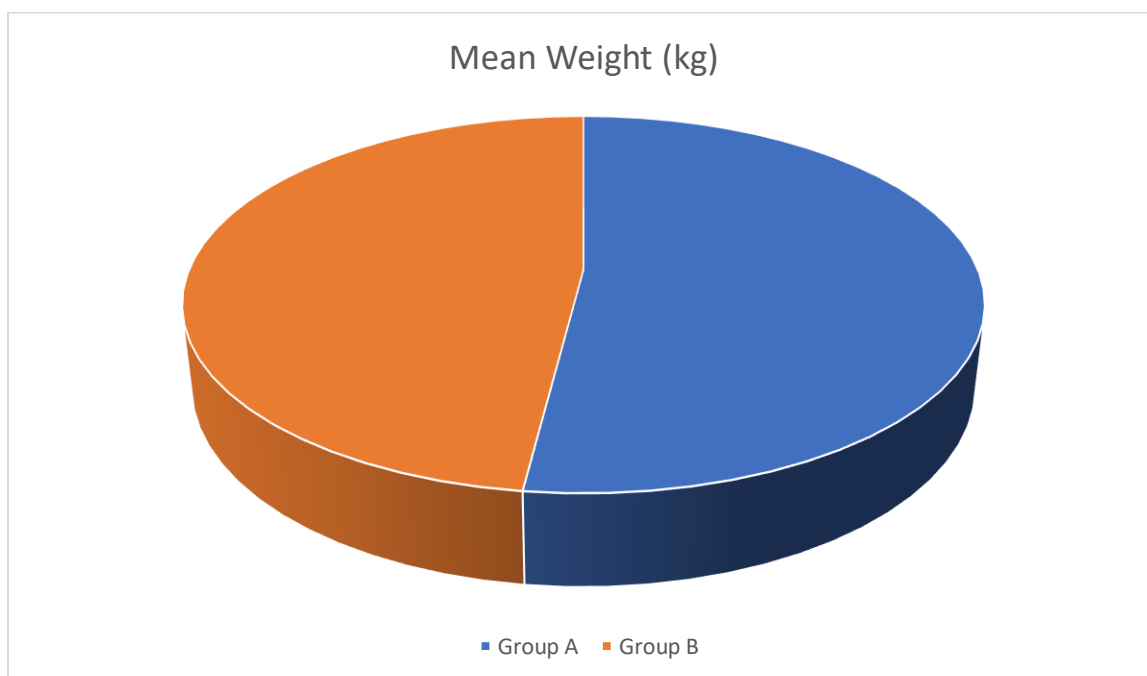


GRAPH 1: COMPARISON OF MEAN AGE (YEARS)

The mean age of participants in **Group A** was **46.21 ± 15.497 years**, while in **Group B**, it was **41.09 ± 13.957 years**. An independent samples t-test was conducted to compare the mean ages between the two groups, yielding a p-value of 0.157. Since this value is greater than the conventional significance threshold of 0.05, the difference in age between the two groups is not statistically significant. This implies that both groups are comparable in terms of age, minimizing the potential influence of age as a confounding factor in the study.

b) TABLE B – MEAN WEIGHT (Kg) OF TWO GROUPS.

WEIGHT(Kg)	Sample size	MEAN± SD	P value
GROUP A	34	68.62±13.298	0.096
GROUP B	34	63.32±12.579	

**GRAPH 2: COMPARISON OF MEAN WEIGHT (Kg)**

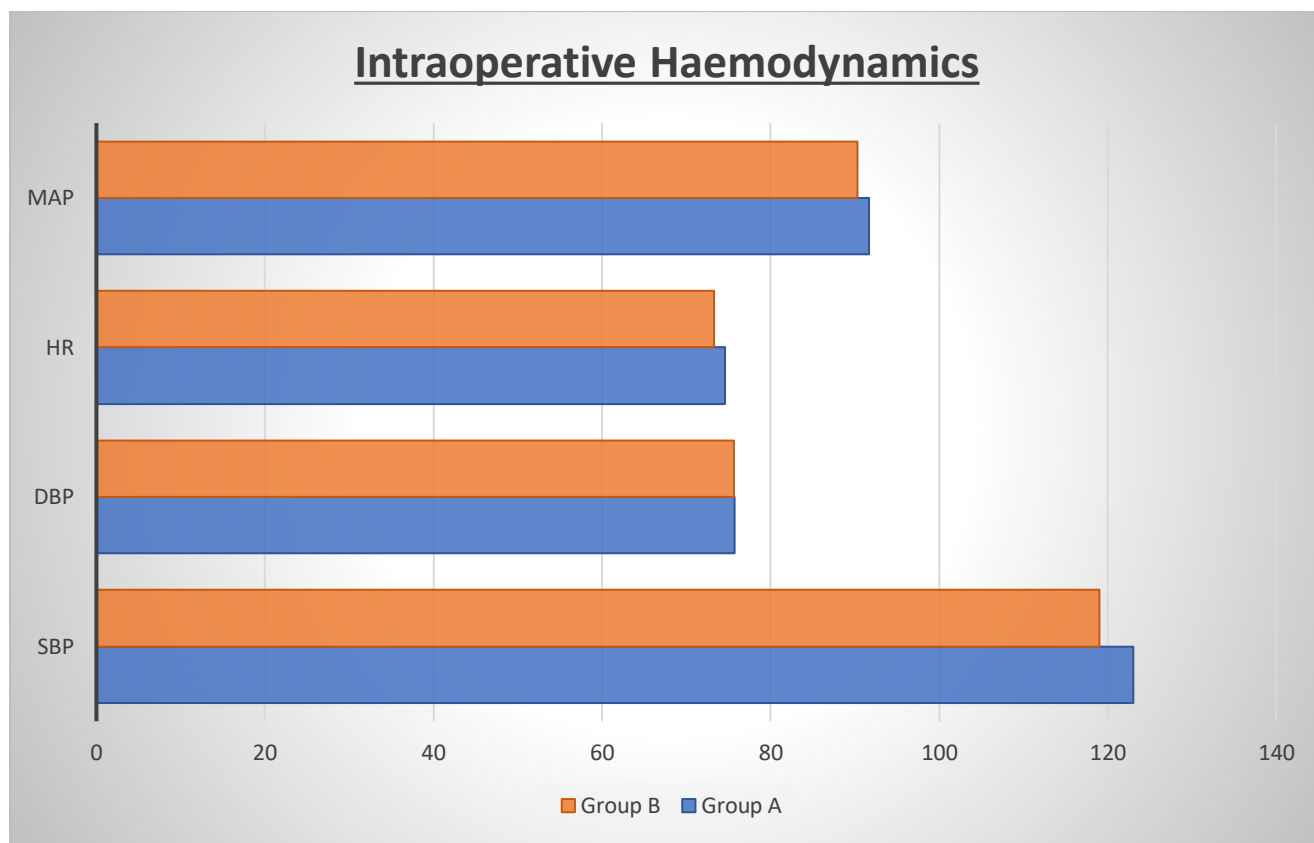
The mean weight of participants in Group A was 68.62 ± 13.298 kg, while in Group B, it was 63.32 ± 12.579 kg. An independent samples t-test was

conducted to compare the mean weights between the two groups, yielding a p-value of 0.096. Hence the difference in weight between the groups is not statistically significant.

c) COMPARISON OF INTRAOPERATIVE HAEMODYNAMICS.

