A COMPARATIVE STUDY OF POSTOPERATIVE ANALGESIC EFFICACY OF LOW DOSE INTRAVENOUS DEXMEDETOMIDINE AND INTRAPERITONEAL DEXMEDETOMIDINE WITH BUPIVACAINE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

By

DR. LAKSHMI SOWJANYA

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Dr. VIJAYA. V. KATTI

PROFESSOR

DEPARTMENT OF ANESTHESIOLOGY

B.L.D.E.(D.U). SHRI B.M.PATIL MEDICAL COLLEGE

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ABSTRACT

Background and aims:

In today's medical practice, the intraperitoneal (IP) delivery of local anaesthetics is a routine procedure. Dexmedetomidine (1 mcg/kg) and bupivacaine were recently studied by certain authors for its prospective use as a postoperative analgesic in patients having laparoscopic cholecystectomy and colorectal cancer surgery. These trials came to the conclusion that dexmedetomidine, when used as an adjuvant, offers greater postoperative analgesia when combined with bupivacaine at a concentration of 0.25%. The dexmedetomidine was administered intraperitoneally at a dose of 1 mcg/kg.

The study aims to determine the postoperative analgesic efficacy of low-dose 0.5 μg/kg dexmedetomidine via Intravenous (IV) and Intraperitoneal (IP) route in laparoscopic cholecystectomy.

Methods

This study was conducted at the Department of Anaesthesiology, B.L.D. E (DEEMED TO BE UNIVERSITY) Shri B.M. Patil Medical College, Hospital, and Research Centre, VIJAYAPURA. The study was conducted from December 2020 to September 2022.

Study design

Randomised controlled study.

Study Period

One and a half year.

Sample size

Ninety-nine patients of both genders were randomly divided into three groups of thirty-two each namely Group IV, Group IP, Control group.

Statistical tests such as CHI SQUARE and the KRUSKAL WALI test were utilized in the analysis of the results.

Results

The IV group had prolonged time for rescue (in minutes) analgesia, with 180.91±41.617, followed by the IP group with 106.06±8.269, and then the Control group with 55.00±6.960. The total amount of diclofenac that was consumed in a period of 24 hours (measured in milligrams) was discovered to be higher in the Control group [241.82±30.767] when compared to the IV group [119.24±40.372] and the IP group [115.30±30.896]. It was discovered that these differences were statistically significant (p=0.0001) for both groups.

Conclusion

In patients undergoing laparoscopic cholecystectomy, this study places an emphasis on the use of dexmedetomidine coupled with bupivacaine through the intraperitoneal (IP) route as an effective post-surgical analgesic regimen.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

ABBREVIATIONS

ASA -American Society of Anaesthesiologists

Bpm -Beats per minute

CO -Cardiac Output

CO2- Carbon Dioxide

DBP -Diastolic Blood Pressure

SBP- Diastolic Blood Pressure

Dex -Dexmedetomidine

DS -Diclofenac Sodium

ECG- Electrocardiography

ETCO2- End Tidal Carbon Dioxide

Hg -Mercury

HR -Heart Rate

i.v. -Intravenous

IP -intra peritoneal

kg -kilogram

MAC -Minimum Alveolar Concentration

mcg -microgram

Min -minute

ml -millilitre

N2O- Nitrous Oxide

ng -Nanogram

NIBP- Non-Invasive Blood Pressure

O2 -Oxygen

PACU -Post Anaesthesia Care Unit

PNP -Pneumoperitoneum

POD -Post Operative Day

PONV- Post operative Nausea and Vomiting

SPO2 -Arterial Oxygen Saturation

VAS-visual analogue scale pain score.

INTRODUCTION

A COMPARATIVE STUDY OF POSTOPERATIVE ANALGESIC EFFICACY OF LOW DOSE INTRAVENOUS DEXMEDETOMIDINE AND INTRAPERITONEAL DEXMEDETOMIDINE WITH BUPIVACAINE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

INTRODUCTION

Dexmedetomidine has gained popularity in the recent era owing to its multiple advantages both in the field of anaesthesia as well as in critical care. In addition to its opioid-sparing, analgesic, sedative, amnestic and sympatholytic characteristics, dexmedetomidine is a highly selective alpha-2 receptor agonist. The majority of the studies that looked at the use of dexmedetomidine via intra venous route (IV) in laparoscopic cholecystectomy employed a dose of 1 mcg/kg followed by an infusion in a dose ranging from 0.2-0.7 mcg/kg/hour. This was done in order to maintain an adequate level of anaesthesia during the procedure. It is known that this dose can elicit a biphasic response, which first manifests as reflex bradycardia, then hypotension, and finally as hypertension. It is possible to avoid this by forgoing the bolus dose. [2] Recent studies have also looked into the use of dexmedetomidine infusions in

low dose in laparoscopic cholecystectomy, with dosages ranging between 0.2 and 0.4 mcg/kg/hour. [3] In these investigations, the reduction of postoperative pain was considered as a secondary objective to the primary focus, which was the dampening of the hemodynamic response. In today's medical practice, the intraperitoneal (IP) delivery of local anaesthetics is a routine procedure. Dexmedetomidine (1 mcg/kg) and bupivacaine were recently studied by certain authors for its prospective use as a postoperative analgesic in patients having laparoscopic cholecystectomy and colorectal cancer surgery. These trials came to the conclusion that dexmedetomidine, when used as an adjuvant, offers greater postoperative analgesia when combined with bupivacaine at a concentration of 0.25%. The dexmedetomidine was administered intraperitoneally at a dose of 1 mcg/kg. Patients who were undergoing laparoscopic cholecystectomy were included in this study, and they were given either a low dose of intravenous (IV) dexmedetomidine (0.5 mcg/kg) as a bolus and intraperitoneal (IP) bupivacaine, or an intraperitoneal (IP) dexmedetomidine (0.5 mcg/kg) and intraperitoneal (IP) bupivacaine.

The most common causes of visceral pain are inflammation and dissection in the area surrounding the gall bladder bed and capnoperitoneum. Shoulder pain is most commonly caused by phrenic nerve neuropraxia as well as increased intra-abdominal pressure, which can lead to straining of the subdiaphragmatic fibres. Intraperitoneal (IP) instillation of local anaesthetics with adjuvants is one

of the many multimodal approaches for post-operative analgesia; yet, it continues to be one of the most preferred methods among anaesthesiologists. Clonidine and dexmedetomidine have each been tested independently alongside a placebo in an effort to produce analgesia for a longer amount of time following surgical procedures[4]. In a recent editorial, the off-label usage of dexmedetomidine in a variety of therapeutic settings and by multiple routes are broken out in detail. However, they have not come across any study that directly compares the effects of clonidine with those of dexmedetomidine in conjunction with bupivacaine for protracted post-operative analgesia in laparoscopic cholecystectomy. Primary and secondary goals have been outlined as the objectives for this project. The magnitude of pain as measured by a Numerical Rating Scale (NRS) score was the primary goal of their research. Some of the secondary goals included the amount of time that passed before the first request for analgesia was made, the need for analgesics within the first 24 hours after surgery, the incidence of shoulder pain among the study groups, and the occurrence of adverse effects over the course of the study.

AIMS AND OBJECTIVES

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AIM:

The study aims to determine the postoperative analgesic efficacy of low-dose 0.5 μg/kg dexmedetomidine via intravenous (IV) and intraperitoneal (IP) route in laparoscopic cholecystectomy.

PRIMARY OBJECTIVES:

- To compare the time of rescue analgesia among 3 groups.
- To compare total consumption of diclofenac in 24 hours.
- To compare visual analogue scale (VAS) pain score.

SECONDARY OBJECTIVES:

- To evaluate the effect of study drugs on intra-operative hemodynamic response.
- The side effects of study drugs.
- Complications if any.

BASIC ANATOMY

Before performing any kind of surgery, you need to have a solid grasp of the necessary anatomy. During the laparoscopic surgery, the area around the gallbladder, and specifically the Calot's triangle, is exposed to a different anatomical view than it is during the open procedure.[5,6]

BASIC ANATOMY:

GALLBLADDER

The gallbladder is an organ that looks like a pear and is situated in a fossa directly below the liver. Both its form and its volume are subjected to change. In most cases, its location in relation to the liver is at the intersection of segments 4 and 5 (also known as main plane or Cantlie's line). For instance, the gallbladder that is referred to as "intrahepatic" may be partially or entirely lodged within the parenchyma of the liver. This might make dissection more challenging and raise the danger of sustaining a harm to the liver during the operation.

The gallbladder is composed of three distinct parts: the fundus, the body and the neck or infundibulum. Each of these parts has a specific function. The so-called "Hartmann's pouch," which is an outpouching of the wall in the region of the neck, is more frequently recognized as a result of disease in the form of dilatation or the presence of stones. [7] There is a wide range of sizes for this

pouch, but if it is particularly large, it can obstruct both the Calot's triangle and the cystic duct . This may be the result of a straightforward expansion of the cystic or bile ducts or an adhesion to either of those structures. Because of this, a small cystic duct has the potential to become entirely buried, and the traction on gallbladder has the potential to cause the bile duct to look like the cystic duct. The condition known as "Mirizzi's syndrome" is an exacerbated variation of the same process known as "Hartmann's pouch adhesion syndrome," in which a huge stone becomes stuck in or erodes into the bile duct. This has the potential to result in significant complications during a cholecystectomy.

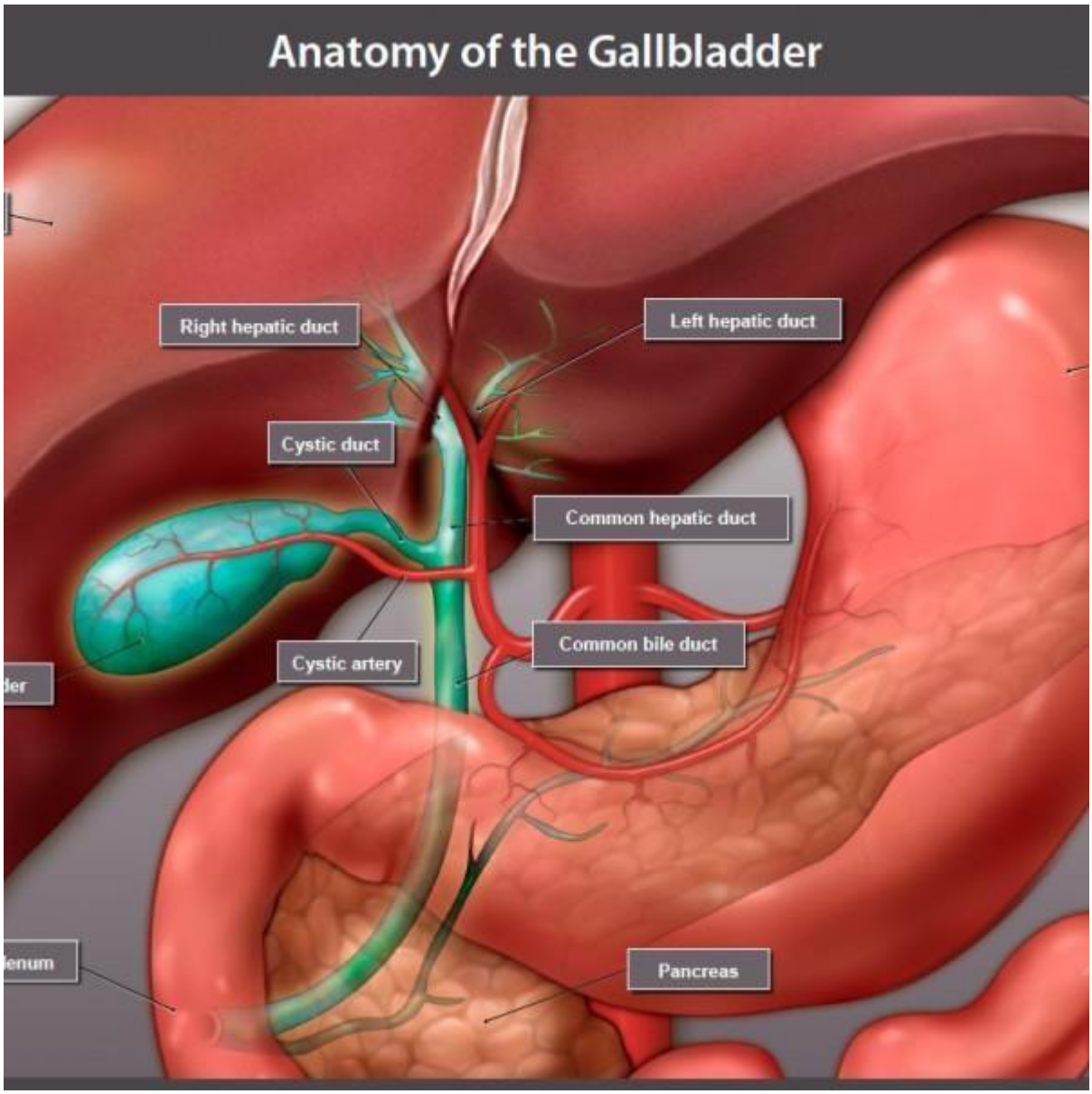


FIGURE 1 ANATOMY OF GALLBLADER

CYSTIC DUCT

During a typical cholecystectomy, the cystic duct is one of the important structures that needs to be located and separated in order to successfully remove the gallbladder. This structure connects the gallbladder to the bile duct. The course that the cystic duct takes might either be completely straight or somewhat convoluted. Its length can range anywhere from 2 centimetres to 4 centimetres, although this is its average range. About twenty percent of cystic ducts are shorter than two centimetres in length. As a direct consequence of this, there might not be much place for clips or ligatures. It is exceedingly unusual for there to be no cystic duct at all, and if one does not appear, the cystic duct is almost certainly concealed. In most cases, the width of the cystic duct is between 2 and 3 millimetres. When there is pathology, the space can become more expansive (stones or passed stones).

The cystic duct makes its connection to the gallbladder at the neck, which is a region that might have an acute angle. There is also the option of an abrupt or smooth tapering joining mode.

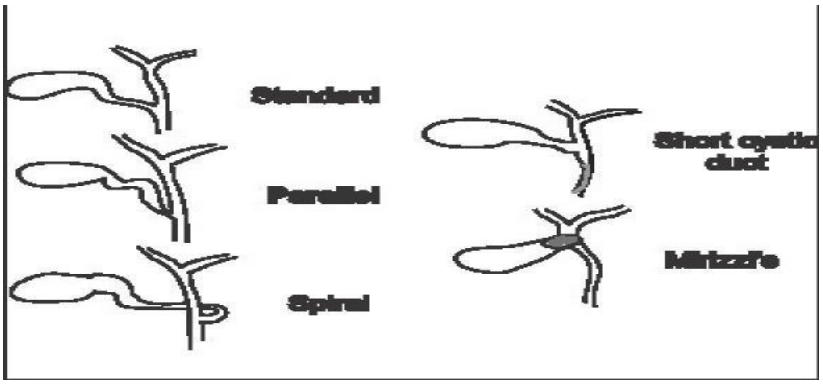


Figure 2 - Modes of union of cystic duct with bile duct

Cystic artery and right hepatic artery

Calot's triangle is the place where the right hepatic artery (RHA) gives off its first branch, which is known as the cystic artery. It can be of varying lengths and can get access to the gallbladder via either the neck or the torso. Both the path taken by the cystic artery and its overall length in the Calot's triangle are variable. In most cases, it gives rise to two branches: an anterior branch, also known as a superficial branch, and a posterior branch, often known as a deep branch.

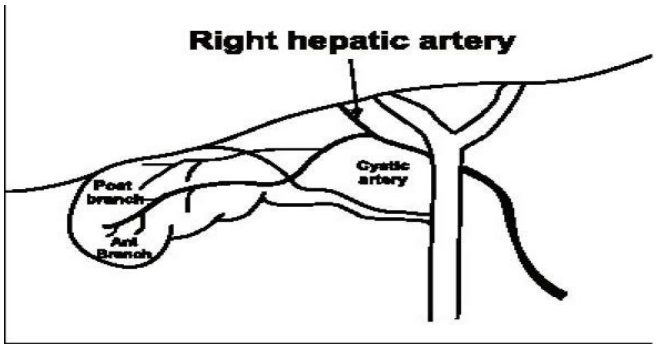


Figure 3- cystic artery & its branches

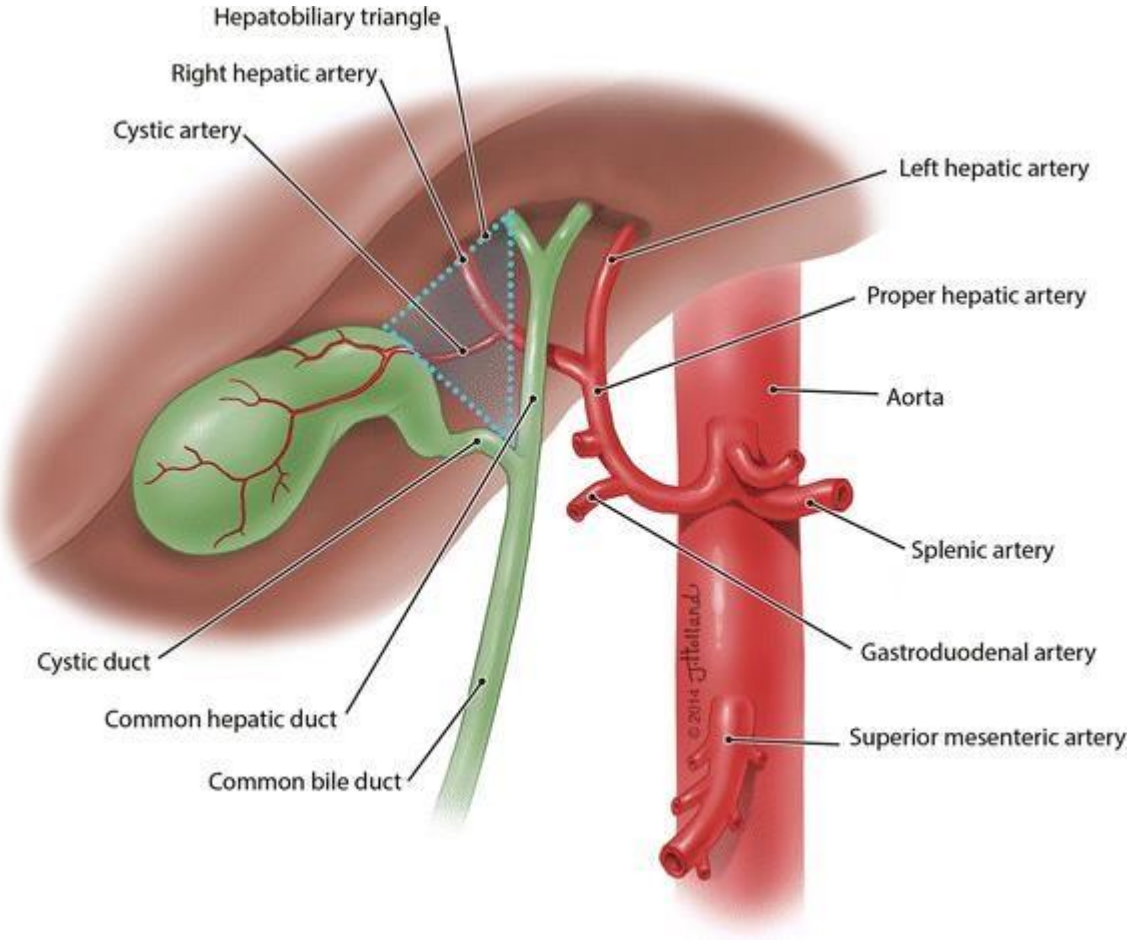


Figure 4-ANATOMY OF CYSTIC ARTERY IN RELATION TO CALOTS TRIANGLE

CALOT'S TRIANGLE:

The bile duct, the cystic duct, and the cystic artery are the three connections that make up Calot's triangle. The upper boundary is formed by the inferior surface of liver, while other two limits are formed by the cystic duct and the portal vein. Components that are shared include the right heart artery (RHA), the cystic artery, the cystic lymph node (of Lund), connective tissue, and lymphatics. It is possible for it to possess additional hepatic ducts and arteries on rare occasions. During a cholecystectomy, this triangular region will be dissected in order to locate the cystic artery and the cystic duct, both of which will then be ligated and divided. The left (or medial) edge of the triangle produced by the bile duct is the most critical structure to protect, and it should be the first priority.[8]

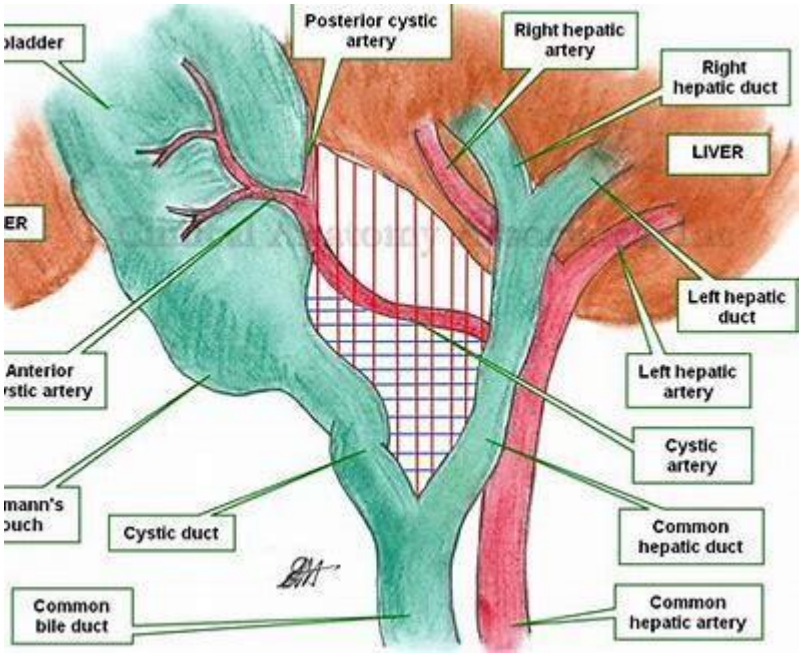


Figure 5- Calot's triangle

INDICATIONS:

- An acute or chronic case of cholecystitis
- Symptomatic cholelithiasis
- Biliary dyskinesia (either hypofunction or hyperfunction)
- Acalculous cholecystitis
- Gallstone pancreatitis
- Gallbladder tumors or polyps.

CONTRAINDICATIONS:

Pneumoperitoneum or general anaesthesia intolerance;

Coagulopathy that cannot be corrected;

Metastatic disease

Although cancer of the gallbladder used to be an indicator where a laparoscopic cholecystectomy should not be performed, the most recent research supports the use of laparoscopic intervention.

EQUIPMENT

- Two laparoscopic monitors.
- One laparoscope with a camera wire and a light source measuring five to ten millimeters and thirty to zero degrees.

- A supply of carbon dioxide and tubing for insufflation.
- Trocars ranging in size from 5 mm to 12 mm (average three 5 mm working trocars one 10 mm to 12 mm trocar).
- Instruments used during laparoscopic surgery include atraumatic graspers, a Maryland grasper, a clip applier, electrocautery (such as hook or spatula), and a retrieval bag.
- Scalpel with a blade measuring 11/15, forceps , a needle driver, and absorbable sutures
- Significant open space, with the possibility of conversion

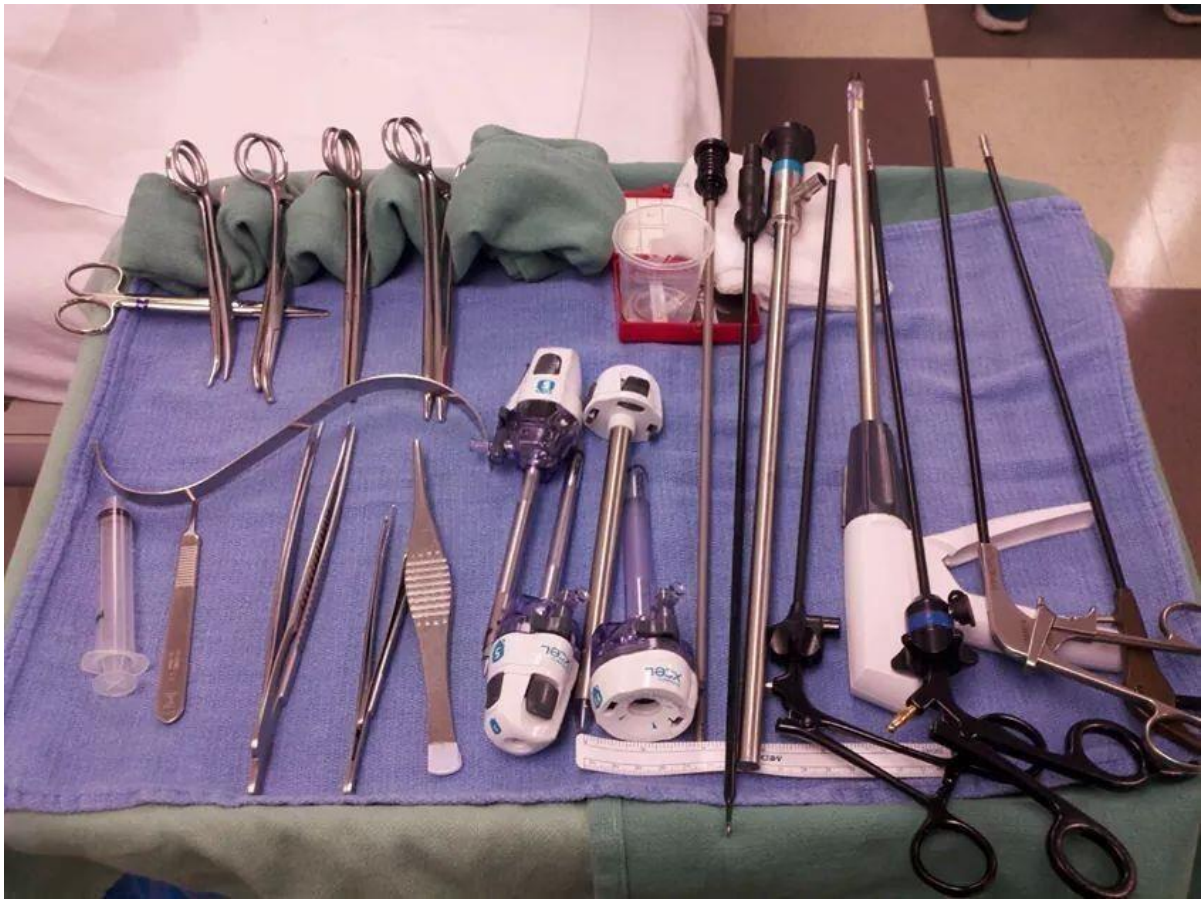


Figure 6-*INSTRUMENTS USED IN LAPAROSCOPIC CHOLECYSTECTOMY*

PERSONNEL:

- The operating surgeon, who will be on the patient's left.
- The surgical assistant, who will be on the patient's right.
- The scrub tech or nurse, who will be on the patient's left.