VARIABLES	Group A (OFA group) (Mean $\pm$ SD)	Group B - Conventional group (Mean $\pm$ SD)	P
SBP (mmHg)	123.6479 $\pm$ 5.672	119.504 $\pm$ 5.720	.004
DBP (mmHg)	75.706 $\pm$ 7.55	75.662 $\pm$ 4.968	.978
HR (bpm)	74.600 $\pm$ 5.354	73.253 $\pm$ 5.507	.310
MAP (mmHg)	91.665 $\pm$ 4.139	90.267 $\pm$ 4.022	.165

A comparison of intraoperative hemodynamic parameters, including systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and mean arterial pressure (MAP) monitored just prior induction and at 5,10,15,30,60 minutes after induction, was conducted between Group A (opioid-free anesthesia, OFA group) and Group B (conventional anesthesia group) using an independent samples t-test to assess statistical significance.



GRAPH 3: COMPARISON OF INTRAOPERATIVE HEMODYNAMICS.

The mean SBP in Group A was 123.65 ± 5.672 mmHg, while in Group B, it was 119.50 ± 5.720 mmHg. Among the assessed intraoperative hemodynamic parameters, SBP was the only variable that exhibited a statistically significant difference ($p = 0.004$), with Group A demonstrating a slightly higher SBP than Group B. However, DBP, HR, and MAP did not differ significantly between the two groups ($p > 0.05$), indicating that intraoperative hemodynamic stability was largely comparable between the two anesthesia techniques.

d) POSTOPERATIVE VAS SCORE COMPARISON.

VARIABLE	Group	N	Mean $\pm$ SD	P
VAS 0 HR	Grp A	34	0.79 $\pm$ 0.88	0.000
	Grp B	34	2.47 $\pm$ 0.615	
VAS 2 HR	Grp A	34	2.06 $\pm$ 0.489	0.000
	Grp B	34	3.32 $\pm$ 0.945	
VAS 4HR	Grp A	34	2.85 $\pm$ 0.744	0.000
	Grp B	34	4.06 $\pm$ 1.774	
VAS6HR	Grp A	34	3.29 $\pm$ 0.871	0.776
	Grp B	34	3.71 $\pm$ 1.697	
VAS12HR	Grp A	34	2.91 $\pm$ 0.830	0.442
	Grp B	34	3.18 $\pm$ 1.058	
VAS24HR	Grp A	34	2.15 $\pm$ 0.50	0.001
	Grp B	34	2.62 $\pm$ 0.604	

The postoperative pain levels were assessed at different time intervals (0, 2, 4, 6, 12, and 24 hours) using the Visual Analog Scale (VAS) in both Group A (opioid-free anesthesia, OFA group) and Group B (conventional anesthesia group). Mann-Whitney U test was used to compare VAS scores between the two groups.

At 0 hours postoperatively, the mean VAS score was 0.79 $\pm$ 0.880 in Group A and 2.47 $\pm$ 0.615 in Group B. The Mann-Whitney U test yielded a p-value of 0.000, indicating a statistically significant difference between the groups, with Group A reporting significantly lower pain scores. At 2 hours postoperatively, the average VAS score was 2.06 $\pm$ 0.489 in Group A and 3.32 $\pm$ 0.945 in Group

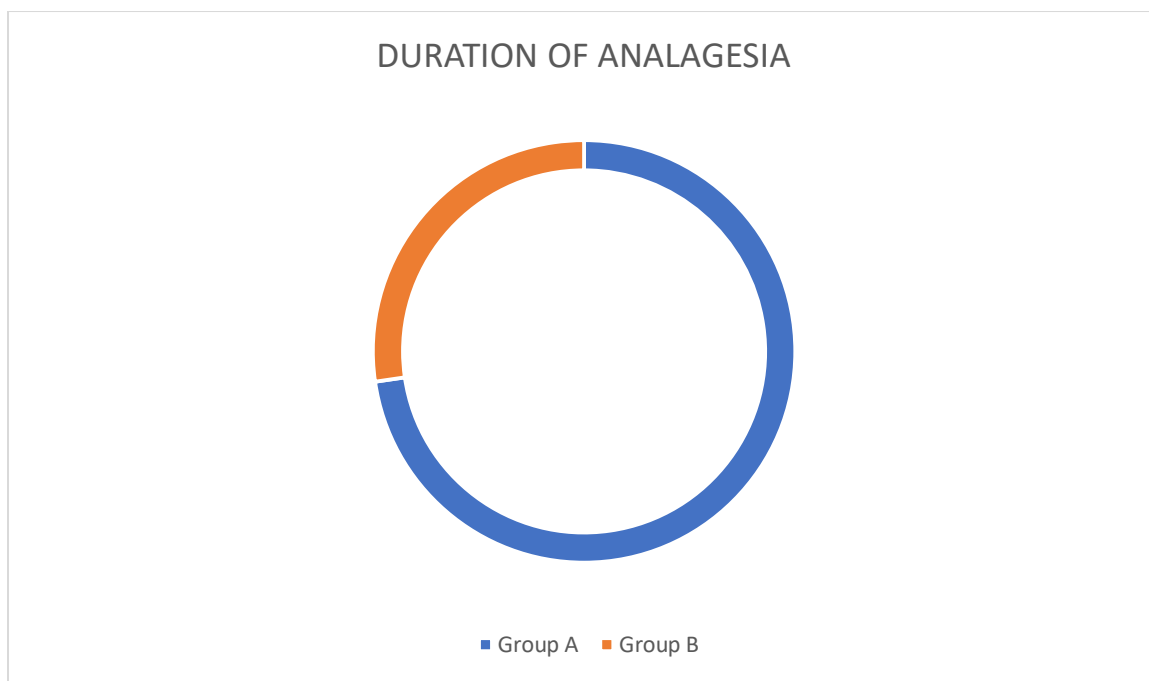
B. The p-value of 0.000 indicates a statistically significant difference, suggesting that pain levels were notably lower in the OFA group than in the conventional group during this period. Similarly at 4 hours postoperatively, the mean VAS scores showed a statistically significant difference in favor of Group A, where patients experienced lower pain levels.

However, no significant differences were observed at 6 and 12 hours postoperatively ($p > 0.05$), suggesting that pain levels became comparable between the groups during this period. At 24 hours postoperatively, the mean VAS scores were 2.15 ± 0.500 in Group A and 2.62 ± 0.604 in Group B. The p-value was 0.001, indicating a statistically significant difference, with Group A experiencing lower pain scores at this time point.

e) DURATION OF ANALGESIA

DURATION OF ANALGESIA (hr.)	Group	N	Mean $\pm$ SD	P
	GROUP A	34	11.35 $\pm$ 7.639	.000
	GROUP B	34	4.26 $\pm$ 2.050	

The mean duration of analgesia was substantially longer in **Group A (11.35 $\pm$ 7.639 hours)** compared to **Group B (4.26 $\pm$ 2.050 hours)**. An independent sample t-test showed a statistically significant difference between the two groups ($p < 0.001$), indicating that the intervention used in Group A resulted in prolonged analgesic effects compared to Group B.



GRAPH 4: COMPARISON OF DURATION OF ANALGESIA.

f) TOTAL CONSUMPTION OF ANALGESICS USING
FREQUENCY TABLE

VARIABLES	OPIOID-FREE ANESTHESIA		CONVENTIONAL group	
	n	%	n	%
Nil dose of analgesic	8	24	0	0
1 dose of paracetamol	24	71	19	56
2 doses of paracetamol	2	6	8	24
1 dose of paracetamol + tramadol	0	0	7	21

n- number

In the OFA group, 24% of patients managed without the need for any analgesics, suggesting that the opioid-free approach may be effective in controlling postoperative pain. Conversely, all patients in the Conventional group required analgesics, as none were able to manage without them. A greater

percentage of patients in the OFA group required only one dose of paracetamol (71%) compared to the Conventional group (56%). This suggests that the opioid-free anesthesia protocol might provide better pain relief with less medication. It also indicates that OFA might result in less severe pain or more effective pain management during the postoperative period. No patients in the OFA group required a combination of paracetamol and tramadol, while 21% of patients in the Conventional group required this combination of analgesics. This suggests that the opioid-free approach was highly effective in controlling pain, as patients did not require additional opioid-based analgesics like tramadol. The conventional group, however, required more potent pain relief, due to higher pain levels.

g) POST-OPERATIVE ADVERSE EFFECTS.

Adverse Effects	Group A	Group B	P
Nausea & vomiting	0	5	0.053
Generalized pruritus	0	1	1.000
Shivering	0	2	0.429
Shoulder tip pain	2	11	0.0115

n- number

The incidence of postoperative adverse effects was notably lower in the opioid-free anesthesia (OFA) group compared to the conventional anesthesia group.

Additionally, shoulder tip pain, attributed to the effects of residual carbon dioxide was more prevalent in Group B. These findings suggest that opioid-free anesthesia may reduce the risk of opioid-related side effects while maintaining comparable postoperative comfort.

DISCUSSION

Since the advent of modern anaesthesia, effective peri-operative pain management has remained a primary concern for both anesthesiologists and patients. Opioids have traditionally been the primary class of analgesics. However, given the risks associated with opioids and the proven benefits of multimodal analgesia, the latter has become the better alternative in surgical pain management.

In the current study, the results indicate that patients in Opioid-free anesthesia group reported significantly lower VAS scores compared to conventional anesthesia group. Our multimodal opioid-sparing regimen included lignocaine and magnesium infusion along with local infiltration and instillation of 0.25% bupivacaine. The postoperative pain levels were assessed at time intervals - 0, 2, 4, 6, 12, and 24 hours using the Visual Analog Scale (VAS) in both Opioid-free anesthesia (OFA group) and the conventional anesthesia group. The mean VAS scores showed a statistically significant difference in favor of OFA group in the first 4 hours postoperatively, where patients experienced lower pain levels. Hence, suggests that opioid-free anesthesia provides a better immediate postoperative pain relief when compared to the conventional opioids in laparoscopic cholecystectomies.

Jun-Ma Yu et al (2023) ^[35] conducted similar study on 150 patients who underwent a 3-port laparoscopic cholecystectomy. Opioid-free anesthesia using Dexmedetomidine, Ketamine and IV Lidocaine combined with local infiltration with 0.5% Ropivacaine showed effective pain relief within 8 hours post-surgery, reduced the need for additional analgesics within 24 hours. This study additionally showed that the time of passing first flatus after surgery was also reduced with no other obvious adverse reactions in patients allotted in the Opioid-free group.

Our study also showed that the average duration of analgesia was considerably longer in OFA group (11.35 ± 7.639 hours) than in conventional opioid groups (4.26 ± 2.050 hours). Also, opioid-free anesthesia (OFA) group had a lower overall requirement for postoperative analgesics compared to the conventional opioid group. A greater proportion of patients in OFA (24%) did not require any analgesics, while all patients in conventional group required at least one dose. Furthermore, no patients in the OFA group required additional opioid analgesic, whereas 21% of patients in the conventional group needed injection tramadol 50 mg in addition to paracetamol 1g. These findings indicate that opioid-free anesthesia may offer more effective postoperative pain relief, thereby decreasing the need for supplementary analgesic medications.

I M Saadawy (2010) ^[36] conducted a double-blind study was conducted to assess and compare the effects of intravenous magnesium and IV lidocaine on

postoperative pain, bowel function, analgesic consumption, and sleep quality in patients undergoing laparoscopic cholecystectomy and concluded that the Intravenous lidocaine and magnesium enhanced postoperative pain relief and decreased the need for both intraoperative and postoperative opioids in these patients. This improvement in recovery quality could contribute to faster hospital discharge. This study also showed Lidocaine was associated with earlier return of bowel function and magnesium was associated with better quality of sleep.

A comparison of intraoperative hemodynamic parameters, including systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and mean arterial pressure (MAP) monitored just prior induction and at 5,10,15,30,60 minutes after induction, was done between both the groups in our current study. Among the assessed intraoperative hemodynamic parameters, SBP was the only variable that exhibited a statistically significant difference ($p = 0.004$), with OFA group demonstrating a slightly higher SBP than conventional group. However, DBP, HR, and MAP did not differ significantly between the two groups ($p > 0.05$), indicating that intraoperative hemodynamic stability was largely comparable between the two anesthesia groups. These findings suggest that the opioid-free anesthesia approach in laparoscopic cholecystectomies did not compromise hemodynamic stability in comparison to conventional anesthesia, except for the observed difference in SBP.

Ragupathy R et al (2022)^[1] had conducted a study on 60 patients posted for laparoscopic surgeries in a tertiary care hospital to compare pain scores in the post-operative period between Opioid-free anesthesia group and the conventional opioid-based group. Anesthetic doses of lidocaine, paracetamol magnesium and in combination with fascial plane block were given for 30 patients, and the other 30 patients received the conventional opioid-based anesthesia using fentanyl. This study concluded the combination of Erector spinae block with intravenous magnesium and lignocaine provided better postoperative pain relief with a lower VAS score and reduced opioid consumption when compared to conventional group. In this study, the intra-operative hemodynamic parameters were comparable between both the groups with systolic blood pressure being lower in the conventional opioid group, but the difference was clinically insignificant.

The incidence of postoperative adverse effects was notably lower in the opioid-free anesthesia (OFA) group in our study when compared to the conventional anesthesia group. Additionally, shoulder tip pain, attributed to the effects of residual carbon dioxide was more prevalent in conventional opioid group. These findings suggest that opioid-free anesthesia may reduce the risk of opioid-related side effects while maintaining comparable postoperative comfort.

Marija Toleska et al (2022)^[6] conducted a clinical trial on 80 patients to assess PONV (Postoperative nausea and vomiting) in patients who received opioids

during laparoscopic cholecystectomy versus patients who received opioid-free anesthesia. Their study showed that PONV have occurred more often in patients who received opioid anesthesia compared to the opioid-free group.

CONCLUSION

The study findings demonstrate that opioid-free anesthesia offers several advantages over conventional opioid-based anesthesia for laparoscopic cholecystectomy. It significantly prolongs postoperative analgesia, reduces early postoperative pain scores, and minimizes the need for additional analgesics.

Moreover, opioid-free anesthesia is associated with a lower incidence of adverse effects which can enhance overall patient comfort and recovery. These findings suggest that opioid-free anesthesia is a viable alternative for improving postoperative outcomes and should be considered as part of enhanced recovery protocols in laparoscopic surgeries.