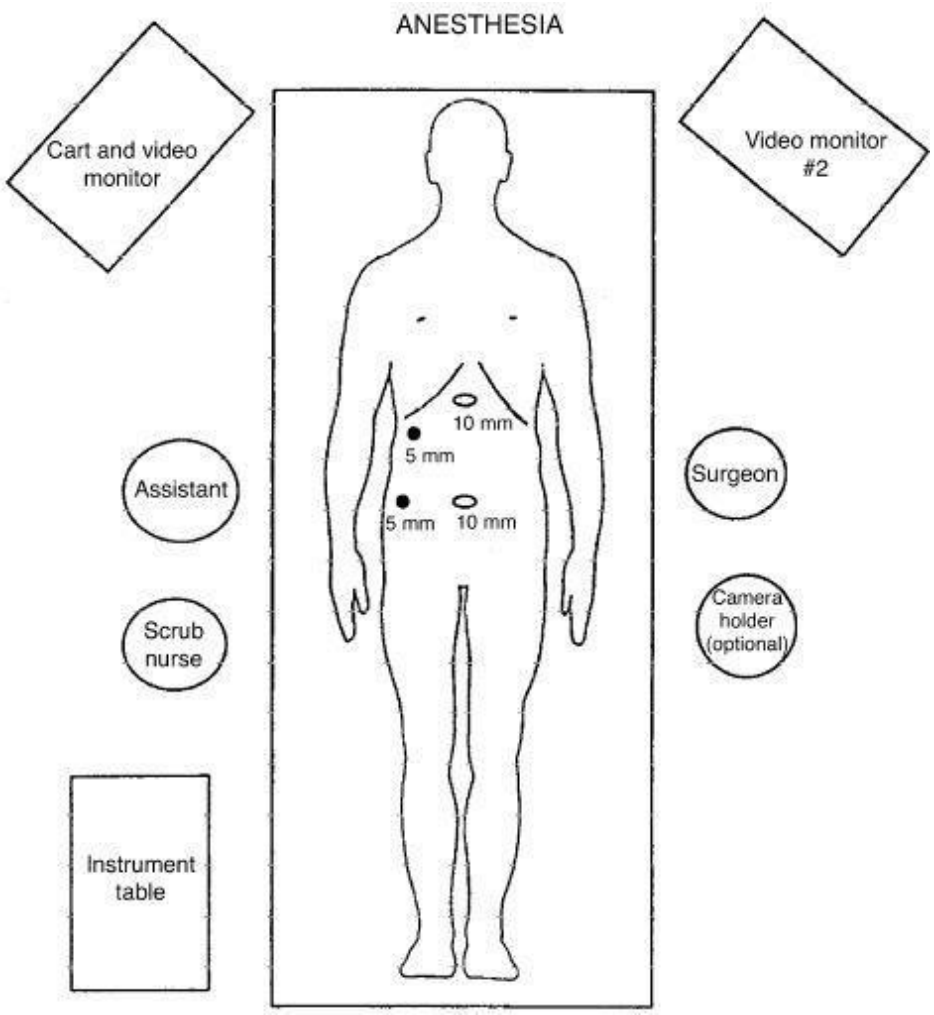


Figure 7-*OPERATING ROOM SETUP FOR LC*

PREPARATION:

- Prior to surgery, the patient needs to have their medical condition improved.
- Ideally, antibiotics should be given preoperatively within thirty minutes of when the incision was made.

An aseptic surgical area is formed slightly above bilateral costal borders, extending to the pubic tubercle, and laterally extending to the right and left sides. If it turns out to be essential, the sterile operating field should be able to accommodate an open procedure.

TECHNIQUE:

After the patient has been intubated and the anaesthesia has been induced, the laparoscopic cholecystectomy can proceed.

In the beginning, carbon dioxide is insufflated into the abdomen to a pressure of 15 mmHg. After that, four very small incisions are made in the patient's abdomen for the installation of the trocars (supra umbilical x1, sub xiphoid x1, and right sub costal x2). Laparoscopic surgery involves the use of a camera (laparoscope) and lengthy instruments to retract the gallbladder over

the liver. Because of this, the region that has been hypothesized to be a hepato cystic triangle can now be seen. A thorough dissection is carried out so that a critical perspective on safety can be attained. This view is defined as

(1) the removal of fibrous fatty tissue from the hepatocystic triangle,

(2) the presence of only two tubular structures entering the gallbladder's base, and

3)the separation of the gallbladder's lower third from the liver to reveal the cystic plate.

After obtaining this image, the operating surgeon will be able to proceed with the procedure knowing for certain that cystic duct, cystic artery have been separated. Both structures have been trimmed and carefully severed in between. After that, either electrocautery or a harmonic scalpel is utilized in order to totally remove the gallbladder from liver bed. Hemostasis should be established after allowing abdomen to gradually deflate to 8 mmHg over the course of two minutes. Utilizing this strategy helps ensure that any potential venous bleeding brought on by increased intra-abdominal pressure is not missed (15 mmHg). When gallbladder is extracted from belly, specimen pouch is utilized during the procedure. Under direct visualization, each trocar needs to be extracted before proceeding. It is recommended to perform fascial closure on

trocar sites that are larger than 5 millimetres in size in order to prevent incisional hernias in the postoperative term.

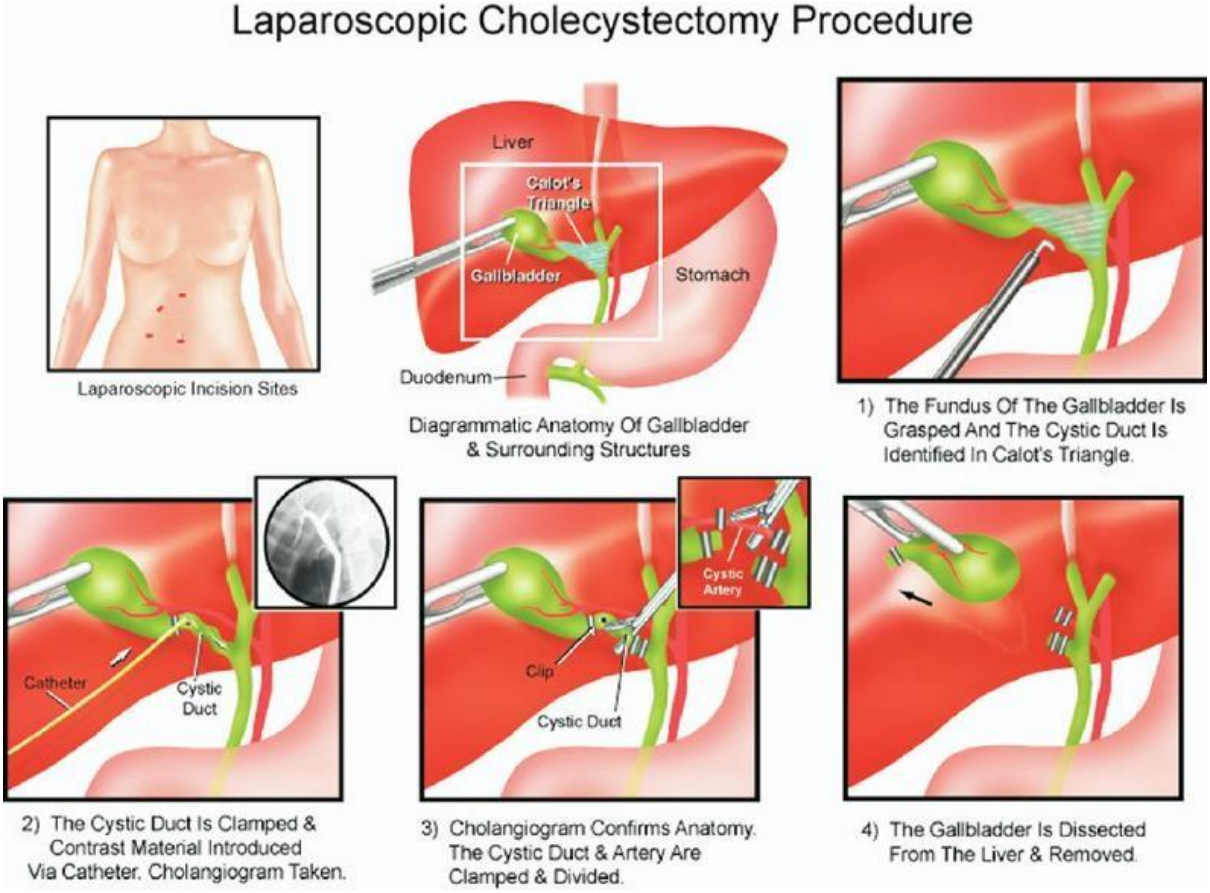


Figure 8-Steps in laparoscopic cholecystectomy

COMPLICATIONS:

Bleeding, infection, and structural damage are all examples of common consequences.The liver is a highly vascular organ, hence bleeding is a typical complication that can occur after liver surgery.[11,12]

In addition to, or instead of, the symptoms of direct hyperbilirubinemia, bile leaks can also induce a vague stomach ache and fever. This can make the process more difficult. Patients who present with complications often do so within the first week after surgery. The first step in treatment should involve either a diagnostic ultrasound or a CT scan of the abdominal region. In cases of retained choledocholithiasis, biliary sphincterotomy is the treatment that is necessary. When treating significant leaks, sphincterotomy and stenting are the procedures of choice. It is recommended to perform a HIDA scan to evaluate bile leakage whenever there is uncertainty regarding the findings of a CT or ultrasonography.

POST OPERATIVE PAIN

POST OPERATIVE PAIN

Pain is defined as "the unpleasant sensory and emotional experience associated with an actual or potential tissue damage or described in terms of such damage" according to the Taxonomy Committee of the International Association for the Study of Pain (IASP), which is an organization dedicated to the study of pain.

Postoperative pain is considered to be sort of acute pain since it is caused by surgical trauma, which in turn triggers an inflammatory response and the firing off of afferent neuronal barrage.

The various causes of pain:

The noxious impulses are carried via a three-neuron circuit that runs from the periphery to the cerebral cortex and is responsible for the sensation of pain.

• First order neuron, which is found in the cell body of the dorsal root ganglia, is responsible for transmitting pain signals from distal receptor to spinal cord's dorsal horn.

•Thalamic 3rd-order neuron sends its fibres to post central gyrus.

• A 2nd order neuron in spinal cord's dorsal horn sends axons that cross the midline and ascend in the spinothalamic tract to the thalamus (via internal capsule).

Typical Processes Involved in Pain

Pain following surgery can be broken down into two categories: acute pain and chronic pain. Pain lasting for more than three months after an injury is regarded to be chronic pain. In contrast to chronic pain, which can lasts longer than seven days, acute pain usually appears after surgery. It's possible for cutaneous, deep somatic, or visceral tissues to be the source of both acute and chronic pain. There are two categories of acute pain:

1. **Superficial somatic pain**: This type of somatic pain originates from the skin, the subcutaneous tissue, or the mucous membrane. The pain is acute and pinpointed to a specific area.Intense somatic pain, which can originate in the muscles, tendons, joints, or bones. It is not as well localized and has a dull aching quality to it. The degree of localisation is influenced not only by the intensity but also the length of the pain.

2. **Visceral Pain**: This type of pain, which can be colicky, cramping, or squeezing in nature, is caused by a disease or an aberrant function of an internal organ or the covering that surrounds the organ. The pain is poorly localized, dull, and nonspecific. Patients who have had laparoscopic cholecystectomy have more than one mechanism at play when it comes to the production of nociception after the procedure There are several possible causes, such as trauma from abdominal incisions that destroy somatic free nerve endings, parietal peritoneal distention, disturbance of visceral nerve endings in the

gallbladder bed, discharge of endogenous pro - inflammatory molecules, discomfort of the phrenic nerve, irritation of the peritoneum brought on by blood, bile spillage, or carbon dioxide, and somatoform or psychogenic causes. The primary benefits of local instillation may be their rapid nociceptive suppression of free nerve endings injured in the gallbladder bed, their progressive peritoneal uptake into the systemic circulation, and their lack of systemic toxicities associated with direct systemic administration of NSAIDs. All these factors combine to produce the preference for local NSAID instillation over targeted systemic administration.

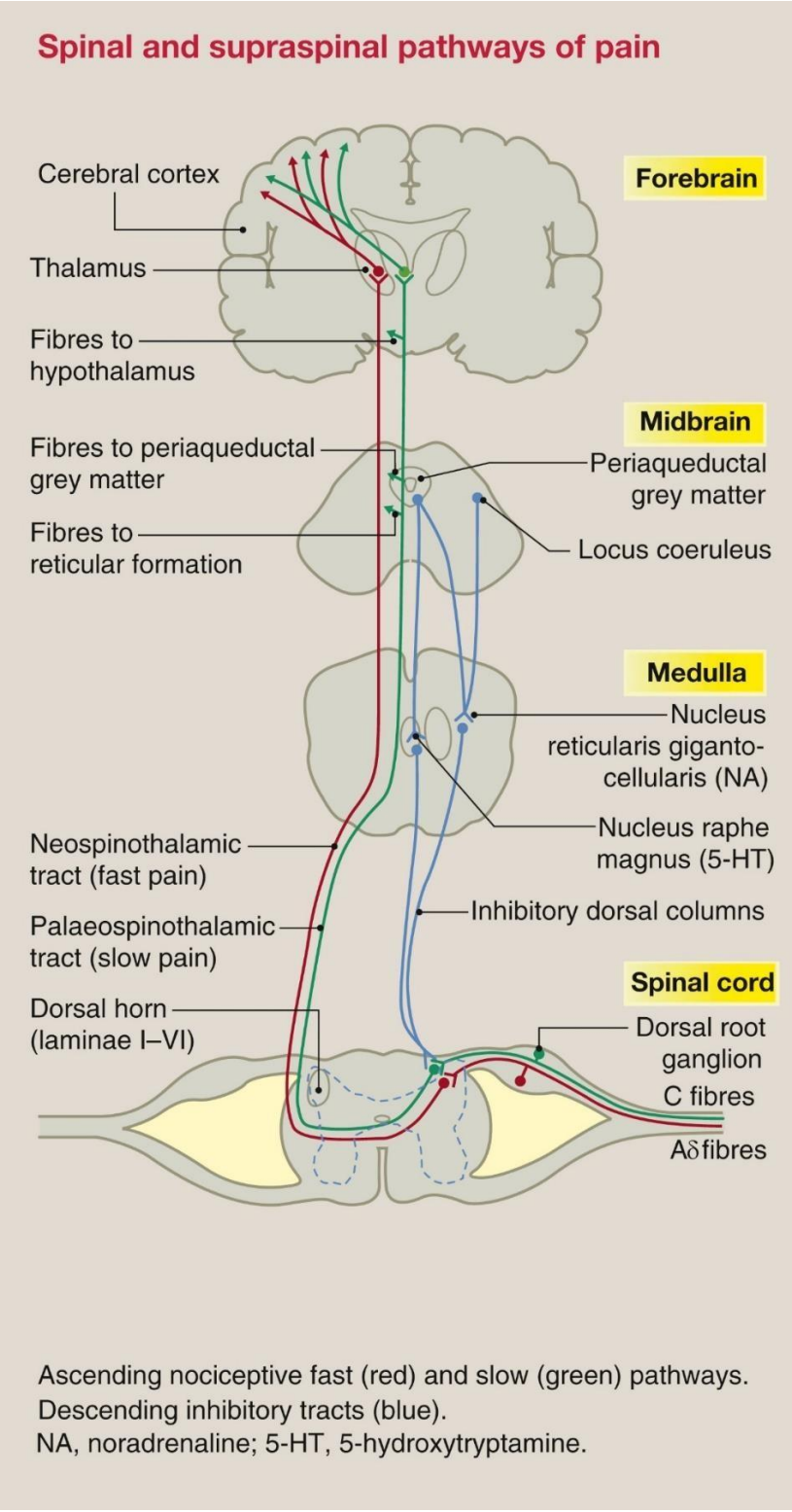


Figure 9 PAIN PATHWAYS

ASSESSMENT OF PAIN: It is an essential component for achieving adequate pain control after surgery. When attempting to measure pain, certain pain evaluation scales are utilized. The most helpful piece of information comes from the patient themselves. As a result, the level of pain should be evaluated to the greatest extent feasible by the patient, provided that the patient is able to articulate and describe what it is like to be in pain. There are a variety of scales that patients can use to evaluate themselves that are available.

VISUAL ANALOGUE SCALE (VAS): Since its introduction in 1966, the visual analogue scale (VAS) has become the tool of choice for evaluating pain. The research on pain makes use of a relatively straightforward scale. The patient evaluates their own level of discomfort on a line that is 10 centimetres long and has two anchor points: "no pain" and "worst pain imaginable." The location of the mark on the line provides a measurement of the amount of pain experienced by the patient.

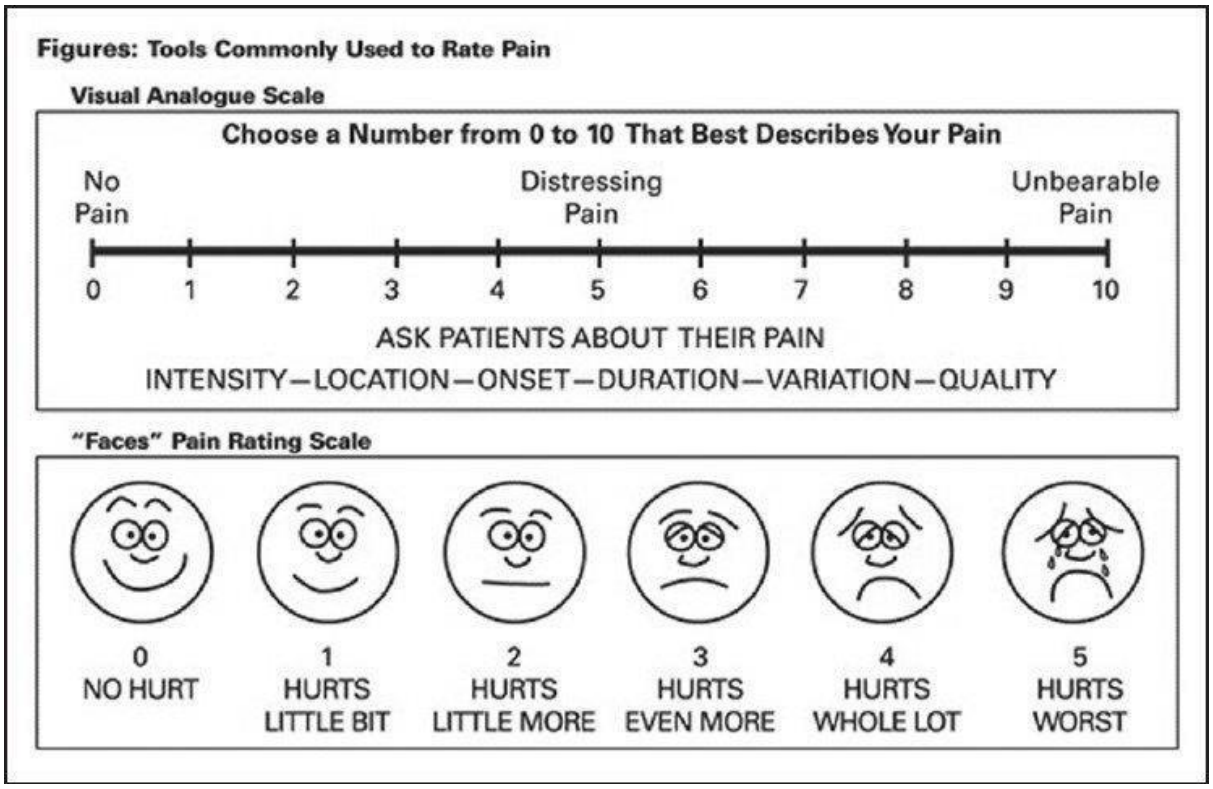


Figure 10 visual analogue scale

The Wong-Baker Pain Rating Scale and Visual Analogue Scale Facial expressions: A pictogram consisting of six faces, each displaying a distinct emotion, ranging from a cheerful smile to a crying one. This scale is appropriate for use with patients who have difficulty communicating, such as younger patients, patients who are elderly, patients who are disoriented, or patients who do not speak the local language.

Numerical rating scale (NRS): It is quite similar to the visual analogue scale, with the two anchors of "no pain" and "worst agony as from 0 to 10," making it an 11-point scale, and the patient is the one who rates their pain.

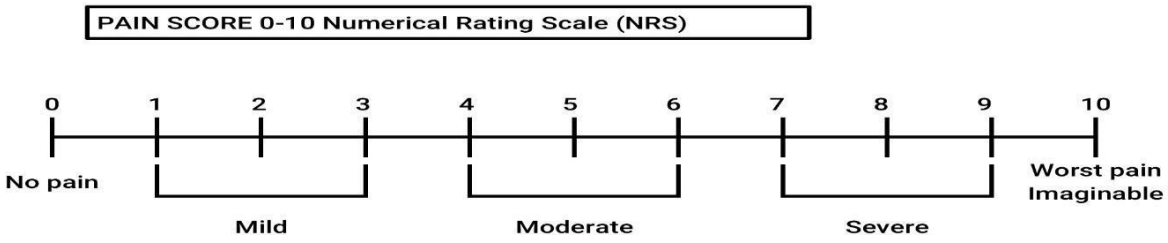


Figure 11 Numerical rating scale

Numerical Pain Scale Verbal rating scale, often known as the VRS: It includes the following categories: no pain, mild pain, moderate pain, and severe pain respectively. It is simple to use and can even be administered to patients with a mild cognitive impairment; nevertheless, it is insensitive to even subtle shifts in the level of pain. The preoperative personality assessment is also important in analyzing the patient's psychological background as well as his psychogenic responses to the surgery and the pain that comes after it. In clinical settings, the most common assessment instruments are the visual analogue scale (VAS), numerical rating scale (NRS), and visual analogue scale (VRS). The visual analogue scale (VAS) is more commonly employed in research settings.

BASIC PHARMACOLOGY

BASIC PHARMACOLOGY OF STUDY DRUGS

Dexmedetomidine

Dexmedetomidine is a sedative medication. It is also used to treat severe agitation caused by schizophrenia or bipolar I or II disorder. [1] [2]

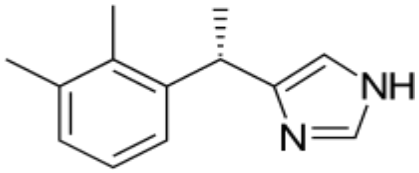


Figure 12 Dexmedetomidine

Formula C13H16N2

Molar mass 200.285 g·mol−1

Dexmedetomidine has an effect that reduces the amount of opioids that are required to achieve the same level of sedation as other sedatives. [13]

There is data to suggest that patients who experience delirium have a shorter time to extubation and fewer hours in which they are dependent on a ventilator. The potential of dexmedetomidine to lower the requirement for additional drugs (such as propofol, benzodiazepines, and opioids) to create a pleasant and compliant patient may be the cause of these reductions. This action has proven

to be extremely helpful in the treatment of elderly people after they have undergone heart surgery. [14] Infusions of dexmedetomidine at doses as high as 1.5 mcg/kg per hour have also become commonplace in the intensive care unit (ICU) as a treatment for inadequate sleep. The use of dexmedetomidine typically produces sleep quality that is comparable to that of stage 2 non-REM sleep, according to research, which lends credence to the practice. On the other hand, there is evidence that typical patterns of sleep are disrupted, and that subjects do not attain the restorative types of sleep known as rapid-eye-movement sleep or slow-wave sleep. In addition, there are not a lot of research that show how beneficial dexmedetomidine is in terms of clinical outcomes that are associated to better sleep.

The drug dexmedetomidine is frequently utilized in the field of anesthesia. Sedation during procedures of all different kinds can be accomplished with its aid. Additionally, it is routinely used to give sedative for patients who are awake while they are being intubated. During the administration of general anesthesia, dexmedetomidine is also administered intravenously as an adjuvant. There is evidence to suggest that dexmedetomidine lessens the need for opioids as well as postoperative pain and nausea. [15] This effect has also been shown when dexmedetomidine is utilized as a sedative in the course of treatments that are carried out while the patient is under the influence of spinal anesthesia. It has been suggested that dexmedetomidine could be used as an adjuvant in the

treatment of postoperative agitation, delirium, and cognitive dysfunction. There is evidence to suggest that emerging agitation in both toddlers and adults can be avoided altogether. [16] Additionally, dexmedetomidine has been utilized to lengthen the duration of analgesia following the administration of peripheral nerve blocks. Dexmedetomidine has been shown in studies to have the ability to extend the duration of a peripheral nerve block by approximately 3 hours. [17]

MECHANISM OF ACTION:

α2-AR agonists are molecules that, once bound to G-protein-coupled α2-AR, produce clinical effects. The clinical effects of each subtype of α2-AR (α 2A, α 2B, and α 2C) are distinct, as are their physiological roles and pharmacological activities. These receptor subtypes are present all over the nervous system, including the peripheral, autonomic, central nervous systems, as well as in important organs and blood arteries. They are also present in the brain and spinal cord. Dexmedetomidine is approximately eight to ten times less selective for α 2-AR than clonidine is. Although neither clonidine nor dexmedetomidine is entirely selective for either of the α 2-AR subtypes, dexmedetomidine appears to have a stronger affinity for α 2A-AR and α 2C-AR than clonidine does.

Both the sedative and analgesic effects are mediated via the locus ceruleus in the brain stem, whereas the spinal cord is responsible for the analgesic effect. Both of these areas work through the 2A-AR receptor. The most important effect that 2A-AR agonists have on the heart is a decrease in tachycardia

(caused by the blockage of the cardioaccelerator nerve) and an increase in bradycardia (caused by the 2A-AR) (through a vagomimetic action). In the peripheral vasculature, there is vasodilation that is mediated by sympatholysis as well as vasoconstriction that is mediated by smooth muscle cell receptors. [18] In spite of extensive research, the mechanism that underlies the anti-shivering and diuretic actions has not been conclusively demonstrated.

Other responses to receptor activation include a decrease in salivation, secretion, and bowel motility in the gastrointestinal tract; contraction of vascular and other smooth muscle; inhibition of renin release, increased glomerular filtration, and sodium and water secretion in the kidney; a decrease in intraocular pressure; and a decrease in insulin release from the pancreas. All of these responses take place in the kidney. [19] Because it combines all of these properties, dexmedetomidine is able to circumvent some of the adverse effects that are typically associated with multiagent therapy.

PHARMACOKINETICS

Absorption and distribution

When given as an intravenous infusion over the course of 24 hours in the recommended dose range of 0.2 to 0.7 g/kg/hr, the pharmacokinetics of dexmedetomidine are linear. With an elimination half-life of roughly two hours

and a distribution half-life of roughly six minutes, the elimination phase lasts far longer than the distribution phase.118 liters is the distribution volume at the steady state. The average level of protein binding is 94%; this level is maintained throughout all plasma concentrations; and males and females exhibit the same level of protein binding. Negligible protein binding displacement occurs as a result of the administration of medications such fentanyl, ketorolac, theophylline, digoxin, and lidocaine, which are frequently utilized during anesthesia and in the intensive care unit. After an 8-hour infusion, the context-sensitive half life of a 10-minute infusion can range anywhere from 4 minutes to 250 minutes. Oral bioavailability is low because significant first-pass metabolism makes it difficult for the drug to be absorbed. However, dexmedetomidine that is given sublingually has a high bioavailability of 84%, which suggests that it may have a function in the sedation and premedication of pediatric patients. [20]

Metabolism and excretion:

Dexmedetomidine almost entirely proceeds through the process of biotransformation into inactive metabolites. This process takes place through direct N-glucuronidation and aliphatic hydroxylation, both of which are mediated by cytochrome P-450 (CYP 2A6). Approximately 95% of metabolites

are eliminated by the urine, while just 4% are eliminated through the feces. Patients who have hepatic failure typically have a slower metabolic rate, thus their doses need to be adjusted accordingly.

CLINICAL PHARMACOLOGY

Dexmedetomidine's effect on the cardiovascular system results in a reaction that is biphasic in nature, with a transient hypertension phase followed by hypotensive effects. It is believed that two distinct 2-AR subtypes are involved for mediating the two phases: the -2B AR is responsible for the initial hypertensive phase, while the 2A-AR is responsible for the hypotensive phase. Anticholinergic drugs were successful in treating bradycardia and sinus arrest in patients who were younger and had higher levels of vagal tone (atropine, glycopyrrolate).

Central nervous system:

The effect that dexmedetomidine has on intracranial pressure (ICP) is unknown, despite the fact that it lowers cerebral blood flow and the metabolic requirement for oxygen in the brain. Dexmedetomidine affects spatial working memory, which improves cognitive function. Additionally, dexmedetomidine acts as a

sedative, analgesic, and anxiolytic via acting on the 2-adrenergic receptor. [21] Studies indicate that it may have a neuroprotective effect by lowering the levels of catecholamines that are circulating throughout the body and in the brain. This would, in turn, balance the ratio of oxygen supplies to the cerebral tissue, reduce excitotoxicity, and improve perfusion in the ischemic penumbra. It brings down the glutamate levels that are responsible for the cellular damage in the brain (helpful in cases of subarachnoid haemorrhage).

Respiratory Effects:

The extent of the effect that dexmedetomidine has on breathing appears to be comparable to that which is observed during the condition of heavy sleep. [22] Dexmedetomidine does not have a suppressive effect on respiratory function, even at large doses. It does not have any unfavorable impact on the patients' respiratory rate or gas exchange when it is used in patients who are spontaneously breathing following surgery in the intensive care unit. It helps to maintain sedation without causing cardiovascular instability or respiratory drive depression, and as a result, it may be of assistance in weaning and extubating trauma and surgical ICU patients who have failed in previous attempts due to agitation and hyperdynamic cardiopulmonary response. [23]

Effects on the endocrine system and the kidneys:

Dexmedetomidine works by activating presynaptic receptors in the periphery, which in turn lowers the production of catecholamines and, as a result, the sympathetic response to surgical procedures. Research conducted on animals has demonstrated that both natriuresis and diuresis can take place. Although dexmedetomidine is an imidazole drug, it does not appear to suppress steroidogenesis when it is administered as an infusion for short-term sedation. This is in contrast to etomidate, which does have this effect. [24]

ADVERSE EFFECTS

A variety of adverse effects, including hypotension, hypertension, nausea, vomiting, dry mouth, bradycardia, atrial fibrillation, pyrexia, chills, pleural effusion, atelectasis, pulmonary oedema, hyperglycemia, hypocalcemia, and acidosis, have been documented. Infusions of dexmedetomidine given quickly (loading dose of 1 microgram per kilogram per hour if given in less than ten minutes) have the potential to cause temporary hypertension due to peripheral α2B-AR vasoconstriction. [25] Hypotension and bradycardia, which are both caused by a reduction in noradrenaline production from the sympathetic nervous system, are possible side effects of long-term therapy that is mediated by the central alpha-2A receptor. The use of dexmedetomidine for an extended period of time promotes super sensitization and upregulation of receptors, which ultimately results in a withdrawal syndrome that includes uneasiness, agitation, headaches, and a hypertensive crisis. Patients who have extensive heart block as

well as ventricular dysfunction are not good candidates for treatment with dexmedetomidine. It has been given a pregnancy risk classification of category C by the FDA, which means that it should only be taken with extreme caution in pregnant women.

Administration:

In the intensive care unit, the average dosage range for sedation is between 0.2 and 0.7 mcg/kg per hour. It is possible to increase the dose to 1.5 milligrams per kilogram per hour in order to reach the appropriate level of drowsiness. Adjustments to the dosage are not required for renal or hepatic impairment; nonetheless, they should be considered, particularly in the event of hepatic impairment.

When it is utilized in anesthesia, a loading dosage of 0.5 to 1.0 mcg/kg is often followed by a continuous infusion of 0.2 to 0.7 mcg/kg per hour, which is titrated to achieve the desired level of sedation. As was said before, increasing the dose of the infusion used can help one get the desired impact.

When used as an adjunct for peripheral nerve block, the amount of dexmedetomidine that is typically administered is 1 mcg/kg. This ensures that the desired prolongation is achieved. [26,27].

Contraindications:

Dexmedetomidine has no absolute contraindications for usage. However, patients who already have bradycardia or low blood pressure should use this drug with extreme caution because it has the potential to make these symptoms much more severe. In addition, individuals who are already diagnosed with heart failure should only use it with extreme caution because there is evidence that dexmedetomidine has the potential to make myocardial dysfunction even worse.

Monitoring:

The monitoring of drugs is not subject to any particular criteria. It is imperative that careful attention be paid to the monitoring of pulse oximetry, sedation, blood pressure, heart rate and rhythm.

Toxicity:

At this time, there is no substance that can reverse the effects of dexmedetomidine or serve as an antidote. Supportive care and thorough monitoring are the two aspects of treatment for overdose that are essential.

Clinical uses:

Premedication:

Because of its sedative, anxiolytic, analgesic, sympatholytic, and stable hemodynamic profile, dexmedetomidine is utilized as an adjuvant for

premedication. This is particularly the case in patients who are more likely to experience preoperative and postoperative stress. Dexmedetomidine lowers the amount of oxygen required during surgery by up to 8%, and it lowers the amount of oxygen required for recovery by up to 17%. The premedication dose ranges from 0.33 to 0.67 mg/kg intravenously, and it is given 15 minutes before surgical incisions are made (this dose minimises side effects of hypotension and bradycardia).

Intraoperative usage:

Dexmedetomidine lowers the hemodynamic stress response to both intubation and extubation. This effect is achieved through sympatholysis. [28] Because it does not cause respiratory depression like some other medicines do, it does not need to be stopped before the extubation process can begin. The anesthetic effect of any and all anesthetic drugs can be magnified by the addition of dexmedetomidine, regardless of the route of administration. Because of the intraoperative administration of dexmedetomidine at lower dosages, there have been fewer interventions required to manage tachycardia, and the incidence of myocardial ischemia has decreased as a result. However, this medication's use is restricted by its side effects, which include bradycardia and hypotension. As a result, pharmacological rescue therapy is required. The combination of volatile anesthetic features, such as vasodilation and cardiac depression, may be responsible for these effects. Because dexmedetomidine has direct effects on the

peripheral vessels, high doses of the drug can cause systemic and pulmonary hypertension. Additionally, dexmedetomidine can damage the function of the heart and raise blood pressure.

Locoregional analgesia:

Because of its extremely lipophilic nature, dexmedetomidine is able to undergo rapid absorption into cerebrospinal fluid and to bind to the 2-AR in the spinal cord, where it has an analgesic effect. Regardless of the route of administration, it lengthens the amount of time that a local anesthetic causes sensory and motor blockage in the affected area (e.g., epidural, caudal, or spinal). In spite of the fact that dexmedetomidine increases the degree to which central and peripheral neural blockade are brought about by local anesthetics, the peripheral neural blockade is brought about because of its binding to 2A-AR. Intracoronary recirculation angiography (IVRA), brachial plexus block, and intraarticular injection have all been demonstrated to be effective uses of dexmedetomidine. [29] The addition of 0.5 micrograms per kilogram of dexmedetomidine to lidocaine for intravenous regional anesthesia (IVRA) increases the quality of anesthesia as well as intraoperative and postoperative analgesia without creating any adverse effects. When used in conjunction with levobupivacaine to perform an axillary brachial plexus block, the inclusion of dexmedetomidine speeds up the start of the block while simultaneously extending its duration and enhancing postoperative analgesia. Patients having arthroscopic knee surgery benefit from

an improvement in the quality and duration of postoperative analgesia when intraarticular dexmedetomidine is administered.

Sedation in intensive care unit:

Patients are able to remain aware, peaceful, and able to articulate their demands while under the influence of dexmedetomidine, making it a popular choice as a sedative agent in the intensive care unit (ICU). This is owing to the fact that dexmedetomidine can generate cooperative sedation. Because it does not disrupt the respiratory drive or create agitation, it enables an early weaning off of the ventilator and, as a result, reduces the overall cost of staying in the intensive care unit. Keeping up a normal sleep pattern while under sedation has the potential to cut down on recovery time in the ICU. Although multiple studies have proven that dexmedetomidine is safe for usage over extended periods of time, the FDA only permits its use in intensive care units (ICUs) for a maximum of 24 hours at a time at this time. Dexmedetomidine has been shown to have sedative and analgesic sparing effects, reduced delirium and agitation, minimal respiratory depression, and favorable cardiovascular effects when compared to traditional sedatives and opiates. Additionally, it has been shown to have beneficial effects on the cardiovascular system. [30]

Procedural sedation:

Dexmedetomidine is a promising agent for short-term procedural sedation. It has been used safely in procedures such as transesophageal echocardiography, colonoscopy, awake carotid endarterectomy, shockwave lithotripsy, vitreoretinal surgery, elective awake fiberoptic intubation, paediatric tonsillectomy, and paediatric MRI. In addition, it has shown promise as a potential agent for long-term procedura The standard dose of dexmedetomidine for procedural sedation is 1 microgram per kilogram, followed by an infusion of 0.2 micrograms per kilogram every hour. It takes fewer than 5 minutes for it to start having an effect, and it takes less than 15 minutes for it to reach its full effectiveness. Because the pharmacologic effects of dexmedetomidine can be reversed by the 2-AR antagonist atipamezole, dexmedetomidine offers a form of hypnotic drowsiness that is both titratable and quickly reversed.[31]

Controlled hypotension:

Because of its central and peripheral sympatholytic action, dexmedetomidine is a drug that is used to treat controlled hypotension that is both safe and effective. It is a near-ideal hypotensive drug due to the ease with which it can be administered, the predictability with which it interacts with anesthetic medicines, and the absence of any harmful side effects while preserving adequate perfusion of the important organs. Surgical procedures such as spinal fusion for idiopathic scoliosis, tympanoplasty and septoplasty operations, and

maxillofacial surgery have all been successfully conducted while the patient's blood pressure was managed by dexmedetomidine.

Analgesia:

Dexmedetomidine works by activating 2-AR in the spinal cord, which in turn decreases the transmission of nociceptive signals like substance P. It helps to alleviate chronic neuropathic pain and has a considerable opioid-sparing impact. [32]

BUPIVACAINE

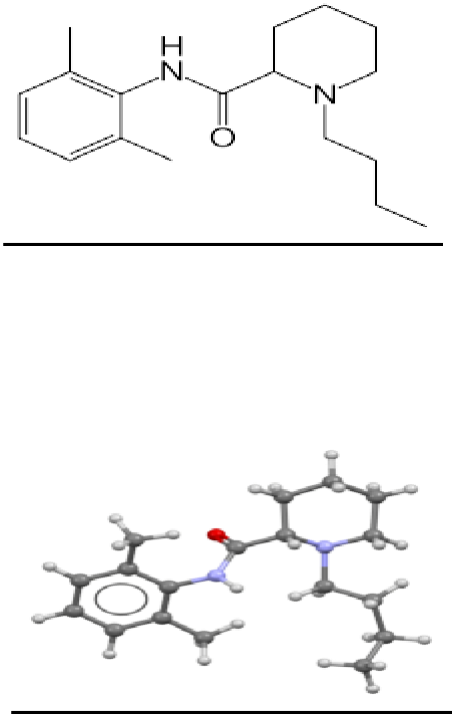


Figure 13 Bupivacaine

Formula C18H28N2O

Molar mass 288.435 g·mol−1

Bupivacaine is a powerful local anesthetic that was developed in 1957. It possesses features that are distinct from those of the amide group of local anesthetics. Local anesthetics are used in all four types of anesthesia: regional anesthesia, epidural anesthesia, spinal anesthesia, and local infiltration. The production of action potentials is inhibited by the use of local anesthetics, which function by increasing the threshold at which nerve cells become electrically excited. The depth of anesthesia is determined by a number of parameters, including the diameter of the nerve fibers, the degree of myelination, and the

conduction velocity. The following is a list of the orders in which nerve function can be lost in clinical practice: [33]

• Temperature • Proprioception • Touch • Pain • Skeletal muscle tone

Mechanism of action:

An aromatic ring, an ester (in the scenario of procaine) or an amide (in the scenario of bupivacaine) linking group, and an ionizable amine group are the structural components that are shared by all local anesthetics. In addition, the activity of each and every LA is determined by two distinct chemical features, which are as follows:

• Lipid solubility

• Ionization constant (pKa)

Local anaesthetic lipid solubility is the primary factor that determines their potency, duration of action, and ability to bind to plasma proteins. When they penetrate nerve fibers, local anesthetics take the form of a neutral-free. This results in rapid dispersion to the cytoplasmic side of the Na+ channel, which itself is desirable.

Action potentials are able to move through axons, dendrites, and muscle tissue thanks to proteins called Na+ channels, which are found in membranes. They are in charge of creating and maintaining electrochemical gradient in heart and

brain specialised cells. The Sodium ion channels found in different tissues each have another one or two smaller beta subunits and a bigger alpha subunit. Each of the three binding sites for local anaesthetics and the ion conduction site has four domains and six segments that span alpha helices in the membrane. Each of these three sites also has a site that is responsible for ion conduction. The channel is able to maintain its correct orientation within the cytoplasmic membrane because to the highly glycosylated surface of the alpha-external subunit. In contrary to local anaesthetics, scorpion venom and tetrodotoxin poisons bind to the outer surface of Na+ channel.

When LAs bind to the Na+ channel and limit the Na+ permeability necessary for an action potential to be generated along an axon, a local anesthetic is produced. As a result, an action potential develops along the axon. The capacity of local anaesthetics to selectively block voltage-gated sodium channels in their open state is unmatched Blocking Na+ channels has the effect of reducing or eliminating transmission within vascular smooth muscle, which induces relaxation.This results in a reduction in the amount of activity produced by the pacemaker and a lengthening of the refractory period in the heart. Bupivacaine increases the maximum rate of depolarization (Vmax), which raises the likelihood of ventricular arrhythmias.This is because bupivacaine has slower action than other anaesthetics at dissociating from inhibited sodium channels. LAs also cause dose-dependent myocardial depression and obstruct the

movement of Ca2+ signals throughout the heart muscle because they bind to and block voltage-gated Calcium as well as Potassium channels in the heart.

It's likely that local anaesthetics adhere to adrenoceptors and prevent epinephrine from inducing the synthesis of cAMP, which would explain why bupivacaine Cardiovascular toxicity is refractory to standard resuscitation methods. After being subjected to local anaesthetics, the central nervous system (CNS) could become more excitable, and this condition may be followed by depression.

Neurons have a unique reaction to the effects of local anesthetics. It is necessary to block between two and three Ranvier nodes in order to completely impede neuronal transmission. Depolarizing currents in nerves move along Ranvier nodes. Because smaller fibers have shorter internodal distances, they are easier for local anesthetics to block.

Administration

There are three different concentrations of bupivacaine that can be purchased: 0.25%, 0.5%, and 0.75%.

peripheral nerve blocks, Local infiltration, spinal anaesthesia, epidural anesthesia/analgesia for labour pain, and caudal blocks are examples of the administration techniques. Local infiltration is used for post-surgical analgesia. Peripheral nerve blocks are used for dental and other minor surgical procedures

as well as orthopaedic surgery (anesthesia and analgesia below the umbilicus, usually for pediatric surgery).When performing nerve blocks, it is common practice to combine local anesthetics with adjuvants in order to extend the anesthetic effects beyond what would be possible with LA alone. It has been demonstrated that the anesthetic effect can be greatly prolonged with the local anaesthetic being combined with alpha-2 agonists like clonidine or dexmedetomidine. Dexamethasone has also been demonstrated to extend the duration of anaesthesia when paired with a local anaesthetic for nerve blocks; however, it is unknown whether this is because of a direct neural action or only the systemic effects of the steroid's anti-inflammatory activities. This effect's underlying mechanism is unknown. It has been demonstrated that magnesium helps to a longer duration of effect for local anaesthetics used for nerve blocks because of its N-methyl D-aspartate receptor antagonist properties. Research is now being done to determine the impact of these and other potential additives that may be added to LAs to boost their efficacy while lowering the probability of their toxicity. Ultrasound-guided neuronal blocks have been linked to a lower risk of local anaesthetic toxicity over the past ten years. It is believed that seeing the nerve and the surrounding structures reduces the probability of injecting into a vasculature and increases the likelihood of early identification of this event, both of which lessen the risk of bupivacaine levels in the bloodstream rising to dangerous levels.[35]

Adverse effects:

Technique, vascularity of tissue, area, segments number that need to be blocked, the depth or length of anesthesia that is necessary, and the patient's physical condition are the factors that decide the amount of bupivacaine that will be administered. There is a possibility that bupivacaine will interact negatively with other drugs, including those used to treat migraines, blood thinners, antidepressants, and monoamine oxidase inhibitors. Immunologic responses induced by a local anesthetic are quite rare. It is extremely rare for patients to experience allergic responses to amide-type local anesthetics that do not contain any preservatives. It would appear that ester local anesthetics or preservatives are more likely to cause true anaphylactic reactions; yet, reactions to epinephrine-containing local anesthetics are frequently mistaken as allergic reactions. Patients might potentially have an adverse reaction to preservatives in local anesthetics, like methylparaben, for example.

Methemoglobinemia is almost always caused by benzocaine or prilocaine; but, in a few extremely unusual instances, bupivacaine has been shown to be the culprit. Methemoglobinemia may not show any symptoms at low concentrations (1% to 3%), but at higher concentrations (10% to 40%), it may result in cyanosis, cutaneous discoloration (grey), tachypnea, dyspnea, exercise intolerance, fatigue, dizziness, syncope, and weakness.

Some of the most frequent adverse effects include chills or shivering, headache, nausea, vomiting, backache, vertigo, , anxiety, vertigo, tinnitus, sexual dysfunction, fuzzy vision, agitation ,and tremors. More severe adverse effects such as myoclonic jerks, seizure, coma, and cardiovascular compromise can develop.

Contraindications:

The following situations are contraindicated: amide anaesthetic hypersensitivity, infection at the site of injection, obstetric paracervical block, obstetric anaesthesia with a 0.75% concentration, intravenous regional anaesthesia, and intra-articular continuous infusion. Patients who, have impaired kidney function, are hypersensitive to sulfites impaired heart function, heart block, hypovolemia, hypotension, and individuals who are elderly, incapacitated, or seriously ill should be treated cautiously. Standard monitoring procedures include doing a continuous electrocardiogram, measuring oxygen saturation in the blood, and taking the patient's blood pressure.

Inquire about any numbness that may be present around the mouth, a taste of metal, tremors, ringing in the ears thoughts of foreboding. When any of these symptoms are reported by the patient, the bupivacaine treatment must be stopped immediately, and the treatment must begin in accordance with the instructions. [36]

Toxicity:

The indications and symptoms caused by the majority of local anesthetics are quite comparable to one another. However, Bupivacaine is the most cardiotoxic of the local anaesthetics, and the proportion of neurotoxicity to cardiotoxicity may vary. One in 1000 to one in 10,000 recorded cases of poisoning are extremely low. Be wary of local anaesthetic toxicity (LAST), which may manifest as unusual signs and symptoms involving the nervous system or the cardiovascular system.The location at which a local anesthetic is administered is another factor that affects the likelihood of adverse effects. Unintentional direct intravenous injection or rapid vascular absorption of medication, which has an upper limit of dose that ranges from 2.5 to 3.5 mg/kg, is the most prevalent cause of bupivacaine toxicity. Another common cause is rapid vascular uptake of the drug. Depending on the degree of vascularity present at the injection site as well as the method used, there is a possibility that the medicine will become toxic if it is given in excess of the recommended maximum dosage. The signs of toxicity may present themselves immediately or gradually.

Patients almost never experience toxicity from bupivacaine at doses that are significantly lower than the upper limits of the recommended dosing range. This unusual situation, which is brought on by a deficiency in L-carnitine, seems to be the root source of this harmful effect. Patients are at risk for developing cardiac toxicity at doses of bupivacaine that are as low as 1.1 mg kg when

administered through subcutaneous injection. There are case reports that describe instances of low-dose toxicity in patients who were afterwards found to be lacking in l-carnitine. These patients were treated using case reports. The efficacy of this model was proved in a study conducted on rats, where it was found that providing the rats with additional l-carnitine might have the opposite effect. [37]

Pathophysiology

At therapeutic levels, local anesthetics block voltage-gated Na-channels at the alpha subunit located inside the channel. This prevents Na+ influx, which would otherwise lead to depolarization and the formation of action potentials. They inhibit K+, Ca2+, and NMDA receptors in the brain, which leads to a toxic effect on Na+ channels in the heart as well as neurons in the brain. In addition, the use of local anesthetics can interfere with some cellular functions, including the generation of cAMP, the utilization of free fatty acids, and oxidative phosphorylation. Toxic doses of local anaesthetics accumulate in the heart and cause conduction anomalies, decreased cardiac smooth muscle contraction, and reduction of vascular tone resulting from excessive vasodilation.

Indicators:

Neurological

Early symptoms include tinnitus ,perioral tingling, blurred vision,tongue paraesthesia's; these symptoms progress to central nervous system supression (slurred speech drowsiness);

Late symptoms include confusion, agitation, agitated myoclonic convulsions, and convulsions.

Cardiovascular

Moderate myocardial depression and hypotension are both correlated with hypertension and tachycardia. The last phases of this syndrome include vasodilation, extreme hypotension, dysrhythmias, transmission blockages, and asystole.

Hypercarbia:

It lowers the threshold for having a seizure and increases the blood flow to the brain, which enables more of the local anesthetic to be absorbed by the brain. Acidosis hinders the ability of the local anesthetic to bind to proteins, which leads to a higher free fraction in plasma. This, in turn, increases the amount of local anesthetic that is delivered to the brain.

Treatment

Because of its high neurologic and cardiac toxicity, the treatment of bupivacaine poisoning has always been a challenging endeavor. In the past, treatment

consisted of the usual procedures for cardiac resuscitation, management of the airway, and seizure control by the use of fast-acting GABA agonists such as midazolam. Because of its very extended duration of action, bupivacaine presented a unique set of challenges for toxicologists. For patients who were in centers where cardiopulmonary bypass was easily available, it was utilized to sustain them while they waited for the medicine to be sufficiently metabolized and expelled from their system, which could take several hours. In the subsequent 15 years, the treatment with lipid emulsion became widely accepted as effective. It was originally thought of as a treatment of last resort for these individuals, but now days it is frequently employed as a treatment that comes first in the line of treatment. Lipid emulsions should always be kept on hand in local anesthetic facilities in case of an unexpected emergency. It is interesting to note that the use of large doses of epinephrine has been associated with lower efficacy of lipid emulsion in the treatment of LAST. These findings highlight how critical it is to initiate therapy with lipid emulsions as soon as there is even a remote possibility that LAST is present. The website of the American Society of Regional Anesthesia has treatment algorithms that are broken down into great detail. The following is a list of the most recent guidelines for the appropriate dosage of lipid emulsion 20%:

In a patient who weighs more than 70 kilograms, administer 100 milliliters of lipid emulsion 20% as a fast bolus over the course of two to three minutes, and

then continue to infuse 200 to 250 milliliters over the next fifteen to twenty minutes. It is possible that a higher dose, up to a maximum of 12 mL/kg, will need to be administered.

A bolus of 1.5 mL/kg lipid emulsion 20% should be given to a patient weighing less than 70 kg over the course of two to three minutes. This should be followed by an infusion of 0.25 mL/kg/min for optimal body weight, with a maximum dose of 12 mL/kg.

In the event that alternative treatments are futile, early consideration should still be given to cardiopulmonary bypass surgery.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

A prospective double-blinded study was carried out by **Oza VP et al. [38] (2016)** on a group of patients who were going to be receiving laparoscopic procedures. Their primary objective was to determine whether or not intraperitoneal administration of bupivacaine alone or a combination of bupivacaine and dexmedetomidine was more effective at relieving pain than the other. During the elective laparoscopic surgery that was performed on 100 patients of either sex, the patients were randomly split into two groups consisting of 50 patients each. In Group B, an intraperitoneal instillation of 50 mL of bupivacaine 0.25% (125 mg) was performed, whereas in Groups B and D, the same dose was performed in addition to the administration of 1 mcg/kg of dexmedetomidine. A visual analogue scale was used to assess the level of pain the patient was experiencing at 0.5 hours, 1 hour, 2 hours, 4 hours, 6 hours, and 24 hours after surgery (VAS). It was determined that analgesics would be necessary for the rescue operation. The duration of analgesia was significantly increased in group B+D (14.5 hours), compared to that of group B (13.06 hours). This difference was statistically significant (P 0.05), with group B+D requiring much less rescue analgesia over the course of 24 hours (1.76 as opposed to 2.56). There was a statistically significant difference between the two groups in terms of the mean total number of rescue analgesics given in 24 hours, with group B+D receiving 1.76 less doses than group 2.56. Because of this, they came to the

conclusion that intraperitoneal instillation of dexmedetomidine, as compared to bupivacaine alone, extends the period of time during which postoperative analgesia is provided. In addition, the use of rescue analgesics following surgery is reduced when dexmedetomidine is administered alongside bupivacaine in the role of an adjuvant.