BIBLIOGRAPHY

1. Ragupathy, Ramanarayanan; Prabhu, S.C.Ganesh; Thiyagarajan, Dhivya; Anto, Vijay1. Opioid-free anaesthesia for laparoscopic surgeries - A prospective non-randomised study in a tertiary care hospital. *Indian Journal of Anaesthesia* 66(3):p 207-212, March 2022. | DOI: 10.4103/ija.ija_785_21
2. Hao C, Xu H, Du J, Zhang T, Zhang X, Zhao Z, Luan H. Impact of Opioid-Free Anesthesia on Postoperative Quality of Recovery in Patients After Laparoscopic Cholecystectomy-A Randomized Controlled Trial. *Drug Des Devel Ther.* 2023; 17:3539-3547
<https://doi.org/10.2147/DDDT.S439674>
3. Toleska M, Dimitrovski A. Is Opioid-Free General Anesthesia More Superior for Postoperative Pain Versus Opioid General Anesthesia in Laparoscopic Cholecystectomy? *Pril (Makedon Akad Nauk Umet Odd Med Nauki)*. 2019 Oct 1;40(2):81-87. doi: 10.2478/prilozi-2019-0018. PMID: 31605587.
4. @article{Ahmed2020OpioidFA,title={Opioid Free Anesthesia in Laparoscopic Cholecystectomy (Comparative Clinical Study)}, author={Osama Helal Ahmed and Tawfik Mohamed Noor El-Din and Waheed Mohamed Ali and Zein Sayed}, journal={The Egyptian Journal of Hospital Medicine} year={2020}
5. Manan A, Khan AA, Ahmad I, Usman M, Jamil T, Sajid MA. Intraperitoneal Bupivacaine as Post-laparoscopic Cholecystectomy Analgesia. *J Coll Physicians Surg Pak.* 2020 Jan;30(1):9-12. doi: 10.29271/jcpsp.2020.01.09. PMID: 31931924
6. Toleska M, Dimitrovski A, Dimitrovska NT. Postoperative Nausea and Vomiting in Opioid-Free Anesthesia Versus Opioid Based Anesthesia in Laparoscopic Cholecystectomy. *Pril (Makedon Akad Nauk Umet Odd Med Nauki)*. 2022 Dec 4;43(3):101-108. doi: 10.2478/prilozi-2022-0042. PMID: 36473040.
7. Das NT, Deshpande C. Effects of Intraperitoneal Local Anaesthetics Bupivacaine and Ropivacaine versus Placebo on Postoperative Pain after Laparoscopic Cholecystectomy: A Randomised Double Blind Study. *J Clin Diagn Res.* 2017 Jul;11(7):UC08-UC12. doi: 10.7860/JCDR/2017/26162.10188. Epub 2017 Jul 1. PMID: 28893013; PMCID: PMC5583910.
8. Nagral S. Anatomy relevant to cholecystectomy. *J Minim Access Surg.* 2005 Jun;1(2):53-8. doi: 10.4103/0972-9941.16527. PMID: 21206646; PMCID: PMC3004105.
9. Hassler KR, Collins JT, Philip K, et al. Laparoscopic Cholecystectomy. [Updated 2025 Jan 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-.<https://www.ncbi.nlm.nih.gov/books/NBK448145/>
10. Blichfeldt-Eckhardt MR, Ording H, Andersen C, Licht PB, Toft P. Early visceral pain predicts chronic pain after laparoscopic cholecystectomy. *Pain.* 2014

- Nov;155(11):2400-7. doi: 10.1016/j.pain.2014.09.019. Epub 2014 Sep 22. PMID: 25250720.
11. Delgado DA, Lambert BS, Boutris N, McCulloch PC, Robbins AB, Moreno MR, Harris JD. Validation of Digital Visual Analog Scale Pain Scoring With a Traditional Paper-based Visual Analog Scale in Adults. *J Am Acad Orthop Surg Glob Res Rev*. 2018 Mar 23;2(3):e088. doi: 10.5435/JAAOSGlobal-D-17-00088. PMID: 30211382; PMCID: PMC6132313.
12. Butterworth JF, Mackey DC, Wasnick JD. Morgan & Mikhail's clinical anesthesiology, 7th edition. New York: McGraw-Hill;
13. Shah J, Votta-Velis EG, Borgeat A. New local anesthetics. *Best Pract Res Clin Anaesthesiol*. 2018 Jun;32(2):179-185. doi: 10.1016/j.bpa.2018.06.010. Epub 2018 Jul 3. PMID: 30322458
14. Karunarathna I, Tharayil AS. Unveiling the Potency of Bupivacaine: A Comprehensive Review of Mechanism, Safety, and Clinical Applications. Uva Clinical Lab. Retrieved from Unveiling the Potency of Bupivacaine: A Comprehensive Review of Mechanism, Safety, and Clinical Applications. 2024.
15. El-Boghdadly K, Pawa A, Chin KJ. Local anesthetic systemic toxicity: current perspectives. *Local and regional anesthesia*. 2018 Aug 8:35-44.
16. Chen C, Tao R. The Impact of Magnesium Sulfate on Pain Control After Laparoscopic Cholecystectomy: A Meta-Analysis of Randomized Controlled Studies. *Surg Laparosc Endosc Percutan Tech*. 2018 Dec;28(6):349-353. doi: 10.1097/SLE.0000000000000571. PMID: 30222695
17. R. R. S. Srisai, et al. "Magnesium in Anesthesia and Intensive Care Medicine." *Anesthesia & Analgesia* 2019; 129(6): 1507-1517.
18. Kogler J. The analgesic effect of magnesium sulfate in patients undergoing thoracotomy. *Acta Clin Croat*. 2009 Mar;48(1):19-26. PMID: 19623867.
19. G. A. Siegel, et al. "Magnesium sulfate in perioperative care: A review of clinical uses." *Journal of Clinical Anesthesia* 2018; 47: 1-10.
20. S. Y. Choi, et al. "Magnesium sulfate as an adjunct to epidural analgesia for pain relief after thoracotomy: a randomized, double-blinded, placebo-controlled study." *Anesthesia & Analgesia* 2017; 124(5): 1436-1443.
21. L. H. Gu, et al. "Effects of magnesium sulfate on postoperative pain: a systematic review and meta-analysis of randomized controlled trials." *Journal of Pain Research* 2020; 13: 803-811.
22. M. J. S. Terao, et al. "Pharmacokinetics of magnesium sulfate in anesthesia and intensive care: implications for clinical use." *Anesthesia and Analgesia* 2021; 132(3): 700-710