Vijayaraghavalu S et al [39] (2021) conducted a study with the primary objective of determining the efficacy of intra peritoneal bupivacaine versus normal saline instillation on post-operative pain relief and the incidence of side effects such as nausea and vomiting. This research was published in 2021.

Participants in this prospective, controlled, and randomized trial ranged in age from 18 to 50 and were all scheduled to undergo laparoscopic cholecystectomy under general anesthesia. Patients were classified as either ASA I or ASA II by the American Society of Anesthesiologists (ASA). The patients were divided into two groups at random, each with the same number of participants. Group B was given an intraperitoneal instillation of 30 ml of plain bupivacaine 0.5%, whereas Group N was given 30 ml of normal saline. During the first twenty-four hours following surgery, patients' reports of postoperative pain were rated on a visual analog scale (VAS). Pain in the shoulder after surgery, nausea, vomiting, and the length of time it took to call for emergency analgesia were all noticed. Patients who received intraperitoneal bupivacaine experienced a significant reduction in postoperative pain during the first six hours ($P = 0.04$);

in addition, the amount of time needed to request rescue analgesia was lengthened (P = 0.04). The researchers' observations showed that these results were statistically significant. Both groups experienced a comparable amount of nausea and vomiting (P = 0.1 and p = 0.09, respectively), however the bupivacaine group reported a significant reduction in shoulder discomfort (P = 0.04).

Chilkoti GT et al [40] (2019) had already conducted a study back in the day. 75 patients ranging in age from 18 to 60 years old and having an ASA physical status of I or II had laparoscopic cholecystectomies performed while they were under general anesthesia. Group C received intraperitoneal (IP) administration of bupivacaine. After having their gall bladders removed, patients in Group IV were given 0.5 mcg/kg dexmedetomidine by intravenous infusion (IV) in addition to bupivacaine 0.25% intraperitoneally (IP). Group IP were given 0.5 mcg/kg dexmedetomidine in bupivacaine 0.25% as 40 mL intraperitoneally (IP). The first analgesic requirement was major goal, and the 'total tramadol consumption in 24 hours' and the 'visual analogue scale (VAS) pain score' were the secondary outcomes. There were a total of 75 patients, with 25 patients assigned to each group. When compared to Group C, the IV (P = 0.001) and IP (P = 0.001) groups had a considerably shorter amount of time before making their initial request for analgesia (59.68 ± 71.05 min). Both the mean amount of tramadol consumed in first 12 hours (152.40± 60.958 vs. 137.64± 52.40 mg)

and amount of pain scored on the VAS scale were found to be comparable between the two treatment methods.

52 children were randomly allocated to either Group B who received intraperitoneal bupivacaine 0.25% (2 mg/kg) or Group BD who received intraperitoneal bupivacaine 0.25% (2 mg/kg) plus dexmedetomidine (1 mcg/kg) for postoperative analgesia in children undergoing laparoscopic appendectomy. This trial was done by **Elnabtity AM et al [41] (2018)** and was a prospective randomized Consumption of postoperative pethidine on day 1 was recorded, and this data was taken into consideration as the primary outcome of the study. Patients were evaluated based on their pain scores at 0 hours, 2 hours, 4 hours, 6 hours, and 24 hours; their time until they made their first request for pethidine; their sedation scores at 0 hours, 2 hours, and 6 hours; the length of their hospital stays; and their parents' levels of satisfaction. For the purpose of analysis, we utilized the Chi-square test, Fisher's exact test, Student's t-test, and the Mann-Whitney U-test. They had discovered that Group BD had lower postoperative visual analogue scale scores at 2, 4, and 6 h (mean = 3, 3, respectively) in comparison to Group B (mean = 4, 5, 4, respectively) (P 0.05). Patients in Group BD had higher sedation scores at 0 hours, 2 hours, and 4 hours (P = 0.05), a relatively lengthy delay to first rescue analgesia (P = 0.03), lower use of rescue analgesics (P = 0.02), a shorter hospital stay (P = 0.02), and higher parental satisfaction (P = 0.01). They came to the conclusion that when

dexmedetomidine was added to bupivacaine intraperitoneally, the analgesia was much improved.

An investigation was carried out by **Praveena BL et al [42] (2019)** in the year 2019. It was a prospective observational study that was randomised and double blinded, and it was carried out on patients who were undergoing laparoscopic cholecystectomy. A total of 80 patients were selected at random to be placed in one of two groups of equal size and given either of the following treatments: The RF (n = 40) received 30 mL of 0.2% ropivacaine with 1 g/kg fentanyl (diluted in 2 mL normal saline), while the RD (n = 40) received 30 mL of 0.2% ropivacaine with 1 g/kg dexmedetomidine through trocars. Both of these solutions were diluted in 2 mL of normal saline (diluted in 2 mL normal saline). The score on the visual analogue scale was utilized in order to assess the level of analgesia provided (VAS). It was recorded when the patient made their initial request for analgesia, how much total analgesic dose they received in the first 24 hours, and any side effects. Both the Students' t-test and the Chi-square test were utilized in order to analyze the data. When compared with the RF group, the RD group had a significantly lower overall VAS in 24 hours (1.68 0.46 vs. 4.47 0.94), a significantly longer time to first request of analgesia (min) (122.7 24.5 vs. 89.3 13.2), and a significantly lower total analgesic consumption (mg) (95.3 15.6 vs. 135.7 75.1). It has been discovered that the antinociceptive impact of ropivacaine in conjunction with dexmedetomidine is significantly

more potent than the antinociceptive effect of ropivacaine in combination with fentanyl.

Between July 2015 and July 2016, **Bisht N et al [43] (2021)** carried out a prospective, randomized, and single-blind comparison study. A total of eighty individuals diagnosed with LC were split evenly between two groups, CLO (n = 40) and DEX (n = 40). Prior to induction, the patients were premedicated with low-dose (one gram per kilogram) bolus intravenous medications in accordance with the group to which they had been assigned. Analgesic-sparing benefits of a multimodal analgesic regimen consisting of intraoperative fentanyl and postoperative tramadol were detected. Individual medication effects on the postoperative visual analogue scale (VAS) score were also noticed. The hemodynamic condition of the patients was also evaluated. They discovered that DEX had a substantial impact in lowering VAS scores 15 minutes after extubation, as well as the number of patients who needed rescue analgesia and the number of injections that were necessary. Both the systolic and diastolic readings of blood pressure were considerably lower in the DEX group. DEX was found to be superior to LC in terms of giving early pain relief and improved hemodynamic stability, despite the fact that both medications were successful for treating LC in the short term. As a consequence of this, using DEX as a routine premedication prior to ambulatory LC treatment might be recommended.

As an adjuvant to local wound infiltration anesthesia, dexmedetomidine was the subject of a meta-analysis that was carried out by **Ren Y et al [44] (2021)** in order to gain a better understanding of both its safety and its effectiveness. The systematic search method made use of a variety of resources, including PubMed, Embase, the Cochrane Library, and Chinese databases. As a consequence of this, 23 randomized controlled trials including 1445 patients were included. Patients who received local anesthesia in addition to dexmedetomidine had a lower rate of rescue analgesia [risk ratio (RR): 0.48; 95% confidence interval [CI]: 0.36-0.65]] and a lower intake of rescue analgesic medication [weighted mean difference (WMD): -10.80 mg; 95% confidence interval [CI]: -13.28 to -8.31 mg]] than patients who received local anesthesia alone. Among the adverse responses that were associated with dexmedetomidine were bradycardia (relative risk: 1.33; 95% confidence interval: 0.32-5.56) and hypotension (relative risk: 3.00; 95% confidence interval: 0.49-18.42). In addition, the time until the first request for analgesia had a WMD of 296.16 minutes and a 95% confidence interval ranging from 165.69 minutes to 426.63 minutes. , the occurrence of postoperative nausea and vomiting (PONV), and the pain scores at 4 hours postoperatively were all considerably lower in individuals who were given dexmedetomidine in combination with local anesthesia. According to the findings of this meta-analysis, the addition of dexmedetomidine to wound infiltration as an adjuvant lowers the frequency of the need for rescue analgesia, as well as the

consumption of rescue analgesics and the risk of PONV. In addition, there is some evidence to show that dexmedetomidine may be able to extend postoperative analgesia for up to five hours. There is a need for additional research on the adverse events that are associated with dexmedetomidine, as well as research into the dose-response impact of dexmedetomidine in wound infiltration.

Chiruvella S et al [45] (2016) had done in patients undergoing laparoscopic procedures. Randomization under double-blind conditions was used to decide which of the following injections would be administered intraperitoneally at the conclusion of laparoscopic hysterectomy. Patients were placed in one of two groups according to their diagnoses: Patients in the ropivacaine group (R group) (N = 30) were given 30 mL of 0.2% ropivacaine along with 2 mL of normal saline through trocars. Patients in the ropivacaine plus dexmedetomidine group (RD group) (N = 30) were given 30 mL of 0.2% ropivacaine along with 1 mcg/kg dexmedetomidine (diluted in 2 mL normal After receiving a visual analogue scale (VAS) rating of 3 for their level of discomfort, the patients were all administered diclofenac sodium. VAS score at various intervals, overall VAS in 24 h was much lower (1.86 0.46 vs. 4.7 0.94) in the RD group than in the R group, duration to the first request of analgesia (min) was longest (126 24 vs. 59 13), and total analgesic intake (mg) was lowest (95 15 vs. 175 75).

Ali WA et al [46] (2020) conducted a study comparing the postoperative analgesia provided by intravenous bupivacaine to that provided by bupivacaine, particularly when combined with nalbuphine, in patients who were undergoing LC. Patients and treatment strategies Participants with LC numbered 90 in this study. They were split up into three groups of 30 patients each by a random process. Postoperatively, group C was given 50 millilitres of normal saline (NS), group B0 was given 100 milligrams of bupivacaine diluted with NS to 50 millilitres, and group BN was given 100 milligrams of bupivacaine mixed with 10 milligrams of nalbuphine diluted with NS to 50 millilitres. The patient's level of pain was measured continuously over the course of one day using a visual analogue scale (VAS), and the time of their initial painkiller request was also noted. We also recorded the total amount of analgesic that was consumed over the course of 24 hours, along with hemodynamic parameters and adverse effects. Up to 24 hours after the operation, the postoperative VAS values in group BN were considerably lower than those in group BN. In addition, the values of the VAS produced by i.p. bupivacaine were lower than those produced by the control group. In groups BN, B0, and C, the duration of analgesia was 11.5 +/- 0.9 hours, 7.5 +/- 0.9 hours, and 1.5 +/- 0.6 hours, respectively (P 0.001). The BN group used a considerable amount fewer of the analgesics throughout the course of 24 hours compared to the other groups. The BN group's hemodynamic parameters were more stable than those of the other groups, and there were no notable detrimental effects seen in this group. They

came to the conclusion that the combination of intravenous nalbuphine and bupivacaine gives better analgesia than bupivacaine on its own does after LC, without increasing the number of side events.

A randomized double-blind study was carried out by **Fares KM et al. [47] (2015)** on 45 patients who were scheduled to undergo laparoscopic colorectal cancer surgery. These patients were randomly assigned to receive either 50 mL of saline (control group; GI, n = 15), 50 mL of bupivacaine 0.25% (125 mg; GII, n = 15), or 50 mL of bupivacaine 0.25% Evaluations of the patients' hemodynamics, visual analogue scale (VAS), time to first request analgesia, total analgesic use, shoulder discomfort, and side effects were performed during the first twenty-four hours following surgery. Their findings indicated that, in compared to GI and GII, the VAS in GIII had dramatically dropped at the baseline, 2, 4, and 24 hours after surgery. Additionally, this decline had taken place 24 hours after surgery (P 0.05). It took significantly longer for GIII patients to have their first need for analgesic medication (P 0.05). The number of rescue analgesic pills taken on a daily basis was much lower on the GIII. They came to the conclusion that intraperitoneal administration of Dex 1 mcg/kg combined with bupivacaine improves the quality and duration of pain control and delivers an analgesic sparing effect compared to bupivacaine alone in patients who underwent laparoscopic colorectal cancer surgery. This was accomplished without significantly causing any adverse effects.

In the research conducted by **Chavan SG et al. [48] (2016)**, there were a total of sixty patients who were randomly split into two groups of thirty each. Patients in Group A received a loading dose of dexmedetomidine intravenously at a rate of 1 mcg/kg spread out over a period of 10 minutes, whereas patients in Group B received normal saline as their treatment. After the induction with propofol, Group A received an infusion of dexmedetomidine at a dosage ranging from 0.2 to 0.8 g/kg/h. Inhalation was accomplished with sevoflurane for both of the groups. It was determined which parameters will be used for postoperative monitoring. The evaluation of recovery and postoperative sedation took place. Making use of statistical research and methods The Chi-square test developed by Pearson was utilized so that demographic data could be analyzed. The changes in heart rate (HR), systolic blood pressure (BP), and diastolic blood pressure were analyzed using paired and unpaired t-tests, respectively. When the findings of the Shapiro-Wilk normality test were uncertain, Mann-Whitney rank sum tests were employed to determine "P" values. These tests were used to assess the significance level. They discovered that dexmedetomidine considerably lowers the stress response during intubation when compared to the group that served as the control. This was demonstrated by a decreased increase in heart rate (86.00 5.16 vs. 102.97 7.07/min.) and mean blood pressure (95.78 5.35 vs. 110.18 5.35). (P 0.05). After the pneumoperitoneum, the patient's heart rate dropped to 85.07 6.23 from 107.10 4.98, and their mean blood pressure dropped from 118.54 6.27 to 98.98 10.16. (P 0.05). improves the stability of the

hemodynamics during the operation. After surgery, there was no statistically significant difference between the test group and the control group in terms of either the extubation time (7.00 0.58 vs. 6.74 0.73) or the responsiveness to oral commands (8.78 0.72 vs. 8.66 0.73) (P > 0.05). Dexmedetomidine is effective in preserving hemodynamic stability during surgical procedures when it is administered as an adjuvant in general anesthesia. Additionally, it attenuates a variety of stress responses. It does not slow down the healing process in any way.

A study involving eighty patients who were scheduled to undergo laparoscopic cholecystectomy was carried out in the past by **Swaika S et al [49] (2013)**. However, in their study, they only included female patients who fell into the ASA grade I category and were between the ages of 19 and 60 years old. These patients were split up into two groups at random, and one group received an infusion of paracetamol while the other group received an infusion of dexmedetomidine. Heart rate (HR), diastolic blood pressure, and mean arterial pressure profiles of intra-operative hemodynamic changes were similar in both groups, with the exception of the systolic blood pressure, which was significantly reduced by dexmedetomidine in comparison to paracetamol (P = 0.014). Heart rate (HR), diastolic blood pressure, and mean arterial pressure profiles of intra-operative hemodynamic changes were similar in both groups. After surgery, there was a statistically significant difference in the mean HR

between the two groups at both 4 and 24 hours. The difference occurred between the two groups (P 0.05). On the visual analogue scale, the Group P had significantly lower scores than the Group D at all three time points (8th, 16th, and 24th h) (P 0.001). The sedation scores of the patients in Group D were statistically higher than those of the patients in Group P at the 4th, 8th, 16th, and 24th post-operative hours (P 0.006).

In order to lessen the need for opioids, a combination of paracetamol and dexmedetomidine infusion was administered. However, paracetamol is capable of providing adequate analgesia with only a moderate amount of sedation during surgery, while dexmedetomidine is capable of providing both analgesia and co-operative sedation.

It was demonstrated by **Kalaskar VP et al [50] (2021)** that dexmedetomidine, an alpha 2 agonist, with its anxiolytic, sympatholytic, and sedative property can be a good adjuvant in anesthesia by modifying the stress response to various stimuli that occur during laparoscopic cholecystectomy. These stimuli include laryngoscopy, intubation, pneumoperitoneum, and extub Theyaimed to investigate low dose dexmedetomidine for minimizing hemodynamic perturbations to stressful situations with secondary purpose of investigating propofol dose reduction and postoperative analgesia. Sixty patients of American Society of Anesthesiologists Physical Status (ASA PS) Classes I and II were randomized to two groups of 30 each to receive dexmedetomidine infusion (0.5

mcg.kg−1.h−1) starting 15 min before induction (Group A) and normal saline (Group B) (Group B). Heart rate (HR) and mean arterial pressure (MAP) were recorded while the patient was inducing and maintaining themselves with propofol infusions to keep their BIS values between 55 and 60 in both groups. During the surgical closure, they halted the infusions. Score on the VAS was recorded up until 24 hours after surgery. Both groups' total propofol requirements were tallied and reported. The SPSS software, version 15.0, was used to do statistical analysis on the collected data. The mean arterial pressure (MAP) and heart rate (HR) of patients in Group B continued to be elevated after intubation and remained elevated throughout the procedure as well as during all stressful events, including CO2 insufflation and tracheal extubation. These findings were statistically significant. When compared to Group B, Group A required dosages of propofol that were much lower by roughly 30 percent in order to obtain the same BIS readings. The score on the Visual Analog Scale remained significantly lower in Group A after 24 hours than it did in Group B. In patients having laparoscopic cholecystectomy, a low dosage of dexmedetomidine (0.5 mcg.kg1.h1) can successfully sustain hemodynamics during stressful events, reduce the necessity for propofol, and improve postoperative analgesia.

El Baz MM [51] (2018) reported remarkably similar findings in their study conducted on 105 patients undergoing laparoscopic cholecystectomy. The

patients all had gallstones removed through laparoscopic surgery. In terms of the Visual Analog Scale (VAS) score as well as the amount of post-operative analgesic consumption, it was discovered that the dexmedetomidine combined with levobupivacaine group was much more effective than levo bupivacaine on its own.

A study was carried out by **Sharan R et al [52] (2018)** on sixty patients who were classified as having an American Society of Anesthesiologists Physical Status (ASA PS) Class I or II and were scheduled to undergo laparoscopic cholecystectomy.

They were split into two groups of thirty each and randomly assigned to receive either an infusion of dexmedetomidine (0.5 mcg.kg-1.h-1) beginning 15 minutes before induction (Group A) or a normal saline solution (Group B) (Group B). Both groups of patients were given an induction and maintenance dose of propofol to maintain a BIS value between 55 and 60, and their heart rate (HR) and mean arterial pressure (MAP) were measured. At the time of surgical closure, we discontinued the infusions. Score on the VAS was recorded up until 24 hours after surgery. Both groups' total propofol requirements were tallied and reported. The SPSS software, version 15.0, was used to do statistical analysis on the collected data. They discovered that after intubation in Group B, both MAP and HR remain elevated throughout the procedure and during all stressful events, such as CO2 insufflation and tracheal extubation, and that these changes

are statistically significant. Additionally, they found that these changes occur continuously throughout the procedure. When compared to Group B, the doses of propofol that were required in Group A to reach values that were comparable to those of Group B were much lower by about 30 percent. After one day, the score on the Visual Analog Scale for Group A continued to be lower than that of Group B. Therefore, they came to the conclusion that A low dosage of dexmedetomidine (0.5 mcg.kg-1.h-1) can effectively sustain hemodynamics during stressful events in patients having laparoscopic cholecystectomy. This can also reduce the requirement for propofol and improve postoperative analgesia.

MATERIALS AND METHODS

MATERIALS AND METHODS

SOURCE OF DATA:

This study was conducted at the Department of Anaesthesiology, B.L.D. E (DEEMED TO BE UNIVERSITY) Shri B.M. Patil Medical College, Hospital, and Research Centre, VIJAYAPURA. The study was conducted from December 2020 to September 2022.

A written informed consent was obtained for this study from all subjects after obtaining approval from the ethical committee.

METHOD OF COLLECTION OF DATA:

Study design: Randomised controlled study.

Study Period: One and a half year.

Sample size: Ninety-nine patients of both genders were randomly divided into three groups of thirty-two each**.**

- The anticipated Mean±SD of VAS score at 0.5htheirs of time interval in the control group 4.36±2.08 and group IV 2.56±1.64 resp. [10] The required minimum sample size is 32 per group (i.e., a total sample size of 96, assuming equal group sizes) to achieve a power of 80% and a level of significance of 1% (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

The formula used is $N = 2\left[\frac{(Z_a + z_\beta) * S}{d}\right]^2$

Level of significance=99%

power of the study=90%

d=clinically significant difference between two parameters

SD=Common standard deviation

Statistical Analysis:

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. One-way analysis of variance (one-way ANOVA) was a technique used to compare means of three or more samples for numerical data (using the F distribution). A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.

Explicit expressions that can be used to carry out various *t*-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a *t*-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

Once a *t* value is determined, a *p*-value can be found using a table of values from Student's t-distribution. If the calculated *p*-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favor of the alternative hypothesis.

P-value ≤ 0.05 was considered for statistically significant.

Randomization:

- 96 patients recruited for the study were randomly allocated by computer-generated slips into three groups of 32 patients in each group.
- Group C: 30 mL of normal saline (NS) Intravenous along with bupivacaine 0.25% as 40 ml is given Intraperitoneally (IP).
- Group IV: 0.5µg/kg dexmedetomidine is given Intravenously (IV) along with bupivacaine 0.25% as 40 ml is given Intraperitoneally (IP).
- Group IP: 30ml of NS intravenously (IV) given and 0.5µg/kg Dexmedetomidine is given in 0.25% bupivacaine in volume of 40 ml intraperitoneally (IP).

INCLUSION CRITERIA:

- Patients aged between 18-60 years of both sexes undergoing laparoscopic cholecystectomy.
- Patients belonging to ASA Grade I and II.
- Mallampati grade I and II.

EXCLUSION CRITERIA:

- BMI >30kg/m2.
- Hypersensitivity to study drugs.
- Patients with hepatic or renal insufficiency.
- Patients with neurologic and psychiatric disease.

- Patients with a preoperative heart rate of <45/min or heart blocks.
- Patients on antihypertensive medication with any α2 agonists like clonidine.
- If surgical procedure gets converted into open cholecystectomy.

METHODOLOGY:

Preliminaries:

• A written informed consent was obtained from all patients, and it was stated to them that they would need to be followed up on for at least 24 hours after surgery.

• It was confirmed that the oral status was nil.

• An intravenous cannula of 18 gauge was used to ensure a secure intravenous access.

Evaluation prior to administration of anesthesia consisted of taking a comprehensive patient history, doing a thorough physical exam, and checking the patient's vitals during the preoperative appointment. Inquiries were made regarding the presence of any serious illnesses in the patient's past. It was determined what was wrong with the airway, the respiratory system, and the cardiovascular system.

In their study, participants had to be ASA grade I or lower patients, be between the ages of 18 and 60, and be of either gender. In addition, they had to be undergoing laparoscopic cholecystectomy.

The procedure consisted of administering 0.25 milligrams of alprazolam orally the night before surgery as well as on the morning of the procedure itself.

• Patients were instructed on how to utilize the visual analogue scale (VAS) during their time in the preoperative room.

• After moving the patient to the operating table, an intravenous access was established on the patient's forearm using an 18-gauge IV cannula, and an intravenous infusion of Ringer's lactate solution at a rate of 10 ml/kg/h was performed. Before beginning the surgery, a multi-parameter monitor was used to record the patient's ECG, baseline ECG, non-invasive blood pressure, and SPO2 levels. Additionally, the breathing rate was recorded.

• Patients were assigned to one of three groups using a random number generator: group C, group IV, or group IP.

• Patients in Group C had an intravenous (IV) infusion of 30 milliliters of normal saline (NS) over a period of ten minutes shortly after the removal of their gallbladders, in addition to an intraperitoneal injection of 40 milliliters of bupivacaine 0.25%.

• Patients in group IV received an infusion of 0.5 mg/kg dexmedetomidine intravenously (IV) in 30 milliliters of normal saline (NS) over a period of ten minutes shortly after the removal of their gallbladder, along with 40 millilitres of bupivacaine 0.25% administered intraperitoneally.

• On other hand in the Group IP patients were received 0.5 milligrams per kilogram of dexmedetomidine in 40 millilitres of 0.25% bupivacaine intraperitoneally shortly after having their gallbladders removed, along with 30 millilitres of normal saline over a period of ten minutes.

• To make an IP injection, a 50-milliliter syringe is used to mix 20 millilitres of bupivacaine at a concentration of 0.5% with 20 millilitres of normal saline.

• As a kind of premedication, glycopyrrolate injection 5mcg/kg, ondansetron injection 0.15mg/kg, and midazolam injection 0.025mg/kg were administered intravenously.

• Following pre-oxygenation with 100% oxygen, the patients were given propofol 2 mg/kg and fentanyl 1-2 micrograms/kg to produce anesthesia.

• Atracurium administered intravenously at a dose of 0.5-0.8 mg/kg aided tracheal intubation.

• Maintenance was performed on a mixture of 60 percent nitrous oxide and 40 percent oxygen, and the proportion of isoflurane was changed as necessary to keep the patient's hemodynamics within the normal range. For the maintenance of muscle paralysis, atracurium was administered initially as a bolus dose, and then on an intermittent basis thereafter.

• A multi-parameter monitor was used to continually monitor the patient's vital signs, including the electrocardiogram (ECG), oxygen saturation (spo2), end-tidal CO2, and intermittent non-invasive blood pressure (NIBP).

• Monitoring of the patient's heart rate and non-invasive blood pressure was performed three minutes after intubation, immediately after the creation of pneumoperitoneum, and at regular intervals of ten minutes.

• After intravenous administration of the study drug at 5-minute intervals up until tracheal extubation, intraoperative monitoring will continue.

• After the gall bladder has been removed, the study solution was administered intravenously gradually over a period of ten minutes.

Before the removal of the trocar in Trendelenburg's position, study solution to be given, was injected into the hepato diaphragmatic space, on the gallbladder bed, near and above the hepatoduodenal ligament in IP group. CO2 is evacuated by manual abdomen compression at the end of surgery with open trocars. After the onset of spontaneous breathing, intravenous neostigmine 0.05mg/kg and glycopyrrolate 0.01 Patients are eligible for extubation once all of the extubation criteria have been met.

• Changes in the hemodynamic parameters, such as hypotension (a fall ranging more than 20% of systolic blood pressure from baseline level), were managed with an injection of mephentermine given as 3-6 mg bolus IV or with a bolus of

ringer lactate solution. Bradycardia was treated with an injection of atropine 0.6 mg IV bolus. The occurrence of any unwanted side effects, such as nausea, vomiting, pruritis, urine retention, and the like, was recorded and handled appropriately.

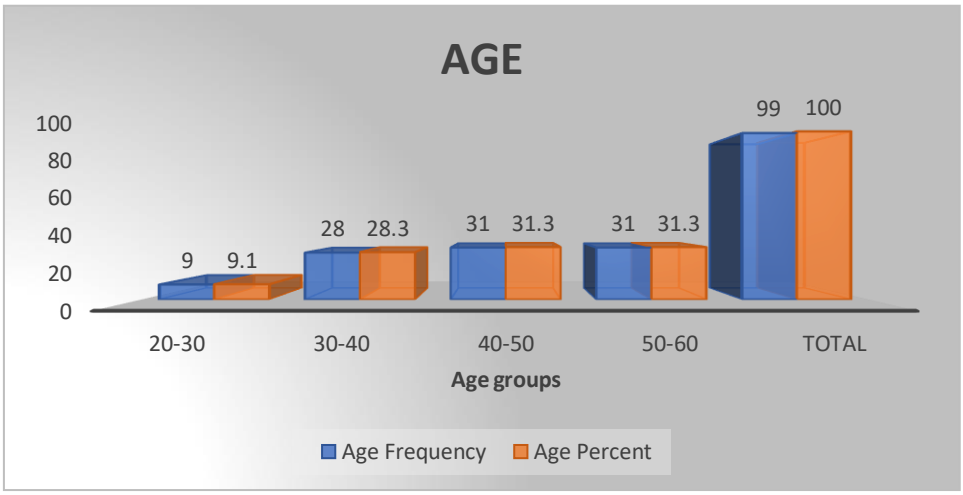
RESULT & ANALYSIS

DEMOGRAPHIC VARIABLES

Table 1: Distribution of Age

Age		
	Frequency	Percent
20-30	9	9.1
30-40	28	28.3
40-50	31	31.3
50-60	31	31.3
Total	99	100.0

GRAPH 1 – Age wise distribution of patients

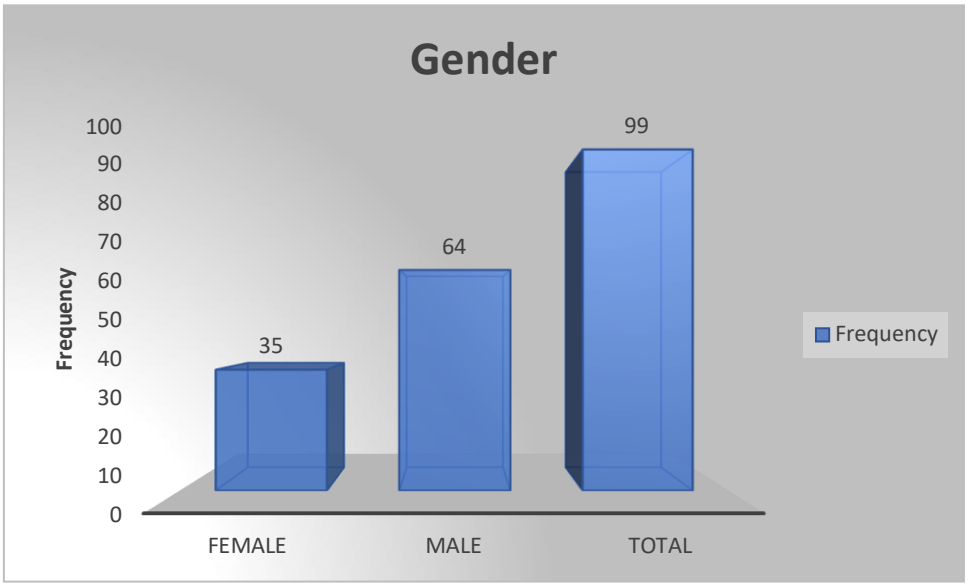


In our study, 9 (9.1%) patients were 20-30 years of age, 28 (28.3%) patients were 30-40 years of age, 31 (31.3%) patient were 40-50 years of age and 31 (31.3%) patients were 50-60 years of age.

Table 2: Distribution of Gender

Gender	Frequency	Percent
Female	35	35.4
Male	64	64.6
Total	99	100.0

GRAPH 2 – Gender wise distribution of study population

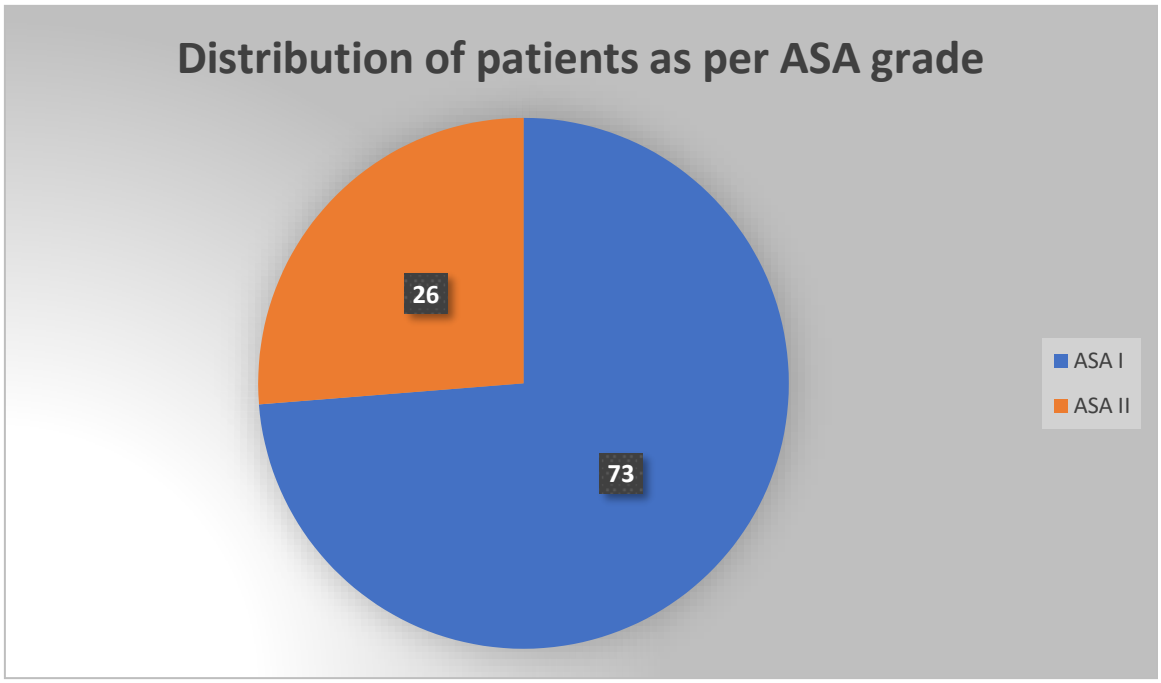


In our study, 35 (35.4%) patients were Female and 64 (64.6%) patients were male.

Table 3: Distribution of ASA Grade

ASA			
		Frequency	Percent
Valid	I	73	73.7
	II	26	26.3
	Total	99	100.0

Graph 3 - Distribution of study population as per ASA grade



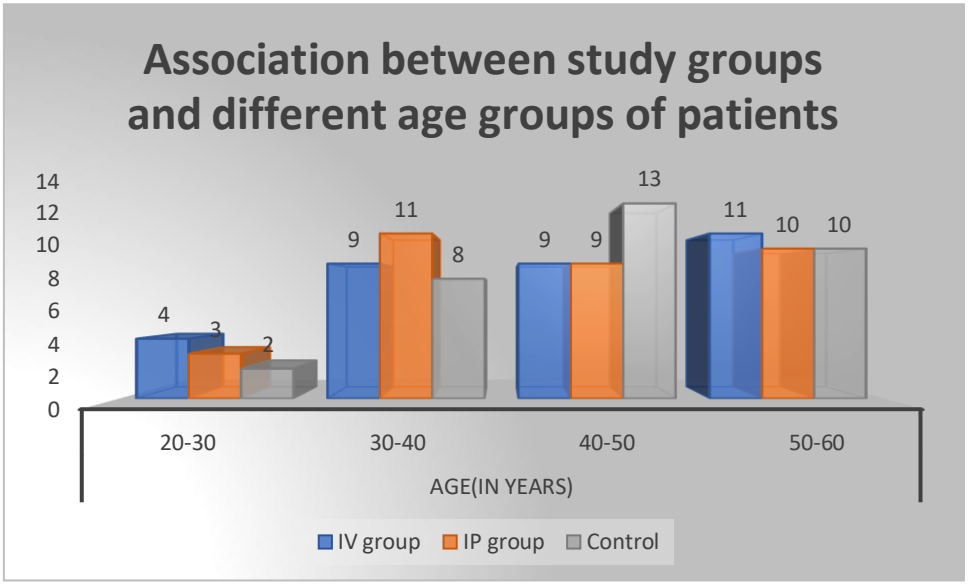
In our study, 73 (73.7%) patients belonged to ASA I and 26 (26.3%) patients belonged to ASA II

Table 4:

Association between study groups and different age groups of patients

			AGE (in years)				Chi-square Value	P-value
			20-30	30-40	40-50	50-60		
GROUPS	IV group	Count	4	9	9	11	2.263	0.894
		% Within group	12.1%	27.3%	27.3%	33.3%		
	IP group	Count	3	11	9	10		
		% Within Group	9.1%	33.3%	27.3%	30.3%		
	Control Group	Count	2	8	13	10		
		% Within Group	6.1%	24.2%	39.4%	30.3%		
Total		Count	9	28	31	31		
		% Within Group	9.1%	28.3%	31.3%	31.3%		

GRAPH 4 – AGE GROUPS COMPARISON



In IV group, 4 (12.1%) patients were 20-30 years of age, 9 (27.3%) patients were 30-40 years of age, 9 (27.3%) patient were 40-50 years of age and 11 (33.3%) patients were 50-60 years of age..

In IP group, 3 (9.1%) patients were 20-30 years of age, 11 (33.3%) patients were 30-40 years of age, 9 (27.3%) patient were 40-50 years of age and 10 (30.3%) patients were 50-60 years of age.

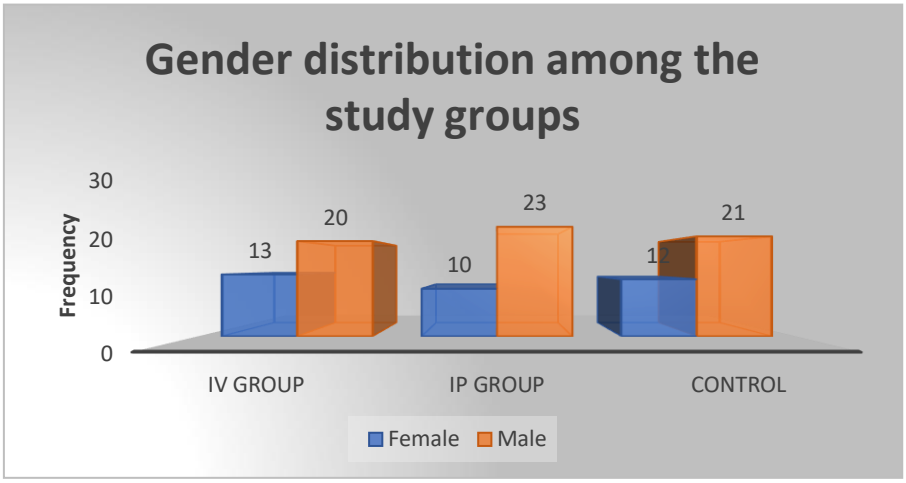
In Control, 3 (9.1%) patients were 20-30 years of age, 11 (33.3%) patients were 30-40 years of age, 9 (27.3%) patient were 40-50 years of age and 10 (30.3%) patients were 50-60 years of age.

Association of Age in Group with study Group was found to be not statistically significant (p=0.894).

Table 5: Association between study group and Gender

			Gender		Chi square test	P value
			Female	Male		
group	IV group	Count	13	20	.619	.734
		within group	39.4%	60.6%		
	IP group	Count	10	23		
		% within group	30.3%	69.7%		
	Control group	Count	12	21		
		% within group	36.4%	63.6%		
Total		Count	35	64		
		% within group	35.4%	64.6%		

GRAPH 5: GENDER DISTRIBUTION-FREQUENCY



In IV group, 13 (39.4%) patients were Female and 20 (60.6%) patients were Male.

In IP group, 10 (30.3%) patients were Female and 23 (67.7%) patients were Male..

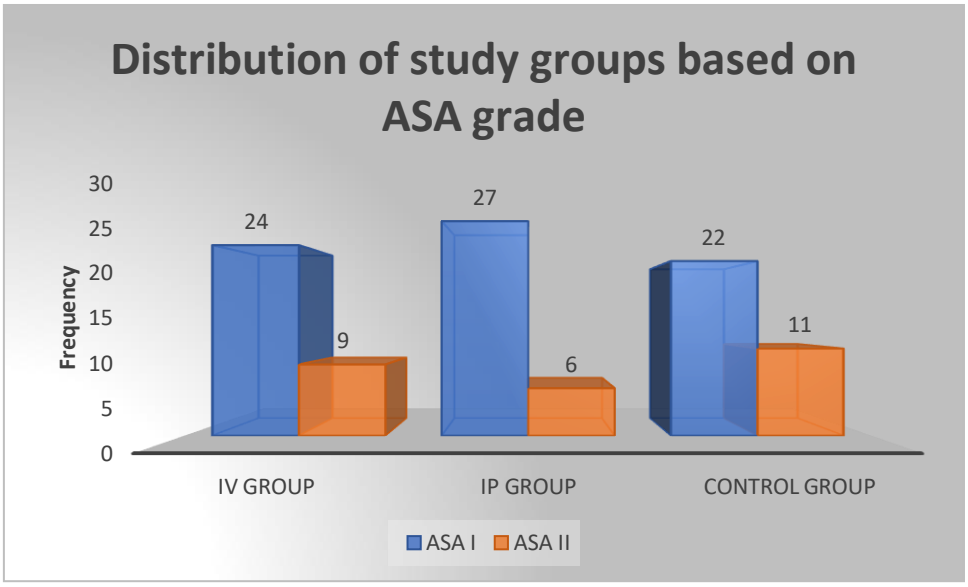
In Control, 12 (36.4%) patients were Female and 21 (63.6%) patients were Male.

Association of Gender with Group was found to be not statistically significant (p=.734)

Table 6 Distribution of study groups based on ASA grade

			ASA		Chi square test	P value
			I	II		
Group	IV group	Count	24	9	1.982[a]	.371
		% within group	72.7%	27.3%		
	IP group	Count	27	6		
		% within group	81.8%	18.2%		
	Control group	Count	22	11		
		% within group	66.7%	33.3%		
Total		Count	73	26		
		% within group	73.7%	26.3%		

GRAPH 6 STUDY GROUPS AND ASA GRADE FREQUENCY



In IV group, 24 (72.7%) patients had ASA I and 9 (27.3%) patients had ASA II.

In IP group, 27 (81.8%) patients had ASA I and 6 (18.2%) patients had ASA II

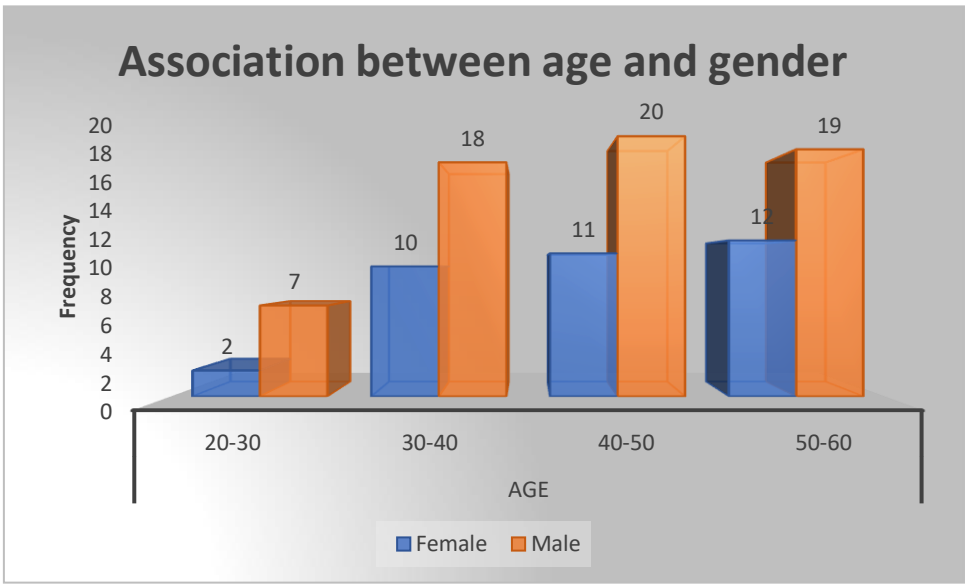
In Control, 22 (66.7%) patients had ASA I and 11 (33.3%) patients had ASA II

Association of ASA with study Group was not statistically significant (p=.371)

TABLE 7 ASSOCIATION BETWEEN GENDER & AGE

			age				Chi square test	P value
			20-30	30-40	40-50	50-60		
Gender	Female	Count	2	10	11	12	.834[a]	.841
		% within Gender	5.7%	28.6%	31.4%	34.3%		
	Male	Count	7	18	20	19		
		% within Gender	10.9%	28.1%	31.2%	29.7%		
Total		Count	9	28	31	31		
		% within Gender	9.1%	28.3%	31.3%	31.3%		

GRAPH 7 ASSOCIATION BETWEEN GENDER & AGE



Among Females, 2 (5.7%) patients were 20-30 years of age, 10 (28.6%) patients were 30-40 years of age, 11 (31.4%) patients were 40-50 years of age and 12 (34.3%) patients were 50-60 years of age.

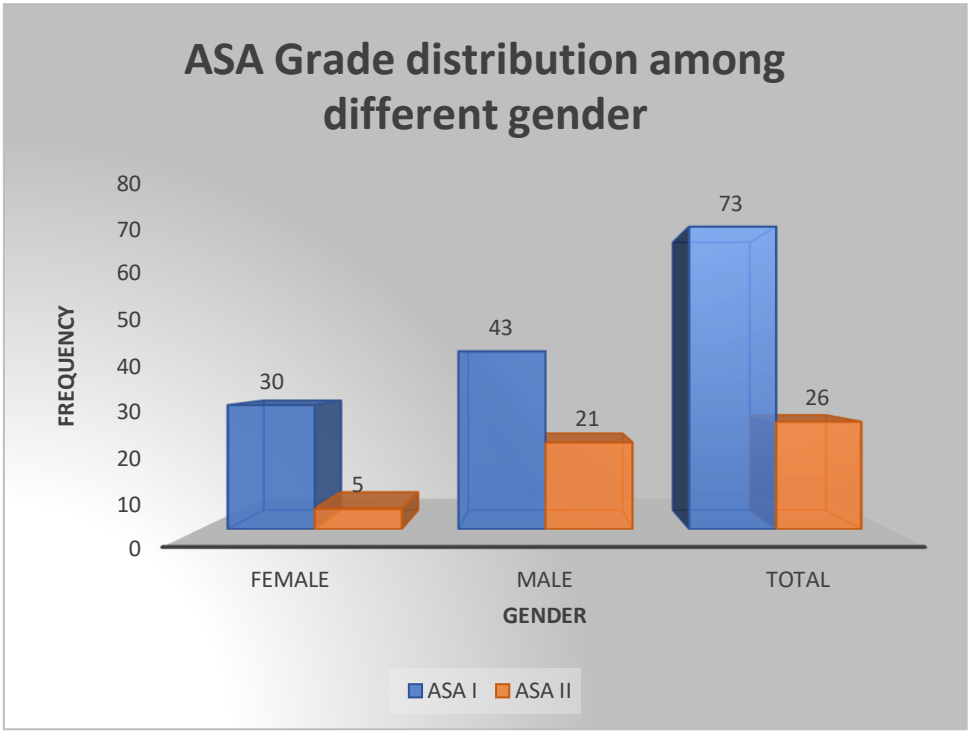
Among males, 7 (10.9%) patients were 20-30 years of age, 18 (28.1%) patients were 30-40 years of age, 20 (31.2%) patients were 40-50 years of age and 19 (29.7%) patients were 50-60 years of age.

Association of Gender with age was not statistically significant (p=0.841).

Table 8 Association between: gender & ASA

			ASA		Chi square test	P value
			I	II		
Gender	Female	Count	30	5	4.010	.057
		% within Gender	85.7%	14.3%		
	Male	Count	43	21		
		% within Gender	67.2%	32.8%		
Total		Count	73	26		
		% within Gender	73.7%	26.3%		

GRAPH 8 Association between: gender &ASA



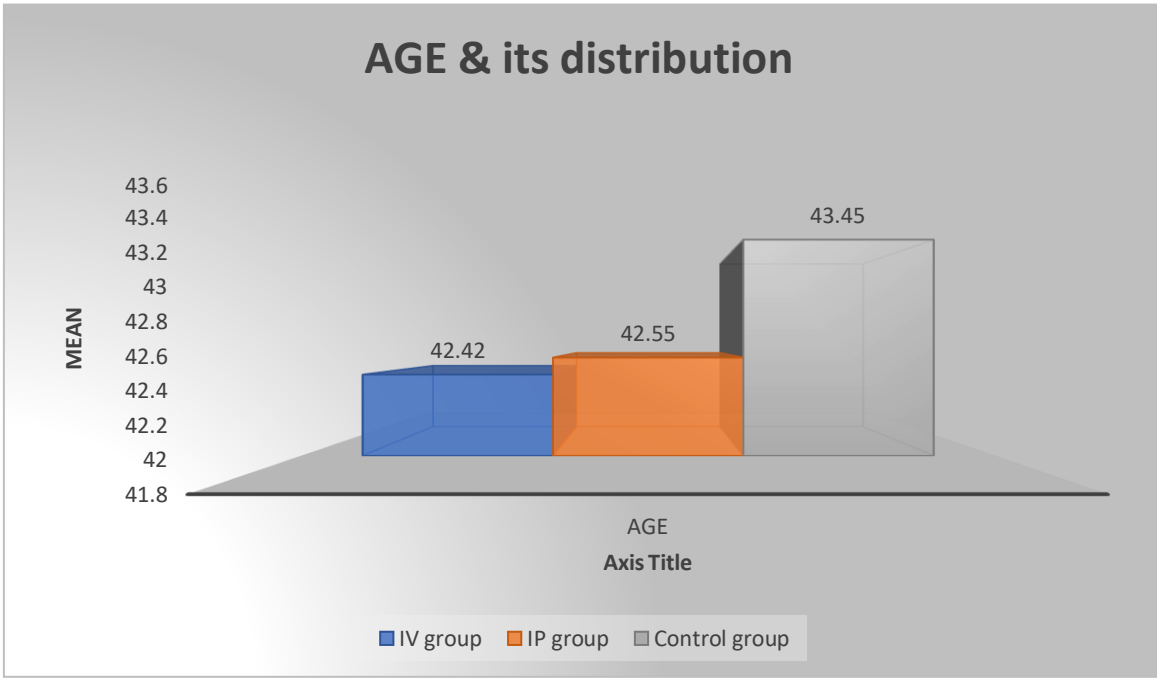
In Female, 30 (85.7%) patients had ASA I and 5 (14.3%) patients had ASA II. In male, 5 (14.3%) patients had ASA I and 21 (32.8%) patients had ASA II. Association of Gender with ASA was not statistically significant (p=0.057).

Statistical analysis of demographic variables and their significance

Table 9 Mean Distribution of Age Among Study Groups

Age(Years)	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
AGE	42.42	9.824	42.55	8.927	43.45	8.588	0.278	0.870
Statistically insignificant								

Graph 9 Mean Distribution of Age



In IV group, the mean Age (mean± s.d.) of patients was 42.42±9.824.

In IP group, the mean Age (mean± s.d.) of patients was 42.55±8.927.

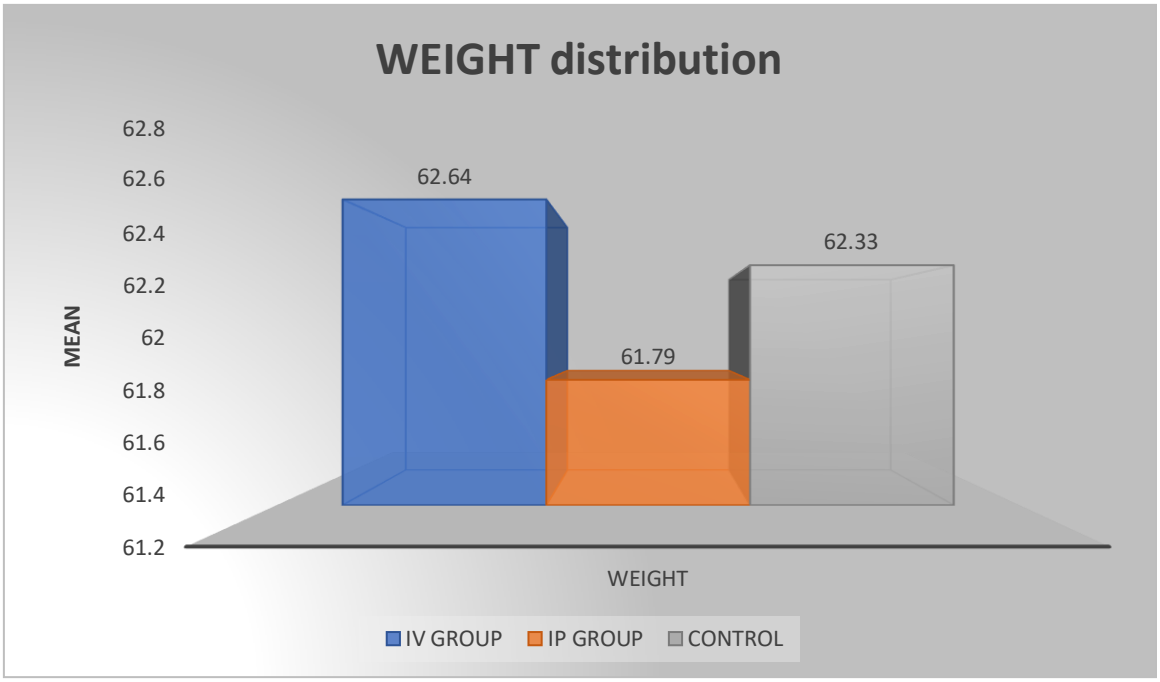
In Control group, the mean Age (mean± s.d.) of patients was 43.45±8.588.