23. R. H. Sharma, et al. "Magnesium sulfate and neuroprotection during anesthesia: A critical review." *Journal of Neurosurgical Anesthesia* 2021; 33(2): 175-184.
24. Beecham GB, Nessel TA, Goyal A. Lidocaine. [Updated 2024 Aug 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK539881/>
25. Lee IW, Schraag S. The Use of Intravenous Lidocaine in Perioperative Medicine: Anaesthetic, Analgesic and Immune-Modulatory Aspects. *J Clin Med*. 2022 Jun 20;11(12):3543. doi: 10.3390/jcm11123543. PMID: 35743617; PMCID: PMC9224677.
26. Miller RD, editor. *Anesthesia* 7th ed. New York: Churchill Livingstone; 2009. p.,1799-800.
13. Benyamin R, Trescot AM, Datta S, Buenaventura R, Adlaka
27. Katzung, B. G., Masters, S. B., & Trevor, A. J. (2017). *Basic and Clinical Pharmacology* (14th ed.). McGraw-Hill Education
28. Aho, J. M., & Tait, G. S. (2021). Clinical pharmacology of lignocaine: Applications and risks in anesthesia. *Journal of Anesthesia*, 32(4), 234-241.
29. Brull, S. J., & Macfarlane, A. J. R. (2014). Mechanisms of action of local anesthetics and antiarrhythmic drugs. *British Journal of Anaesthesia*, 113(3), 486-498.
30. Herring, W. J., & Arora, K. (2020). The pharmacology of intravenous lignocaine in anesthesia: A focus on sodium channel blockade. *Journal of Clinical Anesthesia*, 32, 234-245
31. Kehlet, H., & Dahl, J. B. (2003). The value of multimodal or balanced analgesia in postoperative pain treatment. *Anesth Analg*, 77(5), 1048-1056.
32. Buvenendran, A., & Kroin, J. S. (2009). Multimodal analgesia for controlling acute postoperative pain. *Current Opinion in Anesthesiology*, 22(5), 588-593.
33. Wick, E. C., Grant, M. C., & Wu, C. L. (2017). Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques. *JAMA Surgery*, 152(7), 691-697.
34. Chou, R., Gordon, D. B., de Leon-Casasola, O. A., et al. (2016). Management of postoperative pain: a clinical practice guideline from the American Pain Society. *Journal of Pain*, 17(2), 131-157
35. Yu JM, Tao QY, He Y, Liu D, Niu JY, Zhang Y. Opioid-Free Anesthesia for Pain Relief After Laparoscopic Cholecystectomy: A Prospective Randomized Controlled Trial. *J Pain Res*. 2023 Oct 30;16:3625-3632. doi: 10.2147/JPR.S432601. PMID: 37928062; PMCID: PMC10624184.
36. Saadawy IM, Kaki AM, Abd El Latif AA, Abd-Elmaksoud AM, Tolba OM. Lidocaine vs. magnesium: effect on analgesia after a laparoscopic cholecystectomy. *Acta*

Anaesthesiol Scand. 2010 May;54(5):549-56. doi: 10.1111/j.1399-6576.2009.02165.x.
Epub 2009 Nov 16. PMID: 19919581.

SAMPLE INFORMED CONSENT FORM

BLDE (DEEMED TO BE UNIVERSITY); SHRI B.M. PATIL MEDICAL
COLEGE HOSPITAL AND RESEARCH CENTRE VIJAYAPURA,
KARNATAKA

TITLE OF THE PROJECT: OPIOID-FREE VERSUS OPIOID BASED
ANAESTHESIA FOR LAPAROSCOPIC CHOLECYSTECTOMY-A
RANDOMIZED CLINICAL TRIAL

PRINCIPAL INVESTIGATOR:

Dr.THASKIN

Department of Anaesthesiology

BLDE (Deemed to be University), Shri B.M. Patil Medical College Hospital
and Research Centre, Vijayapura – 586 103, Karnataka.

Email: thaskin.majeed@gmail.com

PG GUIDE:

Dr. BASAVARAJ PATIL MD

Associate Professor

Department of Anaesthesiology,

BLDE (Deemed to be University), Shri B.M. Patil Medical College
Hospital and Research Centre, Vijayapura – 586 103, Karnataka

PURPOSE OF RESEARCH:

I have been informed that this study is on Opioid free versus Opioid based Anaesthesia for Laparoscopic cholecystectomy – A Randomized clinical Trial.

I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given the free choice of either being included or not in the study.

PROCEDURE:

I understand that I will be participating in the study on Opioid free versus Opioid based Anaesthesia for Laparoscopic cholecystectomy – A Randomized clinical Trial

RISKS AND DISCOMFORTS:

I understand that my ward may experience some discomfort during the procedure, and I understand that necessary measures will be taken to reduce them.

BENEFITS:

I understand that my ward participating in this study will help in comparing Opioid free Anaesthesia and conventional opioid techniques for Laparoscopic cholecystectomy.

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this hospital record and will be subjected to the confidentiality and privacy regulation of this hospital. If the data are used for publication in the medical literature or teaching purposes, no names will be used, and other identities such as photographs and audio and videotapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. Dr. THASKIN is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study or later I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. And that a copy of this consent form will be given to me to keep for careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary, and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand Dr. THASKIN will terminate my participation in this study at any time after she has explained the reason for doing so and has helped arrange for my continued care by my own physician or therapist if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely events of injury to me/my ward, resulting directly due to my participation in this study, such injury will be reported promptly, then medical treatment will be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving my legal rights. I have explained the purpose of this research, the procedure required, and the possible risk and benefits to the best of my ability in patients, own language.

DATE

Dr. THASKIN (investigator)

PATIENT/PARENT SIGNATURE

Witness

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. THASKIN has explained to me the purpose of this research, the study procedure that I will undergo, and the possible discomforts and benefits that I may experience in my own language.

I have been explained all the above in detail in my own language, and I understand the same. Therefore, I agree to give my consent to participate as a subject in this research project.

(Participant)

(Date)

(Witness to above signature)

(Date)

B.L.D.E (DEEMED TO BE UNIVERSITY)

ಶ್ರೀ ಬಿ.ಎಂ.ಪಟ್ಟೇಲ್ ಮೆಡಿಕಲ್ ಕಾಲೇಜು, ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ, ವಿಜಯಪುರ-586103

ಪ್ರಬಂಧ/ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಮಾಹಿತಿ ಪಡೆದ ಸಮ್ಮತಿ

ನಾನು, ಕೆಳಗಿನವರು _____ ಸಹಿಯಿಟ್ಟವರು, ಮಗ/ಮಗಳು/ಪತ್ನಿಯ _____ ವಯಸ್ಸು _____ ವರ್ಷಗಳು, ಸಾಮಾನ್ಯವಾಗಿ ನಿವಾಸಿಸುವ ಸ್ಥಳದ ಹೆಸರು _____, ಇಲ್ಲಿ ಹೇಳಿದ್ದೇನೆ/ಘೋಷಿಸುತ್ತೇನೆ ಡಾಕ್ಟರ್ ಹೆಸರು _____ ಅವರು ಆಸ್ಪತ್ರೆ ಹೆಸರು _____ ಅವರು ನನ್ನನ್ನು ಪೂರ್ಣವಾಗಿ ಪರೀಕ್ಷಿಸಿದರು ದಿನಾಂಕದಲ್ಲಿ _____ ಸ್ಥಳ ಹೆಸರು _____ ಮತ್ತು ನನಗೆ ನನ್ನ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ ನಾನು ಒಂದು ರೋಗ (ಸ್ಥಿತಿ) ಅನುಭವಿಸುತ್ತಿದ್ದೇನೆ. ಮುಂದುವರಿದು ಡಾಕ್ಟರ್ ನನಗೆ ತಿಳಿಸಿದ್ದಾರೆ ಅವರು ಒಂದು ಪದ್ಧತಿ/ಸಂಶೋಧನೆ ನಡೆಸುತ್ತಿದ್ದಾರೆ ಶೀರ್ಷಿಕೆಯುಳ್ಳ _____ ಡಾಕ್ಟರ್ _____ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ನನ್ನ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಯನ್ನು ಕೇಳಿದ್ದಾರೆ ಅಧ್ಯಯನದಲ್ಲಿ.

ಡಾಕ್ಟರ್ ನನಗೆ ಇದನ್ನು ಕೂಡಾ ತಿಳಿಸಿದ್ದಾರೆ ಈ ಕ್ರಮದ ನಡೆವಳಿಕೆ ಪ್ರತಿಕೂಲ ಫಲಿತಾಂಶಗಳನ್ನು ಎದುರಿಸಬಹುದು. ಮೇಲೆ ಹೇಳಿದ ಪ್ರಕಟಣೆಗಳಲ್ಲಿ, ಅಧಿಕಾಂಶವು ಚಿಕಿತ್ಸಿಸಬಹುದಾದರೂ ಅದನ್ನು ನಿರೀಕ್ಷಿಸಲಾಗುತ್ತಿಲ್ಲ ಆದ್ದರಿಂದ ನನ್ನ ಸ್ಥಿತಿಯ ಹಿರಿದಾಗುವ ಅವಕಾಶವಿದೆ ಮತ್ತು ಅಪರೂಪದ ಸಂದರ್ಭಗಳಲ್ಲಿ ಅದು ಮರಣಕಾರಕವಾಗಿ ಪರಿಣಮಿಸಬಹುದು ಹೊಂದಿದ ರೋಗನಿರ್ಧಾರ ಮತ್ತು ಯಥಾಶಕ್ತಿ ಚಿಕಿತ್ಸೆ ಮಾಡಲು ಹೊಂದಿದರೂ. ಮುಂದುವರಿದು ಡಾಕ್ಟರ್ ನನಗೆ ತಿಳಿಸಿದ್ದಾರೆ ನನ್ನ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆ ಈ ಅಧ್ಯಯನದ ಫಲಿತಾಂಶಗಳ ಮೌಲ್ಯಮಾಪನದಲ್ಲಿ ಸಹಾಯಕವಾಗುತ್ತದೆ ಇತರ ಸಮಾನ ಪ್ರಕರಣಗಳ ಚಿಕಿತ್ಸೆಗೆ ಉಪಯುಕ್ತ ಉಲ್ಲೇಖವಾಗಿದೆ, ಮತ್ತು ನಾನು ಅನುಭವಿಸುವ ರೋಗದಿಂದ ವಿಮುಕ್ತಿ ಅಥವಾ ಗುಣಮುಖಗೊಳ್ಳುವಲ್ಲಿ ನನಗೆ ಪ್ರಯೋಜನವಾಗಬಹುದು.

ಡಾಕ್ಟರ್ ನನಗೆ ಇದನ್ನು ಕೂಡಾ ತಿಳಿಸಿದ್ದಾರೆ ನನ್ನಿಂದ ನೀಡಿದ ಮಾಹಿತಿ, ಮಾಡಿದ ಪರಿಶೀಲನೆಗಳು / ಪೋರ್ಟೋಗ್ರಾಫ್‌ಗಳು / ವೀಡಿಯೋ ಗ್ರಾಫ್‌ಗಳು ನನ್ನ ಮೇಲೆ ತೆಗೆದುಕೊಳ್ಳಲಾಗುವ ಅನ್ವೇಷಕರು ರಹಸ್ಯವಾಗಿ ಇಡುವರು ಮತ್ತು ನಾನು ಅಥವಾ ನನಗೆ ಕಾನೂನು ದೃಷ್ಟಿಯಲ್ಲಿ ಸಂಬಂಧಿತರಾ ಹೊರತುಪಡಿಸಿ ಇತರ ವ್ಯಕ್ತಿಯಿಂದ ಮೌಲ್ಯಮಾಪನ ಮಾಡಲಾಗುವುದಿಲ್ಲ. ಡಾಕ್ಟರ್ ನನಗೆ ತಿಳಿಸಿದ್ದಾರೆ ನನ್ನ

ಪಾಲೊಳ್ಳುವಿಕೆ ಶುದ್ಧವಾಗಿ ಸ್ವೇಚ್ಛಾಯಿತ, ನನ್ನಿಂದ ನೀಡಿದ ಮಾಹಿತಿಯ ಆಧಾರದ ಮೇಲೆ, ಚಿಕಿತ್ಸೆ / ಅಧ್ಯಯನದ ಸಂಬಂಧದಲ್ಲಿ ರೋಗನಿರ್ಧಾರ, ಚಿಕಿತ್ಸೆಯ ವಿಧಾನ, ಚಿಕಿತ್ಸೆಯ ಫಲಿತಾಂಶ ಅಥವಾ ಆ ಭವಿಷ್ಯದ ಪ್ರವೃತ್ತಿಗಳು ಬಗ್ಗೆ ಯಾವುದೇ ಸ್ಪಷ್ಟತೆ ಕೇಳಬಹುದು. ಅದೇ ಸಮಯದಲ್ಲಿ ನನಗೆ ತಿಳಿಸಲಾಗಿದೆ ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ಪಾಲೊಳ್ಳುವಿಕೆಯನ್ನು ನಿಲ್ಲಿಸಬಹುದು ನಾನು ಬಯಸಿದರೆ ಅಥವಾ ಅನ್ವೇಷಕರು ಅಧ್ಯಯನದಿಂದ ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನನ್ನನ್ನು ನಿಲ್ಲಿಸಬಹುದು.

ಪ್ರಬಂಧ ಅಥವಾ ಸಂಶೋಧನೆಯ ಸ್ವಭಾವ, ಮಾಡಿದ ರೋಗನಿರ್ಧಾರ ಮತ್ತು ಚಿಕಿತ್ಸೆಯ ವಿಧಾನವನ್ನು ಅರ್ಥಮಾಡಿಕೊಂಡು, ನಾನು ಕೆಳಗಿನ ಶ್ರೀ / ಶ್ರೀಮತಿ _____ ನನ್ನ ಪೂರ್ಣವಾದ ಪ್ರಜ್ಞೆಯ ಸ್ಥಿತಿಯಲ್ಲಿ ಹೇಳಿದ ಸಂಶೋಧನೆ / ಪ್ರಬಂಧದಲ್ಲಿ ಪಾಲೊಳ್ಳಲು ಒಪ್ಪುತ್ತೇನೆ.

ರೋಗಿಯ ಸಹಿ

ಡಾಕ್ಟರನ ಸಹಿ

ಸಾಕ್ಷಿಗಳು

1)

2)

PROFORMA:

A. Patient Details:

Name:

Age:

Sex:

Height:

Weight:

IP/OP number:

Diagnosis:

Surgical procedure:

Past history:

Group allotted by Randomization: Group A/Group B

B. General physical examination:

Pallor

Icterus

Cyanosis

Clubbing

Lymphadenopathy

Edema

C. Vital parameters:

Pulse

Blood pressure

Respiratory rate

Temperature

D.Systemic Examination:

- Gastrointestinal system:
- Cardiovascular system:
- Central Nervous system:
- Respiratory system:

E.Airway Assessment:

Mallampatti Grade

Mouth opening

Cervical Spine

Neck movements

F.