Distribution of mean Age with Group was not statistically significant (p=0.870)

TABLE 10 -Mean Weight Distribution Among Study Groups

	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
Weight	62.64	7.004	61.79	7.227	62.33	7.825	0.300	0.861
Statistically insignificant								

GRAPH 10 -Mean Weight Distribution Among Study Groups



In IV group, the mean Weight (in Kg) (mean± s.d.) of patients was 62.64±7.004.

In IP group, the mean Weight (in Kg) (mean± s.d.) of patients was 61.79±7.227.

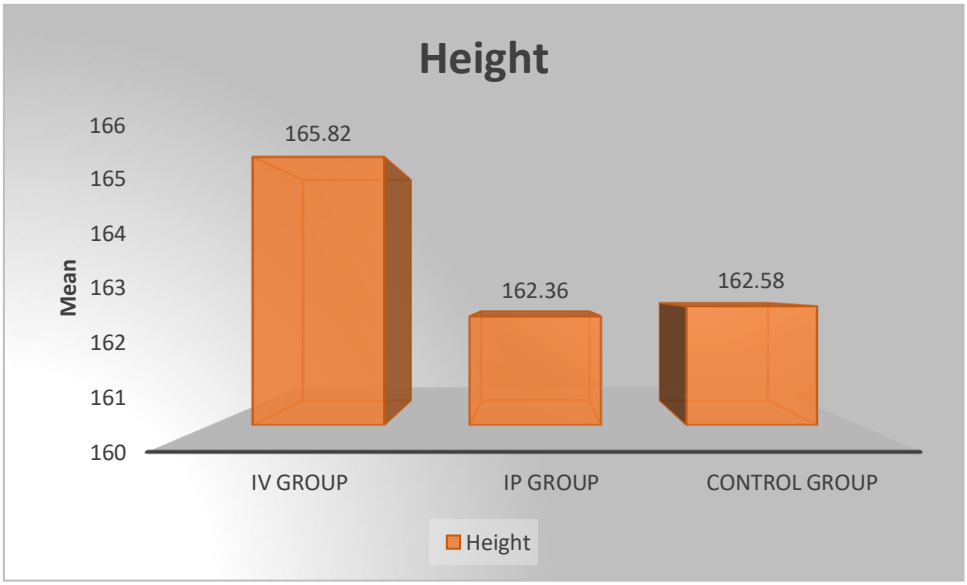
In Control group, the mean Weight (in Kg) (mean± s.d.) of patients was 62.33±7.825.

Distribution of mean Weight (in Kg) with Group was not statistically significant (p=0.861)

TABLE 11 -Mean Height Distribution Among Study Groups

Height (cms)	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
Height	165.82	5.720	162.36	6.020	162.58	6.083	7.395	0.025
Statistically insignificant								

GRAPH 11 -MEAN HEIGHT DISTRIBUTION AMONG STUDY GROUPS



In IV group, the mean Height (in cms) (mean± s.d.) of patients was 165.82±5.720.

In IP group, the mean Height (in cms) (mean± s.d.) of patients was 162.36±6.020.

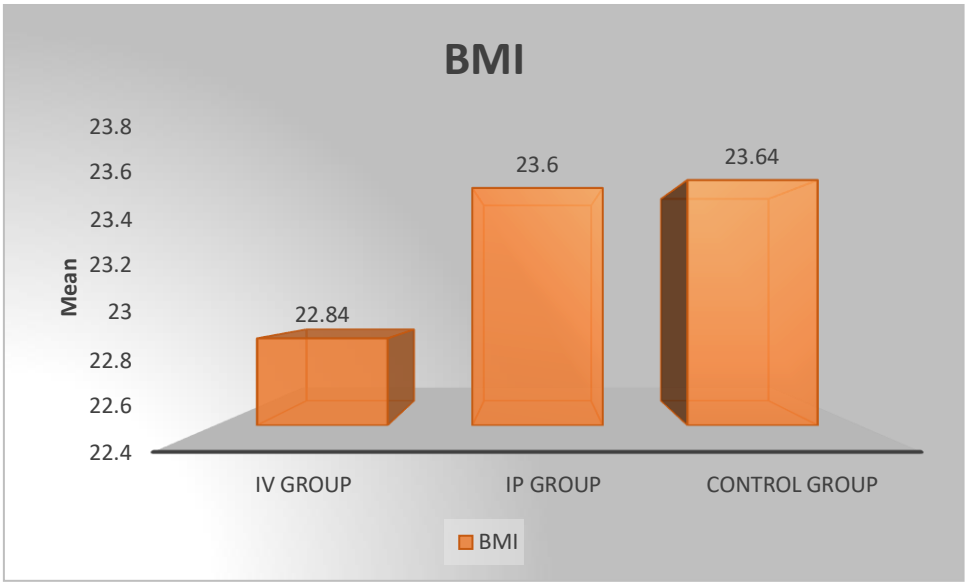
In Control group, the mean Height (in cms) (mean± s.d.) of patients was 162.58±6.083.

Distribution of mean Height (in cms) with Group was not statistically significant (p=0.025).

TABLE 12 -Mean BMI Distribution Among Study Groups

BMI	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
BMI	22.84	2.91	23.60	2.80	23.64	3.16	1.555	0.460
Statistically not significant								

GRAPH 12 -Mean BMI Distribution Among Study Groups



In IV group, the mean BMI (mean± s.d.) of patients was 22.84±2.91.

In IP group, the mean BMI (mean± s.d.) of patients was 23.60±2.80.

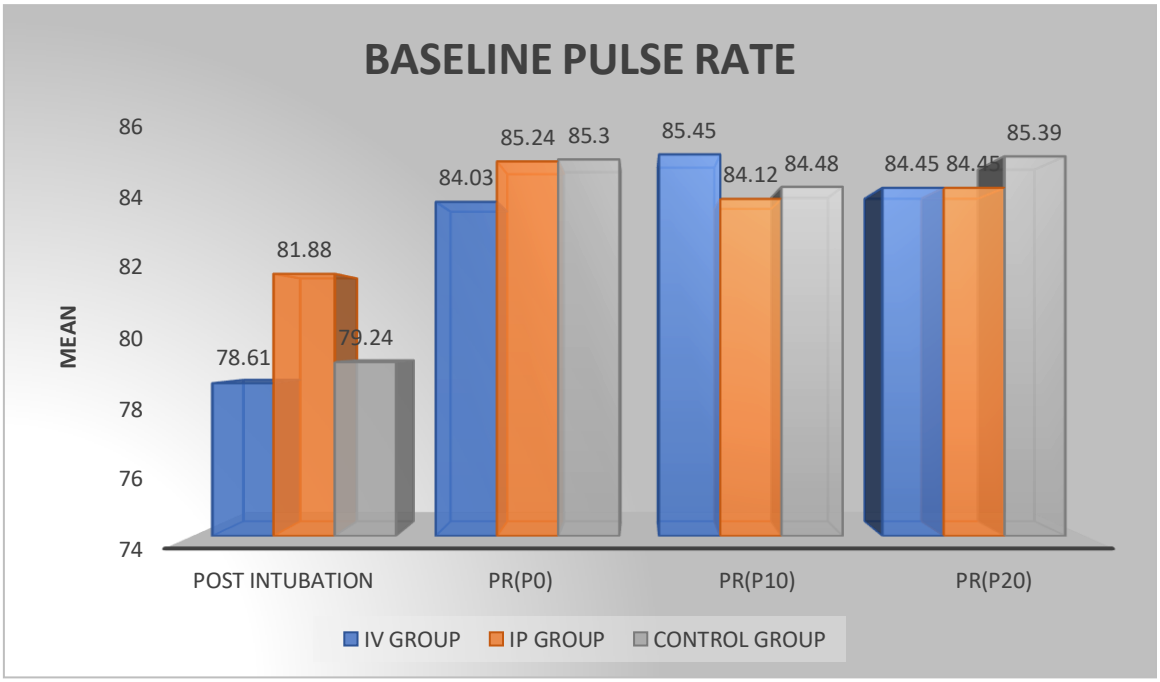
In Control group, the mean BMI (mean± s.d.) of patients was 23.64±3.16.

Distribution of mean BMI with Group was not statistically significant (p=0.460).

Table 13 Comparison of baseline pulse rate among three groups before giving study drug

PR(Baseline)	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
PR(Post intubation)	78.61	5.953	81.88	5.639	79.24	6.011	5.465	0.065
PR(P0)	84.03	3.704	85.24	3.482	85.3	3.504	2.775	0.250
PR(P10)	85.45	3.51	84.12	3.11	84.48	3.289	2.689	0.261
PR(P20)	84.45	3.053	84.45	2.927	85.39	3.791	1.497	0.473

GRAPH 13 MEAN baseline pulse rate comparison (before giving study drug)



In IV group, the mean PR (Post intubation) (mean± s.d.) of patients was 78.61±5.953.

In IP group, the mean PR (Post intubation) (mean± s.d.) of patients was 81.88±5.639.

In Control group, the mean PR (Post intubation) (mean± s.d.) of patients was 79.24±6.011.

In IV group, the mean PR(P0) (mean± s.d.) of patients was 84.03±3.704.

In IP group, the mean PR(P0) (mean± s.d.) of patients was 85.24±3.482.

In Control group, the mean PR(P0) (mean± s.d.) of patients was 85.3±3.504.

In IV group, the mean PR(P10) (mean± s.d.) of patients was 85.45±3.51.

In IP group, the mean PR(P10) (mean± s.d.) of patients was 84.12±3.11.

In Control group, the mean PR(P10) (mean± s.d.) of patients was 84.48±3.289.

In IV group, the mean PR (P20) (mean± s.d.) of patients was 84.45±3.053.

In IP group, the mean PR(P20) (mean± s.d.) of patients was 84.45±2.927.

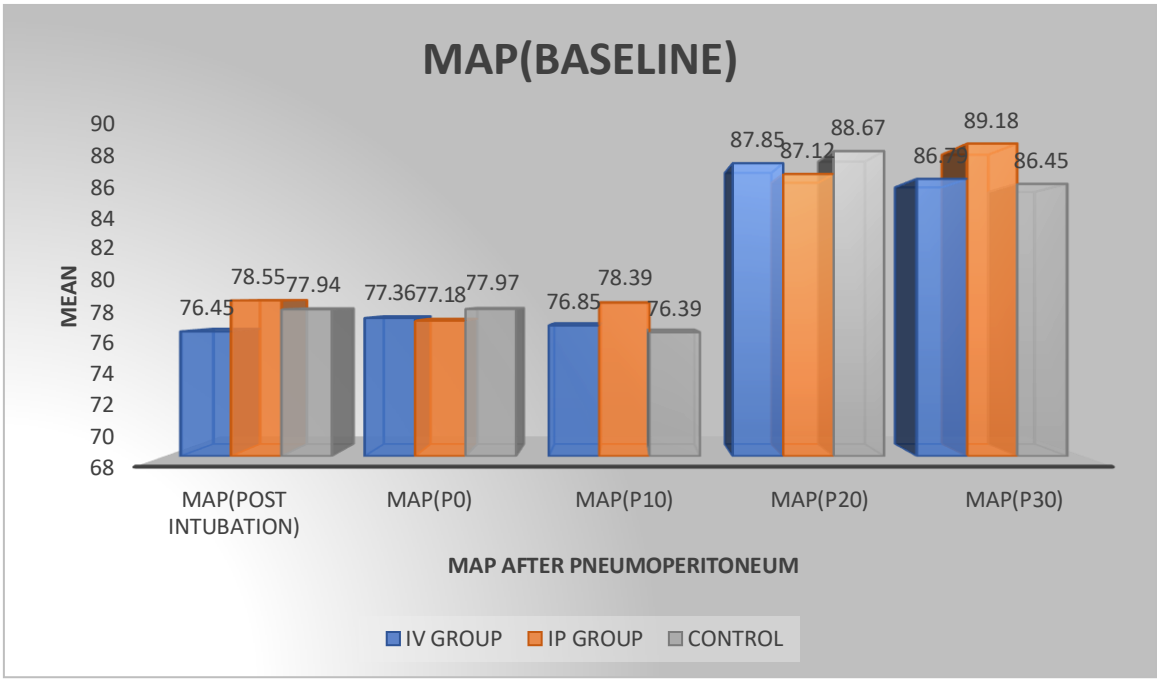
In Control group, the mean PR(P20) (mean± s.d.) of patients was 85.39±3.791.

Upon comparing the baseline pulse rate among three study groups the following results had been obtained and they were found to be statistically not significant. (P >0.005)

TABLE 14 Comparison of Baseline Map Before Giving Study Drug

MAP (Post intubation)	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
MAP (Post intubation)	76.45	4.459	78.55	5.013	77.94	4.337	3.634	0.162
MAP(P0)	77.36	5.024	77.18	5.271	77.97	4.883	0.569	0.752
MAP(P10)	76.85	4.515	78.39	4.376	76.39	4.697	2.962	0.227
MAP (P20)	87.85	4.324	87.12	5.308	88.67	5.066	1.583	0.453
MAP (P30)	86.79	4.702	89.18	4.844	86.45	4.944	5.884	0.053
Statistically insignificant								

GRAPH **14 Comparison of Baseline Map Before Giving Study Drug**



In IV group, the mean MAP (Post intubation) (mean± s.d.) of patients was 76.45±4.459.

In IP group, the mean MAP (Post intubation) (mean± s.d.) of patients was 78.55±5.013.

In Control group, the mean MAP (Post intubation) (mean± s.d.) of patients was 77.94±4.337.

Distribution of mean MAP (Post intubation) with Group was not statistically significant (p=0.162).

In IV group, the mean MAP(P0) (mean± s.d.) of patients was 77.36±5.024.

In IP group, the mean MAP(P0) (mean± s.d.) of patients was 77.18±5.271.

In Control group, the mean MAP(P0) (mean± s.d.) of patients was 77.97±4.883.

Distribution of mean MAP(P0) with Group was not statistically significant (p=0.752).

In IV group, the mean MAP(P10) (mean± s.d.) of patients was 76.85±4.515.

In IP group, the mean MAP (P10) (mean± s.d.) of patients was 78.39±4.376.

In Control group, the mean MAP(P10) (mean± s.d.) of patients was 76.39±4.697.

Distribution of mean MAP(P10) with Group was not statistically significant (p=0.227).

In IV group, the mean MAP (P20) (mean± s.d.) of patients was 87.85±4.324.

In IP group, the mean MAP (P20) (mean± s.d.) of patients was 87.12±5.308.

In Control group, the mean MAP (P20) (mean± s.d.) of patients was 88.67±5.066.

Distribution of mean MAP(P20) with Group was not statistically significant (p=0.453).

In IV group, the mean MAP (P30) (mean± s.d.) of patients was 86.79±4.702.

In IP group, the mean MAP(P30) (mean± s.d.) of patients was 89.18±4.844.

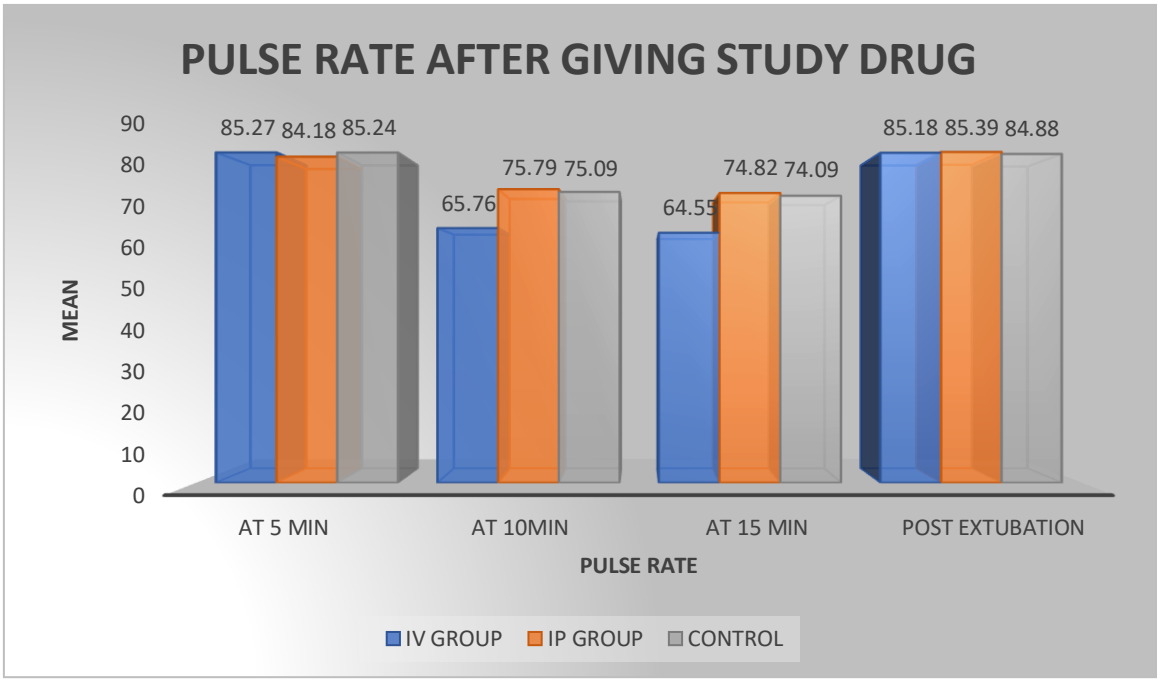
In Control group, the mean MAP(P30) (mean± s.d.) of patients was 86.45±4.944.

Distribution of mean MAP(P30) with Group was not statistically significant (p=0.053).

TABLE 15 Comparison of Mean Pulse Rate After Giving Study Drug

Post study drug PR (study 5min)	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
Post study drug PR (study 5min)	85.27	3.556	84.18	2.755	85.24	3.26	2.337	0.311
PR (10min)	65.76	3.241	75.79	3.199	75.09	3.146	63.866	0.0001*
PR (15min)	64.55	2.818	74.82	3.015	74.09	3.156	64.420	0.0001*
PR(Post extubation)	85.18	3.245	85.39	3.061	84.88	3.305	0.499	0.799
*Statistically significant								

GRAPH 15 COMPARISON OF MEAN PULSE RATE AFTER GIVING STUDY DRUG



At 5min interval after giving study drug :

In IV group, the mean PR (5min) (mean± s.d.) of patients was 85.27±3.556.

In IP group, the mean PR (5min) (mean± s.d.) of patients was 84.18±2.755.

In Control group, the mean PR(5min) (mean± s.d.) of patients was 85.24±3.26.

These values were found to be not statistically significant (p=0.311).

At 10min time interval following study drug :

In IV group, the mean PR (10min) (mean± s.d.) of patients was 65.76±3.241.

In IP group, the mean PR (10min) (mean± s.d.) of patients was 75.79±3.199.

In Control group, the mean PR(10min) (mean± s.d.) of patients was 75.09±3.146.

At 20min time interval following study drug

In IV group, the mean PR(15min) (mean± s.d.) of patients was 64.55±2.818.

In IP group, the mean PR(15min) (mean± s.d.) of patients was 74.82±3.015.

In Control group, the mean PR(15min) (mean± s.d.) of patients was 74.09±3.156.

At extubation

In IV group, the mean PR (Post extubation) (mean± s.d.) of patients was 85.18±3.245.

In IP group, the mean PR (Post extubation) (mean± s.d.) of patients was 85.39±3.061.

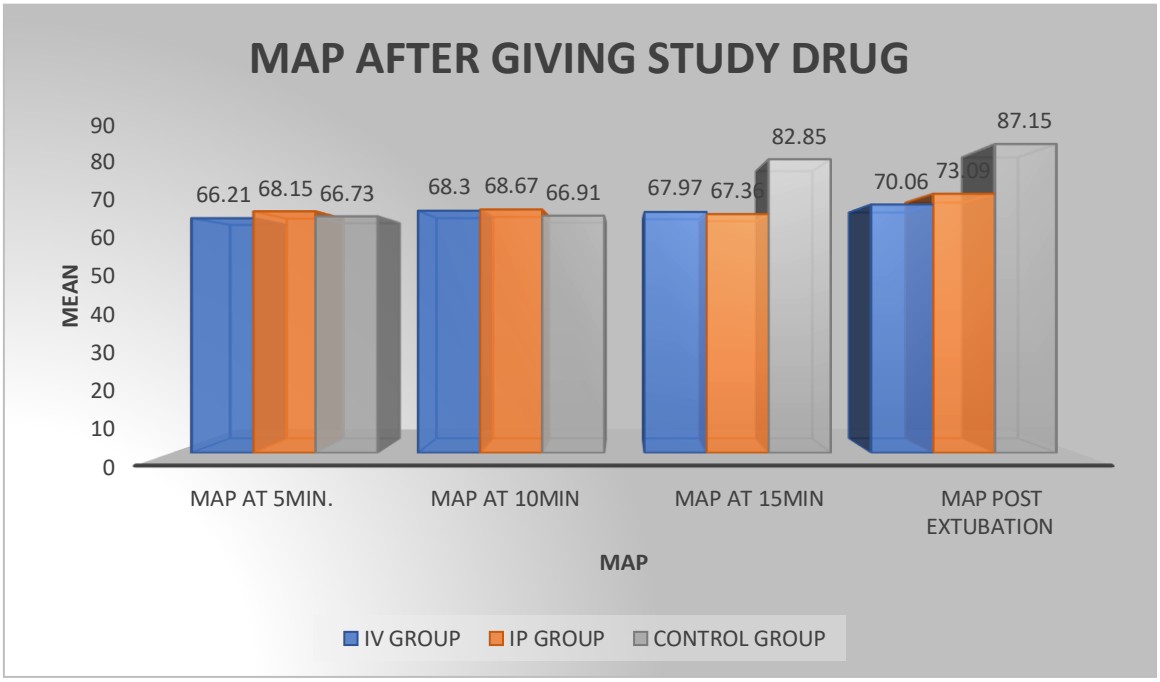
In Control group, the mean PR (Post extubation) (mean± s.d.) of patients was 84.88±3.305.

Statistical significant values are found to be at 10 min and 15 min interval following the administration of study drug.

TABLE 16 Comparison Of Mean Map After Giving Study Drug

MAP(Post study drug)	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
MAP (study drug 5min)	66.21	5.189	68.15	4.529	66.73	4.666	2.765	0.251
MAP(study drug 10min)	68.30	3.917	68.67	4.998	66.91	4.426	2.573	0.276
MAP (study drug 15min)	67.97	1.610	67.36	1.729	82.85	3.977	66.979	0.0001
MAP (Post extubation)	70.06	3.381	73.09	1.259	87.15	4.711	72.025	0.0001
Statistically not significant								

GRAPH 16 Comparison of Mean MAP After Giving Study Drug



MAP After giving study drug :

In IV group, the mean MAP(study drug 5min) (mean± s.d.) of patients was 66.21±5.189.

In IP group, the mean MAP(study drug 5min) (mean± s.d.) of patients was 68.15±4.529.

In Control group, the mean MAP(study drug 5min) (mean± s.d.) of patients was 66.73±4.666.

Distribution of mean MAP(study drug 5min) with Group was not statistically significant (p=0.251).

In IV group, the mean MAP(study drug 10min) (mean± s.d.) of patients was 68.30±3.917.

In IP group, the mean MAP(study drug 10min) (mean± s.d.) of patients was 68.67±4.998.

In Control group, the mean MAP(study drug 10min) (mean± s.d.) of patients was 66.91±4.426.

Distribution of mean MAP(study drug 10min) with Group was not statistically significant (p=0.276).

In IV group, the mean MAP (study drug 15min) (mean± s.d.) of patients was 67.97±1.610.

In IP group, the mean MAP (study drug 15min) (mean± s.d.) of patients was 67.36±1.729.

In Control group, the mean MAP(study drug 15min) (mean± s.d.) of patients was 82.85±3.977.

Distribution of mean MAP(study drug 15min) with Group was statistically significant (p=0.0001).

In IV group, the mean MAP (Post extubation) (mean± s.d.) of patients was 70.06±3.381.

In IP group, the mean MAP (Post extubation) (mean± s.d.) of patients was 73.09±1.259.

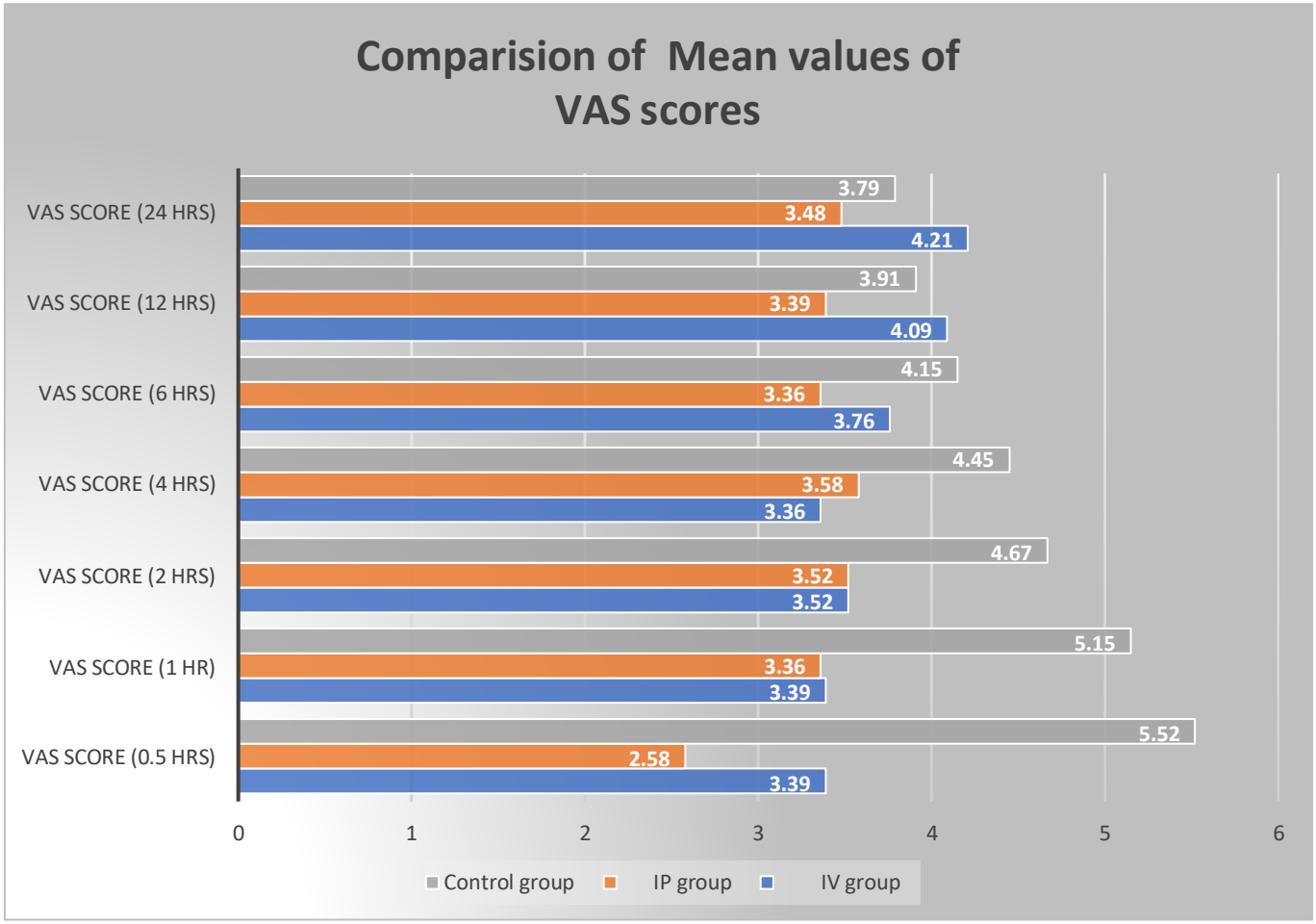
In Control group, the mean MAP (Post extubation) (mean± s.d.) of patients was 87.15±4.711.