ASA (American society of Anaesthesiologist) grade:

Emergency: Y/N

G. Investigations:

- Hemoglobin:
- TLC:
- Platelet count:
- RBS:
- HIV\HBsAg\HCV

SGOT:

SGPT:

Albumin:

ALP:

Blood Urea:

- Creatinine:
- Urine Routine:

- Chest X-ray:

ECG:

INTRA OPERATIVE HAEMODYNAMIC PARAMETERS

Intraoperative parameters	Heart Rate (bpm)	MAP (mm Hg)	SBP (mm Hg)	DBP (mm Hg)
Baseline parameters (Time in minutes)				
5 minutes				
10 minutes				
15 minutes				
30 minutes				
60 minutes				
End of Surgery				

VAS SCORE EVALUATION POSTOPERATIVELY

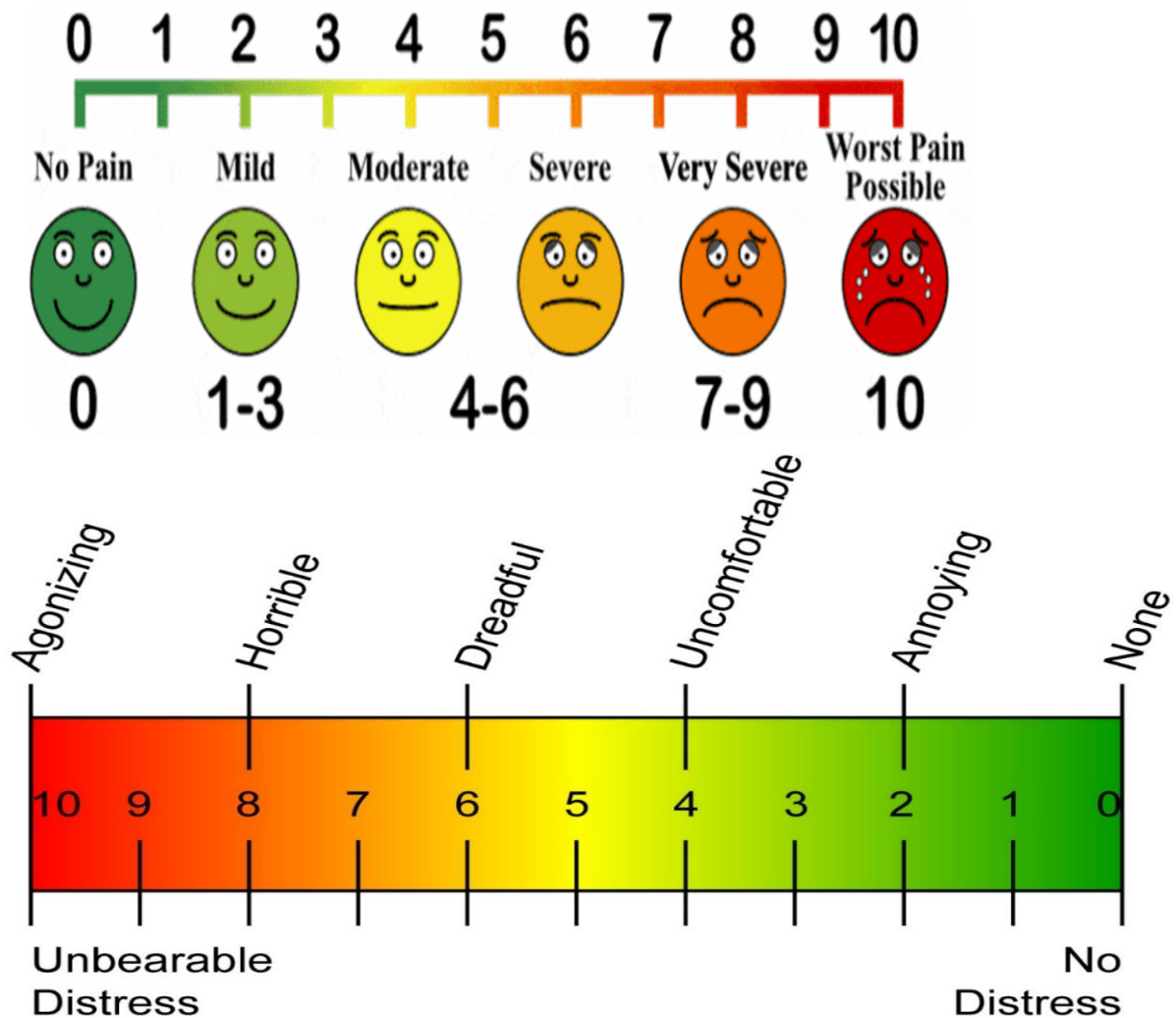
VARIABLES	VAS scoring (1-10)
VAS 0 Hr.	
VAS 2 Hr.	
VAS 4 Hr.	
VAS 6 Hr.	
VAS 12 Hr.	
VAS 24 Hr.	

✓ DURATION OF ANALGESIA:	
✓ TOTAL ANALGESIC CONSUMPTION POSTOPERATIVELY IN 24 HOURS:	
✓ ADVERSE EFFECTS, IF ANY EXPERENCED IN PERI OPERATIVE PERIOD.	

SIGNATURE OF GUIDE

SIGNATURE OF STUDENT

VAS SCORE ASSESSMENT POSTOPERATIVELY



Task _____

Date _____ Start _____ End _____

BIO-DATA

Guide Name: Dr. BASAVARAJ PATIL

Date of Birth: 22/07/1982

Education: MBBS, MD Anaesthesiology (MP SHAH Medical College, Jamnagar, Gujarat)

Designation: Associate Professor

Department of Anaesthesiology

Teaching: UG Teaching-14Years

PG Teaching-11Years

Address: Associate Professor

Department of Anaesthesiology, BLDE (Deemed to be University), Shri B.M. Patil Medical College and Research Centre, Vijayapura-586103, Karnataka

Contact no: 7829655342

INVESTIGATOR:

Name: Dr. THASKIN

Qualification: MBBS (2010-2016), MES Medical College, Kerala

Address: Shri B.M Patil Medical College

Hospital and Research Centre, Vijayapura-586103, Karnataka

Contact no: 7034467286.



BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle-2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 958/2023-24

10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology**, scrutinized the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "OPIOID- FREE VERSUS OPIOID BASED ANAESTHESIA FOR LAPAROSCOPIC CHOLECYSTECTOMY-A RANDOMISED CLINICAL TRIAL".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.THASKIN

NAME OF THE GUIDE: DR.BASAVARAJ PATIL, ASSOCIATE PROFESSOR, DEPT. OF ANAESTHESIOLOGY.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA