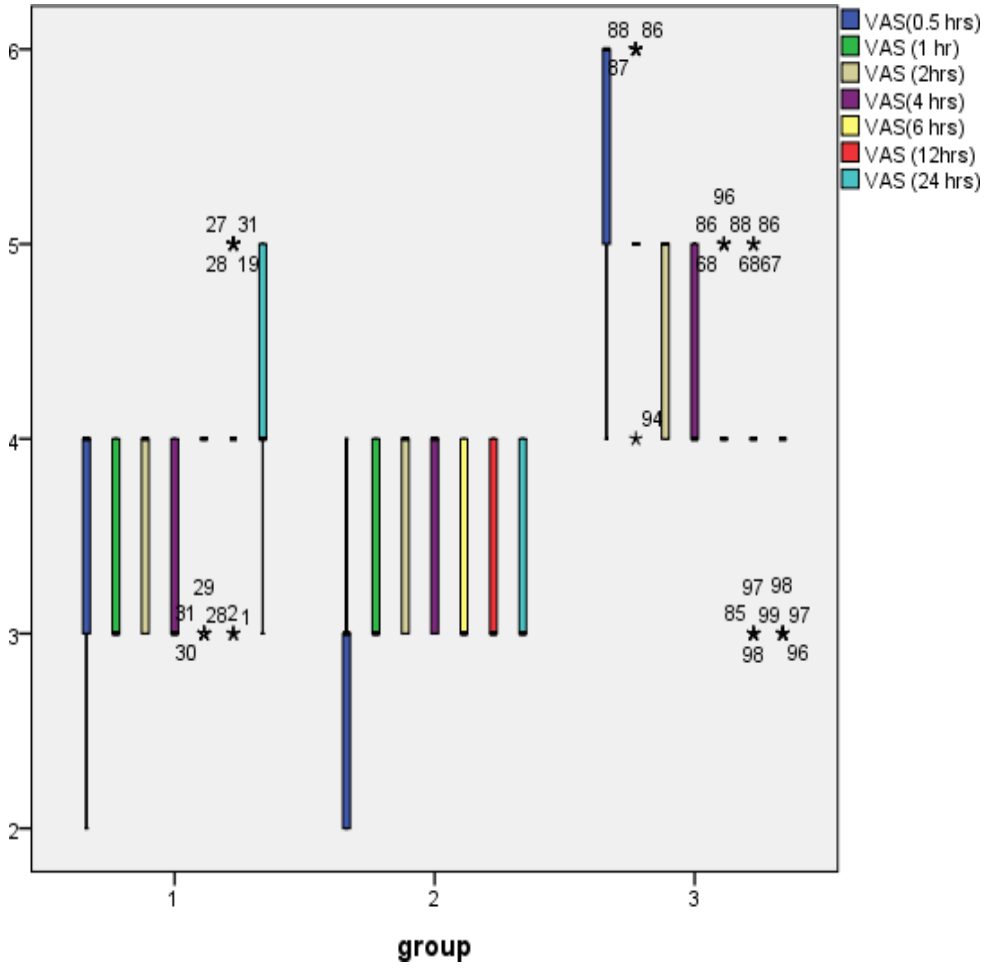
Distribution of mean MAP (Post extubation) with Group was statistically significant (p=0.0001).

TABLE 17 Comparison of mean VAS Scores

VAS score (0.5 hrs)	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
VAS score (0.5 hrs)	3.39	0.704	2.58	0.561	5.52	0.619	74.781	0.0001
VAS score (1 hr)	3.39	0.496	3.36	0.489	5.15	0.442	71.553	0.0001
VAS score (2 hrs)	3.52	0.508	3.52	0.508	4.67	0.479	52.038	0.0001
VAS score (4 hrs)	3.36	0.489	3.58	0.502	4.45	0.506	45.401	0.0001
VAS score (6 hrs)	3.76	0.435	3.36	0.489	4.15	0.364	35.879	0.0001
VAS score (12 hrs)	4.09	0.522	3.39	0.496	3.91	0.522	25.611	0.0001
VAS score (24 hrs)	4.21	0.696	3.48	0.508	3.79	0.415	21.149	0.0001
Statistically significant								

GRAPH 17 Comparison of mean VAS Scores





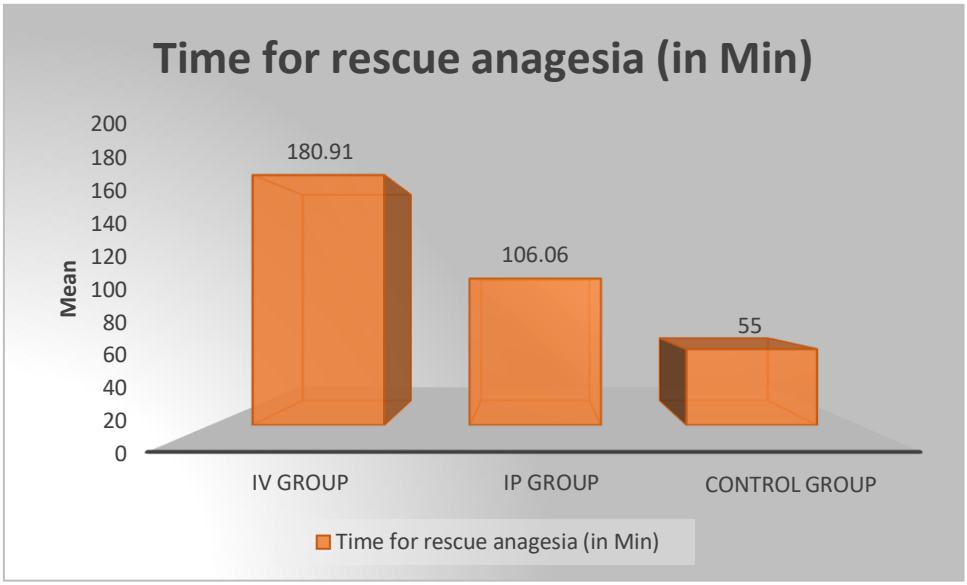
GRAPH 18 Box And Whisker Plot Of Vas Score

In the study, the VAS scores were compared during the post operative period at 0.5 hours,1 hour, 2 hours, 4 hours, 12 hours and 24 hours respectively. It was observed that the mean VAS scores at those respective time intervals were found to be statistically significant(p=0.0001) among all the three study groups.

Table 18 Time for rescue anagesia (in Min)

Time for rescue anagesia (in Min)	IV group		IP group		Control group		Kruskal wallis test	P value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
Time for rescue anagesia (in Min)	180.91	41.617	106.06	8.269	55.00	6.960	84.346	0.0001
Statistically significant								

GRAPH 19 Time for rescue anagesia (in Min)



In IV group, the mean Time for rescue anagesia (in Min) (mean± s.d.) of patients was 180.91±41.617.

In IP group, the mean Time for rescue anagesia (in Min) (mean± s.d.) of patients was 106.06±8.269.

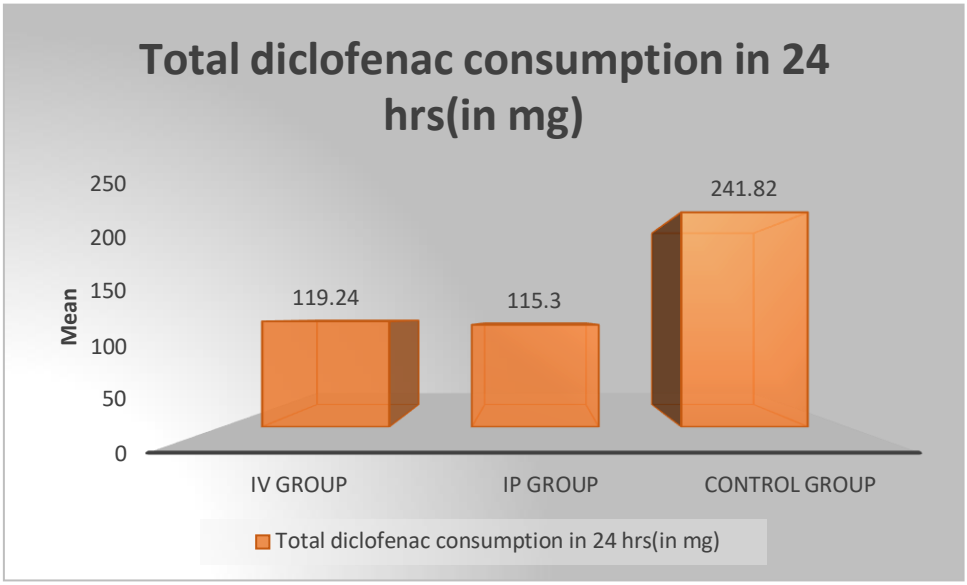
In Control group, the mean Time for rescue anagesia (in Min) (mean± s.d.) of patients was 55.00±6.960.

Distribution of mean Time for rescue anagesia (in Min) with Group was statistically significant (p=0.0001).

Table 19 Total diclofenac consumption in 24 hrs(in mg)

Total diclofenac consumption in 24 hrs(in mg)	IV group		IP group		Control group		Kruskal wallis test	P val
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std deviation		
Total diclofenac consumption in 24 hrs(in mg)	119.24	40.372	115.30	30.896	241.82	30.767	65.389	0.00
Statistically significant								

Graph 20 Total diclofenac consumption in 24 hrs (in mg)



In IV group, the mean Total diclofenac consumption in 24 hrs(in mg) (mean± s.d.) of patients was 119.24±40.372.

In IP group, the mean Total diclofenac consumption in 24 hrs(in mg) (mean± s.d.) of patients was 115.30±30.896.

In Control group, the mean Total diclofenac consumption in 24 hrs(in mg) (mean± s.d.) of patients was 241.82±30.767.

Distribution of mean Total diclofenac consumption in 24 hrs(in mg) with Group was statistically significant (p=0.0001).

DISCUSSION

DISCUSSION

Due to the fact that laparoscopic cholecystectomy is a day case surgery, it is essential to have appropriate analgesia and to recover as quickly as possible. Postoperative discomfort is the most typical problem that arises following laparoscopic surgery. It takes approximately six hours after the surgery for the patient to experience the worst of the pain, after which it begins to lessen progressively over the course of a few days; however, this time frame varies widely depending on the patient.

The peritoneum is a serous membrane that surrounds the bulk of the organs that are located within the abdominal cavity. It also surrounds the abdominal cavity itself. It is a very thin layer that is readily damaged, and it was not meant to be resilient against changing conditions such as dry and cold carbon dioxide.

When undergoing laparoscopic surgery, patients may have postoperative discomfort that is either somatic (at the incision site) or visceral (caused by residual carbon dioxide in the peritoneal cavity). The primary factors that contribute to visceral discomfort are inflammation of the peritoneum and stimulation of the phrenic nerve.

Due to differences in individual threshold, subjectivity, and the complexity of measuring, accurate pain evaluation can be challenging. It was found that IP administration of Inj. Bupivacaine and dexmedetomidine in LC is a safe alternative approach that significantly reduces the requirement for analgesics

and significantly reduces post-operative pain management in laparoscopic cholecystectomy cases utilising intra peritoneal Bupivacaine 0.5% and dexmedetomidine 0.5mcg/kg.

The main benefit of using local anaesthetics and alpha 2 agonists, like dexmedetomidine, is that they don't have the negative side effects of opioids, which can prolong the patient's recovery and ability to leave the hospital. By using these medicines, this can be avoided. Only a few of the possible adverse effects include post-operative nausea, sleepiness, a slow recovery of gastrointestinal motility, and itching. Additionally, if local anaesthetics rather than opioids are used as the anaesthetic technique, the recovery period needed to resume normal bowel function may be shortened. When used at a low dose, dexmedetomidine offered a number of additional benefits. These included improved control over intra-operative hemodynamics, a higher post-operative sedation score, and enhanced cognitive function in the post-operative period.

The present study was a randomized controlled study that was carried out between December 2020 and September 2022 at the Department of Anaesthesiology of the B.L.D. E (DEEMED TO BE UNIVERSITY) Shri B. M. Patil Medical College, Hospital, and Research Centre in VIJAYAPURA. The study was blinded to both participants and observers. There were a total of 99 patients who participated in this trial, and they were divided at random into three groups: the IV group, the IP group, and the Control group. Patients who

fulfilled the inclusion criteria and were scheduled to undergo laparoscopic cholecystectomy under general anesthesia are included in the study. The primary purpose of the research was to compare the three different study groups with regard to post-operative VAS score, amount of time needed for rescue analgesia, and total amount of diclofenac consumed.

Despite the fact that patients were assigned at random by a computer-generated slip, the majority of the patients belonged to the age group of 40-50 and 50-60 years [31 (31.3%); only 9 patients were between the ages of 20-30; 28 patients (28.3%) belonged to the age group of 30-40; however, this was not statistically significant (p=0.894).

DEMOGRAPHIC VARIABLES: AGE In our research, the age of participants in the Control group was significantly older than those in the IP group [42.55±8.927] and the IV group [42.42±9.824], but this difference did not reach the level of statistical significance (p=0.870).

Comparing the sexes: The male population in our research was higher (64,64.6%) than the female population (35,35.4%), but this difference did not reach the level of statistical significance (p=0.734).

ASA grade comparison: Our research revealed that the incidence of ASA I was highest in the IP group (27 out of 81.8% of patients), followed by the IV group (24 out of 72.7%), and then the control group (22 out of 66.7%). However, this did not reach the level of statistical significance (p=0.371).

It was discovered that a greater proportion of patients in the female group had ASA I [30 (85.7%)] compared to the male group [5 (14.3%)], however this difference was not statistically significant (p=0.057).

Other demographic factors, such as height, weight, and body mass index (BMI), were found to be comparable across all three groups, and their differences were not statistically significant ($p > 0.05$).

HEMODYNAMIC VARIABLES:

BASELINE PARAMETERS:

Pulse rate (PR) - The PR following intubation, which served as the baseline, was discovered to be higher in the IP group [81.88±5.639] in comparison to the Control group [79.24±6.011] and the IV group [78.61±5.953], however this difference did not reach statistical significance (p=0.065). PR(P0) was higher in the IP group [85.24±3.482] compared to the Control group [85.3±3.504] and the IV group [84.03±3.704], but this did not reach statistical significance (p=0.250), and PR(P10) was higher in the IV group [85.45±3.51] compared to the Control group [84.48±3.289] and the IP group [84.12±3.11], but this also did not reach

statistical significance (p= According to the results of our research, the PR (P20) was significantly higher in the Control group (85.39±3.791) compared to the IV group (84.45±3.053) and the IP group (84.45±2.927), but this difference did not reach the level of statistical significance (p=0.473).

Mean arterial pressure (MAP): We found that, MAP (Post intubation) was higher in the IP group [78.55±5.013] in comparison to the Control group [77.94±4.337] and the IV group [76.45±4.459], although this difference did not reach statistical significance (p=0.162).

It was discovered that the MAP (P0) was higher in the Control group (77.97±4.883) in comparison to the IP group (77.36±5.024) and the IV group (77.36±5.024), but this difference did not reach the level of statistical significance (p=0.752).

In our research, the MAP (P10) was greater in the IP group [78.39±4.376] compared to the IV group [76.85±4.515] and the Control group [76.39±4.697], but this did not reach the level of statistical significance (p=0.227). Furthermore, the MAP (P20) was greater in the Control group [88.67±5.066] compared to the IV group [87.85±4.324] and the IP group [87.12±5.3 Although the MAP (P30) was significantly higher in the IP group (89.18±4.844) compared to the IV group (86.79±4.702) and the control group (86.79±4.702), this difference did not reach statistical significance (p=0.053).

Hemodynamic variables after delivering study drug:

Following the administration of the medicine under research, the subjects' hemodynamic parameters were assessed at 5, 10, and 15 minutes, as well as after extubation. The following is a summary of our findings:

Pulse rate (PR) - We found that the PR (5min) was significantly higher in the IV group [85.27±3.556] in comparison to the Control group [85.24±3.26] and the IP group [84.18±2.755]; however, this difference did not reach statistical significance (p=0.311). It was discovered that the PR (10min) was significantly higher in the IP group [75.79±3.199] in comparison to the Control group [75.09±3.146] and the IV group [65.76±3.241]. This difference was statistically significant (p=0.0001) Similarly, the PR (study 15min) was found to be significantly higher in the IP group [74.82±3.015] in comparison to the Control group [74.09±3.156] and the IV group [64.55±2.818]; this difference was shown to be statistically significant (p=0.0001)

According to the results of our research, the proportion of patients with PR (Post extubation) was highest in the IP group [85.39±3.061], followed by the IV group [85.18±3.245], and then the Control group [84.88±3.305]. However, this difference did not reach statistical significance (p=0.799).

Mean arterial pressure (MAP) was determined following the administration of the study drug at intervals of 5, 10, and 15 minutes, as well as after extubation. The following has been taken into consideration.

MAP (study drug 5min) was significantly higher in the IP group (68.15±4.529) compared to the Control group (66.73±4.666) and the IV group (66.21±5.189), but this difference did not reach statistical significance (p=0.251).

It was discovered that the MAP (study drug 10 min) was higher in the IP group [68.67±4.998] in comparison to the IV group [68.30±3.917] and the Control group [66.91±4.426], although this difference did not reach the level of statistical significance (p=0.276).

In our research, the MAP (mean arterial pressure at 15 minutes) was found to be significantly higher in the control group (82.85± 3.977) than in the IV group (67.97 ±1.610) and the IP group (67.36± 1.729), despite the fact that this difference was statistically significant (p = 0.0001).

Despite the fact that the MAP (Post extubation) in the Control group was higher (87.15±4.711) than it was in the IP group (73.09±1.259) and the IV group (70.06±3.381), we observed that this difference was statistically significant (p=0.0001).

Comparing the post-operative VAS scores of the three groups, as well as the efficacy of the study drug on reducing the requirement for rescue analgesia and

increasing the amount of time it may be used, is the primary purpose of our research.

Comparison of the VAS Score - Based on the findings of our research, we found that the VAS score in the Control group was consistently higher compared to the IP group and the IV group at all of the supplied time intervals - 1, 2, 4, 6, and 12 hours correspondingly.

At the one-hour mark, the VAS score for the Control group was [5.15±0.442], whereas the IV group's score was [3.39±0.496] and the IP group's score was [3.36±0.489].

When we examined the VAS score at the second hour between the IP group, which had a score of [3.52±0.508], and the IV group, which had a score of [4.67±0.479], we observed that the score in the Control group was significantly higher.

The VAS score at the fourth hour was highest in the Control group [4.45±0.506], followed by the IP group [3.58±0.502], and then the IV group [3.36±0.489].

During the sixth hour after surgery, the VAS score was highest in the Control group [4.15±0.364], followed by the IV group [3.76±0.435] and the IP group [3.36±0.489].

Surprisingly, the VAS score at 12 hours was highest in the IV group [4.09±0.522], next the Control group [3.91±0.522], and finally the IP group [3.39±0.496]

Similar findings were observed in the 24th hour, where it was found that the VAS score (24 hrs) was higher in the IV group [4.21±0.696] in comparison to the Control group [3.79±0.415] and the IP group [3.48±0.508].

It has been determined that all of these findings are statistically significant (p = 0.0001)

In the past, a great number of research had been carried out, all of which had conclusively demonstrated that dexmedetomidine was an effective component of multimodal analgesia in a variety of surgical operations.

A study involving eighty patients who were scheduled to undergo laparoscopic cholecystectomy was carried out in the past by Swaika S et al 57 (2013). However, in their study, they only included female patients who fell into the ASA grade I category and were between the ages of 19 and 60 years old. These patients were split up into two groups at random, and one group received an infusion of paracetamol while the other group received an infusion of dexmedetomidine. Heart rate (HR), diastolic blood pressure, and mean arterial pressure profiles of intra-operative hemodynamic changes were similar in both groups, with the exception of the systolic blood pressure, which was significantly reduced by dexmedetomidine in comparison to paracetamol (P =

0.014). Heart rate (HR), diastolic blood pressure, and mean arterial pressure profiles of intra-operative hemodynamic changes were similar in both groups. After surgery, there was a statistically significant difference in the mean HR between the two groups at both 4 and 24 hours. The difference occurred between the two groups (P 0.05). On the visual analogue scale, the Group P had significantly lower scores than the Group D at all three time points (8th, 16th, and 24th h) (P 0.001). The sedation scores of the patients in Group D were statistically higher than those of the patients in Group P at the 4th, 8th, 16th, and 24th post-operative hours (P 0.006).

In order to lessen the need for opioids, a combination of paracetamol and dexmedetomidine infusion was administered. However, paracetamol is capable of providing enough analgesia with only a moderate amount of sedation during surgery, while dexmedetomidine is capable of providing both analgesia and co-operative sedation.

In a study that compared the effects of remifentanil and dexmedetomidine on intraoperative hemodynamics and postoperative analgesia, Hs Jung et al. 68 (2011) discovered that alertness scores were significantly lower in the dexmedetomidine group at 0, 5, and 10 minutes after arrival in the PACU than they were in the remifentanil group at those times. This was the case at all three time points. In the PACU, the group that received dexmedetomidine had considerably lower levels of blood pressure and heart rate compared to the

group that received remifentanil. Dexmedetomidine shown a considerable advantage over remifentanil with regard to the stability of the patient's hemodynamics after the operation.

In a study that was carried out by Usha Shukla et al 69 (2015), the researchers discovered that, in general, the VAS in 24 h was significantly lower (1.80± 0.36, 3.01± 0.48, 4.5 ±0.92), the time to first request of analgesia (min) was longest (128± 20, 118± 22, 55± 18), and the total analgesic consumption (mg) was lowest (45 15, 85)

In their research, Vijayaraghavalu S et al 39 (2021) gave bupivacaine and normal saline intra peritoneal injections to two separate groups of individuals. They discovered that patients who received intraperitoneal bupivacaine after surgery experienced significantly less postoperative pain for the first six hours (P = 0.04); additionally, it took longer for patients to request rescue analgesia (P = 0.04). These findings suggest that intraperitoneal bupivacaine is an effective treatment for postoperative pain. The group that received bupivacaine reported considerably less shoulder pain (P = 0.04) than the other group, despite the fact that side effects such as nausea and vomiting were comparable across the two groups (P = 0.1 and p = 0.09, respectively). They came to the conclusion that bupivacaine is an effective way to minimize the agony felt after surgery, while also extending the amount of time before additional pain relief is required. In

addition to this, it decreases the likelihood of experiencing shoulder pain after surgery, but it has no impact whatsoever on postoperative nausea and vomiting.

Analogy between the use of rescue analgesia and the time it takes:

According to the findings of our research, the amount of time needed to rescue anagesia was longer in the IV group [180.91±41.617] compared to the IP group [106.06±8.269] and the Control group [55.00±6.960]

The total amount of diclofenac that was consumed in 24 hours (in mg) was higher in the Control group [241.82±30.767] compared to the IV group [119.24±40.372] and the IP group [115.30±30.896]. It was determined that both of these values were statistically significant (p=0.0001)

When comparing the IV (59.68 ±71.05 min, P = 0.00) and IP (90.80 ±80.46 min, P = 0.001) groups to Group C (59.68 ±71.05 min), the researchers found that the time to first request analgesia was significantly shorter in the IV group (59.68 ±71.05 min, P = 0.00) than it was in the Group C group (59.68 ±71.05 min). This finding was In contrast to the intravenous diclofenac that was employed in our research, the rescue analgesia that they used was intravenous tramadol. Both the mean consumption of tramadol (152.40± 60.958 vs 137.64 ±52.40 mg) and the mean VAS pain score in the first 12 hours were comparable in both the IV and IP groups. According to the findings of the study, a low bolus

dosage of intravenous (IV) dexmedetomidine (0.5 mcg/kg) combined with intravenous (IV) bupivacaine is just as effective as intravenous (IV) dexmedetomidine (0.5 mcg/kg).

In addition, Vijayan NK et al 67 (2019) carried out a study with the intention of determining whether or not dexmedetomidine and pregabalin are effective in reducing the stress response to laryngoscopy when taken as a premedication. Dexmedetomidine significantly reduced the stress reaction to laryngoscopy, intubation, and pneumoperitoneum, as well as the necessity for anesthetic, in comparison to the other two groups. Dexmedetomidine was found to be associated with significantly lower mean arterial pressures and higher sedation scores in the preoperative and postoperative periods. Additionally, dexmedetomidine was found to be associated with significantly lower heart rate and arterial pressures as well as a reduced requirement for anesthetics during the intraoperative period. It was discovered that adding dexmedetomidine to the balanced anesthesia technique was an effective way to preserve hemodynamic stability.

Similar findings were reported by Khare A et al 66 (2017), and they demonstrated that the use of dexmedetomidine stabilizes intraoperative hemodynamics and reduces the amount of propofol needed for induction and maintenance during propofol-based anesthesia for laparoscopic

cholecystectomy, all without negatively impacting the patient's ability to recover from the procedure.

In their study, Praveena BL et al 44 (2019) came to the conclusion that intra peritoneal installation of local anesthetics like ropivacaine is found to be more superior in its anti-nociceptive properties when used in combination with dexmedetomidine rather than in combination with fentanyl. This was one of the main takeaways from their research.