Chairman,


Dr. Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee

S.NO.	PT. NAME	AGE (Y)	SEX	WT. (Kg)	ASA	INTRAOPERATIVE HAEMODYNAMIC PARAMETERS						POSTOPERATIVE VAS SCORE EVALUATION						DURATION OF ANALGESIA		TOTAL ANALGESIC CONSUMPTION IN 24 HRS				POST OP ADJ EFFECT
						SYS BP (mmHg)	DIAS BP (mmHg)	HR (bpm)	SPO2 (%)	MAP (mm Hg)	VAS 0 HR	VAS 2 HR	VAS 4 HR	VAS 6 HR	VAS 12 HR	VAS 24 HR	(Hr)		No dose	1 dose of Pmol	2 doses of Pmol	1dose pmol+ tramadol	NIL	
1	Bouramma	37 F		60	ASA-I	133.37	68.06	68.89	100	93	1	2	2	2	4	2	12	--	√	--	--	--	NIL	
2	vetabhai pujari	65 F		65	ASA-II	120.69	67.95	76.16	100	94	1	1	3	3	4	2	12	--	√	--	--	--	NIL	
3	Radhabai	60 F		45	ASA-I	128.36	67.52	73.54	100	89.83	0	2	2	3	3	2	24	√		--	--	--	NIL	
4	Ningania	69 M		88	ASA-II	117.73	81.56	77.87	100	85.53	1	2	4	2	2	2	4	--	√	--	--	--	NIL	
5	Prabhusonda	65 M		85	ASA-II	130.04	80.09	73.63	100	87.8	0	2	2	3	2	3	24	√		--	--	--	NIL	
6	Sharanbai	60 F		70	ASA-II	122.79	79.35	67.36	100	93.62	0	2	3	5	3	2	6	--	√	--	--	--	NIL	
7	Parvati	53 F		68	ASA-I	132.69	78.27	80.01	100	96.74	1	2	2	2	4	2	12	--	√	--	--	--	NIL	
8	Siddavia	60 F		84	ASA-I	121.16	83.18	75.2	100	93.83	0	2	4	3	2	2	4	--	√	--	--	--	NIL	
9	Laxmibai	62 F		88	ASA-II	117.28	71.7	82.8	100	96.41	2	2	3	3	4	3	12	--	√	--	--	--	NIL	
10	Shobha	57 F		65	ASA-I	133.17	71.61	71.81	100	95.84	0	1	2	2	2	2	24	√		--	--	--	NIL	
11	Bhagavathi	52 F		60	ASA-I	116.35	87.73	81.42	100	86.89	2	2	5	3	3	2	4		√	--	--	--	NIL	
12	Sujata	35 F		60	ASA-I	121.81	84.37	78.53	100	92.13	1	2	3	2	2	2	24	√		--	--	--	NIL	
13	Hanamma	40 F		65	ASA-I	119.72	87.5	71.88	100	97.27	0	2	3	4	2	2	6		√	--	--	--	NIL	
14	Pundalik	43 M		88	ASA-I	122.43	67.26	84.17	100	96.85	2	2	2	3	2	2	24	√		--	--	--	NIL	
15	Vilas	29 M		78	ASA-I	116.78	75.7	79.23	100	98.24	0	2	3	4	2	2	6		√	--	--	--	NIL	
16	Shantabai	45 F		76	ASA-I	122.96	77.29	68.82	100	85.65	1	2	3	3	4	2	12		√	--	--	--	NIL	
17	Shantabai	64 F		66	ASA-I	115.53	71.89	67.68	100	89.39	0	1	3	4	3	3	6		√	--	--	--	NIL	
18	Radhabai	67 F		55	ASA-II	123.32	65.59	76.3	97	92.51	1	2	2	3	3	2	24	√		--	--	--	NIL	
19	Roopa	24 F		56	ASA-I	126.37	73.71	81.64	100	86.44	2	2	3	4	2	2	6	--	√	--	--	--	NIL	
20	Anasoda	45 M		76	ASA-I	126.36	83.28	71.35	100	84.83	1	3	2	4	3	1	6	--	√	--	--	--	NIL	
21	Amira	22 F		54	ASA-I	120.66	76.02	83.16	100	91.26	0	2	2	3	4	3	12	--	√	--	--	--	NIL	
22	Kaveri	26 F		50	ASA-I	115.86	84.21	68.65	100	97.64	1	2	2	3	2	3	24	√	--	--	--	--	NIL	
23	Rakshita	19 F		48	ASA-I	132.04	70.39	82.1	100	90.9	0	2	4	3	4	2	4	--	--	√		--	NIL	
24	Wheeda	48 F		78	ASA-I	115.01	92.63	81.16	100	94.76	2	2	3	4	3	1	6	--	√	--	--	--	NIL	
25	Venkappa	56 M		88	ASA-II	123.44	71.8	70.45	99	90.94	0	2	4	2	2	2	4	--	√	--	--	--	NIL	
26	Komal	22 F		65	ASA-I	129.29	73.39	74.02	100	91.2	0	3	3	5	3	2	6	--	√	--	--	--	NIL	
27	Champalal	60 M		77	ASA-I	125.98	82.06	72.05	100	89.01	2	2	3	4	3	3	6	--	√	--	--	--	NIL	
28	Fatima	34 F		76	ASA-I	123.97	71.52	77.37	100	92.02	1	2	2	4	3	2	6	--	√	--	--	--	NIL	
29	Meenalshi	30 F		70	ASA-I	132.77	61.33	66.56	100	96.7	2	2	3	3	4	2	12	--	√	--	--	--	NIL	
30	Arjun	38 M		80	ASA-I	122.35	80.25	72.11	100	89	0	3	3	5	4	2	6	--	--	√		--	NIL	
31	Shankarrao	69 M		88	ASA-I	119.36	74.5	71.1	100	85.14	2	3	3	4	2	2	6	--	√	--	--	--	NIL	
32	Chandralala	40 F		56	ASA-I	131.85	60.87	68.72	100	94.28	0	2	3	4	3	3	6	--	√	--	--	--	NIL	
33	Nisha	31 F		47	ASA-I	119.74	77.9	67.26	100	92.45	2	2	3	3	4	2	12	--	√	--	--	--	NIL	
34	Chandralala	44 F		58	ASA-II	122.8	73.53	73.6	100	84.53	2	3	3	3	2	2	24	√	--	--	--	--	NIL	

THASKIN

OPIOID-FREE VERSUS OPIOID BASED ANAESTHESIA FOR
LAPAROSCOPIC CHOLECYSTECTOMY- A RANDOMIZED CLINI...

 BLDE University

Document Details

Submission ID
trn:oid:::3618:88385986

Submission Date
Mar 28, 2025, 4:59 PM GMT+5:30

Download Date
Mar 28, 2025, 5:01 PM GMT+5:30

File Name
Dr Thaskin.docx

File Size
1.4 MB

57 Pages

8,862 Words

52,985 Characters

9% Overall Similarity

The combined total of all matches, including overlapping sources, for each database.

Filtered from the Report

- ▶ Bibliography
- ▶ Quoted Text
- ▶ Small Matches (less than 10 words)

Exclusions

- ▶ 2 Excluded Websites

Match Groups

-  45 Not Cited or Quoted 7%
Matches with neither in-text citation nor quotation marks
-  9 Missing Quotations 2%
Matches that are still very similar to source material
-  0 Missing Citation 0%
Matches that have quotation marks, but no in-text citation
-  0 Cited and Quoted 0%
Matches with in-text citation present, but no quotation marks

Top Sources

- 8%  Internet sources
- 6%  Publications
- 0%  Submitted works (Student Papers)

Integrity Flags

0 Integrity Flags for Review

No suspicious text manipulations found.

Our system's algorithms look deeply at a document for any inconsistencies that would set it apart from a normal submission. If we notice something strange, we flag it for you to review.

A flag is not necessarily an indicator of a problem. However, we'd recommend you focus your attention there for further review.