CONCLUSION

In recent times, laparoscopic cholecystectomy has surpassed open operation in terms of popularity, as a result of the numerous benefits that it offers. Despite the fact that it offered a number of benefits, post-operative discomfort had been a major cause for concern, not only for the operating surgeon but also for the patient, in terms of a slowed recovery and an extended stay in the hospital. Not only does anesthesia management involve intraoperative patient care, but it also involves improved postoperative patient care, which makes the recovery phase pain-free and more comfortable for the patient. In order to accomplish this goal, a wide variety of multi-modal analgesia approaches were utilized. It was established that intra peritoneal installation of alpha 2 agonists such dexmedetomidine and bupivacaine was successful in giving superior post-surgical analgesia after being tried in a large number of patients.

According to the findings of our research, dexmedetomidine, when administered in a low dose of 0.5 mcg/kg together with bupivacaine through the intra peritoneal route, was successful in reducing the post-operative VAS score, analgesic demand, and the amount of time needed for rescue analgesia. Additionally, it helps to attenuate the hemodynamic changes that are involved with having a laparoscopic procedure done.

Because of this, the findings of our research suggest that patients undergoing laparoscopic cholecystectomy might benefit from receiving dexmedetomidine

through the intraperitoneal route in conjunction with local anesthetics as an alternative method of post-operative analgesia that is both safe and effective

SUMMARY

The study **"A comparative study of postoperative analgesic efficacy of low dose intravenous dexmedetomidine and intraperitoneal dexmedetomidine with bupivacaine in patients undergoing laparoscopic cholecystectomy** "was carried out in the Department of Anaesthesiology, B.L.D.E. (Deemed to be university) Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura amongst patients admitted for laparoscopic cholecystectomy under General Anesthesia .The goal of the study was to detect the efficacy of dexmedetomidine and bupivacaine via intra peritoneal route in providing post operative analgesia. The primary objectives of the study was :

1. To analyze the differences in the length of time needed for rescue analgesia between three groups.

2. to evaluate how much diclofenac they took in total over the course of 24 hours.

3. To compare the visual analogue scale (VAS) pain score.

The evaluation of the influence of study medicines on intra-operative hemodynamic response and the identification of the adverse effects of study drugs were the secondary goals of this research.

• Complications.

A prospective controlled study with blinding on both participants and observers was carried out on a total of 99 participants. These participants were split up into three distinct groups using a random number generator: the IV group, the IP group, and the Control group, with 33 participants in each group. This was accomplished throughout the course of a study that lasted around one and a half years, from December 2020 to August 2022. The people who participated in the research were divided into groups using a computerized random number system. This was accomplished throughout the course of a study that lasted around one and a half years, from December 2020 to August 2022. The participants in the study were divided into Group-IV, Individual Participant, and Control groups using a computerized random number table.

A proforma that had been created in accordance with the aims and objectives of the study was used to record the study's findings. Patients who had met the inclusion criteria and had been scheduled for an elective laparoscopic cholecystectomy procedure were considered for participation in the trial. Initial measurements of vital parameters were taken. Any changes that occurred in the patient's vital parameters after the intubation were recorded. After the gall bladder had been removed, the study drug, which contained dexmedetomidine at a dose of 0.5 mcg per kg of body weight, was given to the appropriate study groups intravenously (IV) and intraperitoneally (IP), coupled with intraperitoneal (IP) bupivacaine.

Statistical tests such as CHI SQUARE and the KRUSKAL WALI test were utilized in the analysis of the results. It was discovered that demographic data such as age, gender, body mass index (BMI), height, and weight were equivalent between all three groups. It was discovered that vital indicators such as pulse rate, MAP, respiratory rate, and ETCO2 were equivalent to one another and lacked statistical significance.

The post-operative VAS score was found to be greater in the control group at all provided time intervals, comparable and low in the IV group and the IP group, with the exception of the 24th post-operative hour (IV group had higher VAS score than IP group).

It was discovered that the IV group had the prolonged time for rescue (in minutes), with 180.9141.617, followed by the IP group with 106.068.269, and then the Control group with 55.006.960. The total amount of diclofenac that was consumed in a period of 24 hours (measured in milligrams) was discovered to be higher in the Control group [241.8230.767] when compared to the IV group [119.2440.372] and the IP group [115.3030.896]. It was discovered that these differences were statistically significant (p=0.0001) for both groups.

In patients undergoing laparoscopic cholecystectomy, this study places an emphasis on the use of dexmedetomidine coupled with bupivacaine through the intraperitoneal (IP) route as an effective post-surgical analgesic regimen.

REFERENCES

1. Alexander JI. Pain after laparoscopy. Br J Anaesth. 1997;79:369–78. [PubMed] [Google Scholar] [Ref list]
2. Ickeringill M, Shehabi Y, Adamson H, Rutteimann R. Dexmedetomidine infusion without loading dose in surgical patients requiring mechanical ventilation: Haemodynamic effects and efficacy. Anaesth Intensive Care. 2004;32:741–5. [PubMed] [Google Scholar] [Ref list]
3. Ahmed B, Ashraf AE, Doaa R. Antinociceptive effect of adrenoceptor agonist dexmedetomidine vs meperidine topically, after laparoscopic gynecological surgery. J Med Sci. 2008;8:400–4. [Google Scholar] [Ref list]
4. Brummett CM, Hong EK, Janda AM, Amodeo FS, Lydic R. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current. Anaesthesiology. 2011;115:836–43. [PMC free article] [PubMed] [Google Scholar] [Ref list]
5. Eisendrath DN. Anomalies of the bile ducts and blood vessels as the cause of accidents in biliary surgery. JAMA. 1918;71:864–7. [Google Scholar] [Ref list]
6. Strasberg SM, Hertl M, Soper NJ. An analysis of the problem of biliary injury during laparoscopic cholecystectomy. J Am Coll Surg. 1995;180:101–25. [PubMed] [Google Scholar] [Ref list]
7. Adams DB. The importance of extra hepatic biliary anatomy in preventing complications at laparoscopic cholecystectomy. Surg Clin N America. 1993;73:861–71. [PubMed] [Google Scholar] [Ref list]
8. Hugh TB, Kelly MD, Mekisic A. Rouviere's sulcus; a useful landmark in laparoscopic cholecystectomy. Br J Surg. 1997;84:1253–4. [PubMed] [Google Scholar] [Ref list]

9. Xu F, Xu CG, Xu DZ. A new method of preventing bile duct injury in laparoscopic cholecystectomy. World J Gastroenterol. 2004;10:2916–8. [PMC free article] [PubMed] [Google Scholar] [Ref list]
10. Way LW, Stewart L, Gantert W, Liu K, Lee CM, Whang K, Huntyer JG. Causes and prevention of laparoscopic bile duct injuries. Analysis of 252 cases from a human Factors and cognitive psychology perspective. Ann Surg. 2003;237:460–9. [PMC free article] [PubMed] [Google Scholar] [Ref list]
11. Schreuder AM, Busch OR, Besselink MG, Ignatavicius P, Gulbinas A, Barauskas G, Gouma DJ, van Gulik TM. Long-Term Impact of Iatrogenic Bile Duct Injury. Dig Surg. 2020;37(1):10-21. [PMC free article] [PubMed] [Reference list]
12. Chinnery GE, Krige JE, Bornman PC, Bernon MM, Al-Harethi S, Hofmeyr S, Banderker MA, Burmeister S, Thomson SR. Endoscopic management of bile leaks after laparoscopic cholecystectomy. S Afr J Surg. 2013 Oct 25;51(4):116-21. [PubMed] [Reference list]
13. McLaughlin M, Marik PE. Dexmedetomidine and delirium in the ICU. Ann Transl Med. 2016 Jun;4(11):224. [PMC free article] [PubMed] [Reference list]
14. Zhang DF, Su X, Meng ZT, Li HL, Wang DX, Xue-Ying Li, Maze M, Ma D. Impact of Dexmedetomidine on Long-term Outcomes After Noncardiac Surgery in Elderly: 3-Year Follow-up of a Randomized Controlled Trial. Ann Surg. 2019 Aug;270(2):356-363. [PubMed] [Reference list]
15. Blaudszun G, Lysakowski C, Elia N, Tramèr MR. Effect of perioperative systemic α2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. Anesthesiology. 2012 Jun;116(6):1312-22. [PubMed] [Reference list]

16. Patel A, Davidson M, Tran MC, Quraishi H, Schoenberg C, Sant M, Lin A, Sun X. Dexmedetomidine infusion for analgesia and prevention of emergence agitation in children with obstructive sleep apnea syndrome undergoing tonsillectomy and adenoidectomy. Anesth Analg. 2010 Oct;111(4):1004-10. [PubMed] [Reference list]
17. Kirksey MA, Haskins SC, Cheng J, Liu SS. Local Anesthetic Peripheral Nerve Block Adjuvants for Prolongation of Analgesia: A Systematic Qualitative Review. PLoS One. 2015;10(9):e0137312. [PMC free article] [PubMed] [Reference list]
18. Macdonald E, Koblka BK, Scheinin M. Gene targeting–homing in on alpha 2-adrenoceptor-subtype function. Trends Pharmacol Sci. 1997;18:211–9. [PubMed] [Google Scholar] [Ref list]
19. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative-analgesic agent. Proc (Bayl Univ Med Cent) 2001;14:13–21. [PMC free article] [PubMed] [Google Scholar]
20. Anttila M, Penttilä J, Helminen A, Vuorilehto L, Scheinin H. Bioavailability of dexmedetomidine after extravascular doses in healthy subjects. Br J Clin Pharmacol. 2003;56:691–3. [PMC free article] [PubMed] [Google Scholar]
21. Franowicz JS, Arnsten AF. The alpha-2a noradrenergic agonist, guanfacine, improves delayed response performance in young adult rhesus monkeys. Psychopharmacology (Berl) 1998;136:8–14. [PubMed] [Google Scholar] [Ref list]
22. Venn RM, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care. 2000;4:302–8. [PMC free article] [PubMed] [Google Scholar] [Ref list]
23. Siobal MS, Kallet RH, Kivett VA, Tang JF. Use of dexmedetomidine to facilitate extubation in surgical intensive-care-unit patients who failed previous weaning attempts following prolonged mechanical ventilation:

A pilot study. Respir Care. 2006;51:492–6. [PubMed] [Google Scholar] [Ref list]

24. Venn R, Bryant A, Hall GM, Grounds RM. Effects of dexmedetomidine on adrenocortical function and the cardiovascular, endocrine and inflammatory responses in post-operative patients needing sedation in the intensive care unit. Br J Anaesth. 2001;86:650–6. [PubMed] [Google Scholar] [Ref list]
25. Afsani N. Clinical application of dexmedetomidine. S Afr J Anaesthesiol Analg. 2010;16:50–6. [Google Scholar] [Ref list]
26. Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care. 2000;4:302–8. [PMC free article] [PubMed] [Google Scholar] [Ref list]
27. Correction to: Drugs That May Cause or Exacerbate Heart Failure: A Scientific Statement From the American Heart Association. Circulation. 2016 Sep 20;134(12):e261. [PubMed] [Reference list]
28. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. Br J Anaesth. 1992;68:126–31. [PubMed] [Google Scholar] [Ref list]
29. Paul S, Bhattacharjee DP, Ghosh S, Dawn S, Chatterjee N. Efficacy of intra-articular dexmedetomidine for postoperative analgesia in arthroscopic knee surgery. Ceylon Med J. 2010;55:111–5. [PubMed] [Google Scholar] [Ref list]
30. Pandharipande PP, Pun BT, Herr DL, Maze M, Girard TD, Miller RR, et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: The MENDS randomized controlled trial. JAMA. 2007;298:2644–53. [PubMed] [Google Scholar] [Ref list]

31. Phan H, Nahata MC. Clinical uses of dexmedetomidine in pediatric patients. Pediatric Drugs. 2008;10:49–69. [PubMed] [Google Scholar] [Ref list]
32. Bekker A, Sturaitis MK. Dexmedetomidine for neurological surgery. Neurosurgery. 2005;57:1–10. [PubMed] [Google Scholar] [Ref list]
33. Shah J, Votta-Velis EG, Borgeat A. New local anesthetics. Best Pract Res Clin Anaesthesiol. 2018 Jun;32(2):179-185. [PubMed] [Reference list]
34. Iskander A, Gan TJ. Novel analgesics in ambulatory surgical patients. Curr Opin Anaesthesiol. 2018 Dec;31(6):685-692. [PubMed] [Reference list]
35. Barrington MJ, Uda Y. Did ultrasound fulfill the promise of safety in regional anesthesia? Curr Opin Anaesthesiol. 2018 Oct;31(5):649-655. [PubMed] [Reference list]
36. Wolfe RC, Spillars A. Local Anesthetic Systemic Toxicity: Reviewing Updates From the American Society of Regional Anesthesia and Pain Medicine Practice Advisory. J Perianesth Nurs. 2018 Dec;33(6):1000-1005. [PubMed] [Reference list]
37. Wong GK, Pehora C, Crawford MW. L-carnitine reduces susceptibility to bupivacaine-induced cardiotoxicity: an experimental study in rats. Can J Anaesth. 2017 Mar;64(3):270-279. [PubMed] [Reference list]
38. Oza VP, Parmar V, Badheka J, Nanavati DS, Taur P, Rajyaguru AM. Comparative study of postoperative analgesic effect of intraperitoneal instillation of dexmedetomidine with bupivacaine and bupivacaine alone after laparoscopic surgery. Journal of minimal access surgery. 2016 Jul;12(3):260.
39. Vijayaraghavalu S, Sekar EB. A Comparative Study on the Postoperative Analgesic Effects of the Intraperitoneal Instillation of Bupivacaine Versus Normal Saline Following Laparoscopic Cholecystectomy. Cureus. 2021 Mar 27;13(3).

40. Chilkoti GT, Kumar M, Mohta M, Saxena AK, Sharma N, Singh J. Comparison of postoperative analgesic efficacy of low-dose bolus intravenous dexmedetomidine and intraperitoneal dexmedetomidine with bupivacaine in patients undergoing laparoscopic cholecystectomy: A randomised, controlled trial. Indian Journal of Anaesthesia. 2019 Feb;63(2):106.
41. Elnabtity AM, Ibrahim M. Intraperitoneal dexmedetomidine as an adjuvant to bupivacaine for postoperative pain management in children undergoing laparoscopic appendectomy: A prospective randomized trial. Saudi Journal of Anaesthesia. 2018 Jul;12(3):399.]
42. Praveena BL, Bharathi B, Sahana VR. Intraperitoneal ropivacaine with dexmedetomidine or fentanyl for postoperative analgesia following laparoscopic cholecystectomy: a comparative randomized trial. Anesthesia, Essays and Researches. 2019 Jan;13(1):169.
43. Bisht N, Muniraju T, Hasan A, Kumar V, Bhaumik D. Premedication with clonidine and dexmedetomidine as multimodal analgesia for overnight stay laparoscopic cholecystectomy: A randomized comparative study. in The Indian Anaesthetists Forum 2021 Jan 1 (Vol. 22, No. 1, p. 79). Medknow Publications.
44. Ren Y, Wei M, Liu H, Wang Y, Chen H, Li Z, Shi W, You F. Efficacy and safety of dexmedetomidine as an adjuvant to local wound infiltration anaesthesia: A meta-analysis with trial sequential analysis of 23 randomised controlled trials. International wound journal. 2021 Feb;18(1):32-48.
45. Chiruvella S, Nallam SR. Intraperitoneal instillation of ropivacaine plus dexmedetomidine for pain relief after laparoscopic hysterectomy: A comparison with ropivacaine alone. Journal of Dr. NTR University of Health Sciences. 2016 Apr 1;5(2):93.

46. Ali WA, Ali NS, Sewefy AM, Ahmed AH. Comparative study between intraperitoneal bupivacaine and bupivacaine-nalbuphine for postoperative pain relief after laparoscopic cholecystectomy. Research and Opinion in Anesthesia and Intensive Care. 2020 Jan 1;7(1):57.
47. Fares KM, Mohamed SA, Abd El-Rahman AM, Mohamed AA, Amin AT. Efficacy and safety of intraperitoneal dexmedetomidine with bupivacaine in laparoscopic colorectal cancer surgery, a randomized trial. Pain Medicine. 2015 Jun 1;16(6):1186-94.
48. Chavan SG, Shinde GP, Adivarekar SP, Gujar SH, Mandhyan S. Effects of dexmedetomidine on perioperative monitoring parameters and recovery in patients undergoing laparoscopic cholecystectomy. Anesthesia, Essays and Researches. 2016 May;10(2):278.
49. Swaika S, Parta N, Chattopadhyay S, Bisui B, Banarjee SS, Chattarjee S. A comparative study of the efficacy of intravenous Paracetamol and Dexmedetomidine on peri-operative hemodynamics and post-operative analgesia for patients undergoing laparoscopic cholecystectomy. Anesthesia, Essays and Researches. 2013 Sep;7(3):331.
50. Kalaskar VP, Ruparel DH, Wakode RP. Effects of dexmedetomidine infusion in low dose on dose reduction of propofol, intraoperative hemodynamics, and postoperative analgesia in patients undergoing laparoscopic cholecystectomy. Anesthesia, Essays and Researches. 2021 Oct;15(4):391.
51. El Baz MM, Farahat TE. Intraperitoneal levobupivacaine alone or with dexmedetomidine for postoperative analgesia after laparoscopic cholecystectomy. Anesthesia, essays and researches. 2018 Apr;12(2):355.
52. Sharan R, Singh M, Kataria AP, Jyoti K, Jarewal V, Kadian R. Intraperitoneal instillation of bupivacaine and ropivacaine for postoperative analgesia in laparoscopic cholecystectomy. Anesthesia, essays and researches. 2018 Apr;12(2):377

ANNEXURE -1

ETHICAL CLEARENCE CERTIFICATE

IEC/No-09/2021
22-01-2021

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

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: Postoperative analgesic efficacy of low dose intravenous dexmedetomidine and intraperitoneal dexmedetomidine with bupivacaine in patients undergoing laparoscopic cholecystectomy: A comparative study

Name of PG student: Dr Lakshmi Sowjanya C Department of Anaesthesiology

Name of Guide/Co-investigator: Dr Vijay V Katti, Associate Professor of Anaesthesiology

DR .S.V.PATIL
CHAIRMAN, IEC

Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

6

ANNEXURE – II

SAMPLE INFORMED CONSENT FORM

B.L.D.E(DEEMED TO BE UNIVERSITY) SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA – 586103, KARNATAKA

TITLE OF THE PROJECT: "A COMPARATIVE STUDY OF POSTOPERATIVE ANALGESIC EFFICACY OF LOW DOSE INTRAVENOUS DEXMEDETOMIDINE AND INTRAPERITONEAL DEXMEDETOMIDINE WITH BUPIVACAINE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY."

PRINCIPAL INVESTIGATOR: Dr.LAKSHMI SOWJANYA C
DEPARTMENT OF ANAESTHESIOLOGY,
BLDE'S (DEEMED TO BE UNIVERSITY),
SHRI.B.M. PATIL MEDICAL COLLEGE
VIJAYAPURA–586103.

GUIDE: DR.VIJAY V KATTI
ASSOCIATE PROFESSOR,
DEPARTMENT OF ANAESTHESIOLOGY,
BLDE (DEEMED TO BE UNIVERSITY),
SHRI B.M.PATIL MEDICAL COLLEG HOSPITAL
RESEARCH CENTRE,VIJAYAPURA -586103.

PURPOSE OF RESEARCH:

I have been informed that this study is: "A COMPARATIVE STUDY OF POSTOPERATIVE ANALGESIC EFFICACY OF LOW DOSE INTRAVENOUS DEXMEDETOMIDINE AND INTRAPERITONEAL DEXMEDETOMIDINE WITH BUPIVACAINE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY."

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

PROCEDURE:

I understand that I will be doing ‘‘A COMPARATIVE STUDY OF POSTOPERATIVE ANALGESIC EFFICACY OF LOW DOSE INTRAVENOUS DEXMEDETOMIDINE AND INTRAPERITONEAL DEXMEDETOMIDINE WITH BUPIVACAINE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY."

RISKS AND DISCOMFORTS:

I understand that I/my ward may experience hypotension while doing the procedure, and I understand that necessary measures will be taken to reduce these complications as and when they arise.

BENEFITS:

I understand that I/my wards participation in this study will help in finding out A COMPARATIVE STUDY OF POSTOPERATIVE ANALGESIC EFFICACY OF LOW DOSE INTRAVENOUS DEXMEDETOMIDINE AND INTRAPERITONEAL DEXMEDETOMIDINE WITH BUPIVACAINE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY.

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time.

Dr. Lakshmi Sowjanya C 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 that **Dr. Lakshmi Sowjanya C** will terminate my participation in this study at any time after he has explained the reasons 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 event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would 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 any of my legal rights

.

I have explained to_____, the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

Date: Dr.VIJAY.V.KATTI Dr. LAKSHMI SOWJANYA C

Time: (Guide) (Investigator)

STUDY SUBJECT CONSENT STATEMENT

I confirm that **Dr. LAKSHMI SOWJANYA C** 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

ANNEXURE – III

SCHEME OF CASE TAKING

PROFORMA

Name: Age: Sex:

Ip No: Height: Weight:

Address:

Religion:

Occupation:

Group allotted by randomization: IV IP CONTROL

Chief Complaints:

Past history:

Personal history:

1. Diet- Veg/Mixed
2. Appetite:
3. Sleep:
4. Bowel and bladder habits:

Family history:

Menstrual history:

Treatment history:

GENERAL PHYSICAL EXAMINATION

Conscious/oriented/cooperative:

Built and nourishment:

Height:

Weight:

BMI:

Mallampati grading:

Pallor

Icterus

Cyanosis

Clubbing

Lymphadenopathy

Edema

Airway assessment:

1. Mouth opening:
2. Neck extension:
3. TMJ movement:

Vitals: PREOP:

1. Temperature:
2. Pulse:
3. BP:
4. Respiratory rate:
5. Spo2:

SYSTEMIC EXAMINATION

Central Nervous System:

Respiratory System:

Cardiovascular System:

P/A:

INVESTIGATIONS:

1) Cbc: Hb- Plt- TLC- Eosinophils-

2) Serum electrolytes

3) Urine examination

4) HCV HIV HBSAG

5) ASA Grade

PARAMETERS OBSERVED INTRA-OP:

TIME	**PR**	**SPO2**	**NIBP**	**ETCO2**
3 min after intubation				
Soon after pneumoperitoneum (p0)				
10 mins after pneumoperitoneum (p10)				
20 mins after pneumoperitoneum (p20)				
30 mins after pneumoperitoneum (p30)				
5 min after giving study drug				

10min after giving study drug				
15 min after giving study drug				
After Tracheal Extubation				

Postoperative VAS score:

Time interval (hrs)	Group 1 (NS)	Group 2 (IV Dexmedetomidine)	Group 3 (IP Dexmedetomidine)
0.5			
1			
2			
4			
6			
12			
24			

Time to first request of analgesia –

(Extubation time -Time 0)

Total diclofenac consumption in 24 hrs –

Complications	**Group IV or IP or C**
Nausea	
Vomiting	
Hypotension	
Bradycardia	
Desaturation spells	

BIODATA OF THE GUIDE

GUIDE NAME : DR. VIJAY V. KATTI

DATE OF BIRTH: 12/01/1976

EDUCATION : M.B.B.S.
B.L.D.E.A.'s SHRI B.M. PATIL MEDICAL COLLEGE AND RESEARCH CENTRE, VIJAYAPURA – 586103

M.D. ANAESTHESIOLOGY
B.L.D.E.A.'s SHRI B.M. PATIL MEDICAL COLLEGE AND RESEARCH CENTRE, VIJAYAPURA – 586103

K.M.C. REG. NO. : 51716

DESIGNATION : ASSOCIATE PROFESSOR
DEPARTMENT OF ANAESTHESIOLOGY

TEACHING : 16 YEARS

ADDRESS : ASSOCIATE PROFESSOR
DEPARTMENT OF ANAESTHESIOLOGY
B.L.D.E(DEEMED TO BE UNIVERSITY)
SHRI B.M.PATIL MEDICAL
COLLEGE AND RESEARCH CENTRE,
VIJAYAPURA – 586103

PHONE : (08352)262770 EXT 2052

MOBILE NO : 9844585900

Email : drvijaykatti@gmail.com

INVESTIGATOR

NAME : DR. LAKSHMI SOWJANYA.C

QUALIFICATION : M.B.B.S., NRI MEDICAL COLLEGE

K.M.C. REG. NO. : 0001984

ADDRESS : DEPARTMENT OF ANAESTHESIOLOGY
B.L.D.E(DEEMED TO BE UNIVERSITY)
SHRI B.M.PATIL MEDICAL COLLEGE AND
RESEARCH CENTRE, VIJAYAPURA – 586103

Contact Number : 7995959903

Email : akhil.reddy.342@gmail.com

MASTER CHART

INTRA VENOUS GROUP

Sl. No.	Name	Age in Year	Gender	Group	VAS(0.5 hrs	VAS (1 hr)	VAS (2hrs	VAS(4 hrs	VAS(6 hrs	VAS (12hrs	VAS (24 hrs	rescue anage	ofenac con	mplicati
1	Gangadhar	57	M	IV	4	3	4	3	3	3	3	240 min	85	none
2	Vani	37	F	IV	3	3	4	3	4	3	3	220 min	190	none
3	Iranna	38	M	IV	4	3	3	3	4	3	3	200 min	150	none
4	Sachin	48	M	IV	4	3	3	3	4	4	3	120 min	100	none
5	Mahadevi	53	F	IV	3	3	3	4	4	4	3	150 min	100	none
6	Shanta	45	F	IV	2	4	3	4	4	4	5	175 min	150	none
7	Dundappa	53	M	IV	2	3	3	4	4	4	5	170 min	160	none
8	Muttappa	45	M	IV	4	4	4	3	4	4	5	200 min	100	none
9	Manju	55	M	IV	4	3	3	3	4	4	4	220 min	200	none
10	Gururaj	27	M	IV	3	4	3	4	4	4	4	200 min	150	none
11	handra kan	54	M	IV	3	3	4	3	4	4	4	210 min	190	none
12	Sushma	34	F	IV	4	3	4	3	4	4	5	175 min	120	none
13	Bhimaraya	54	M	IV	2	4	3	4	4	4	4	170 min	100	none
14	Aarati	28	F	IV	4	4	3	4	4	4	4	200 min	90	none
15	Ganesh	34	M	IV	3	3	3	4	4	5	5	180 min	110	none
16	Muktabai	33	F	IV	4	3	3	4	4	4	5	180 min	120	none
17	Dayanand	50	M	IV	4	4	3	3	4	5	4	180 min	90	none
18	Janaki	54	F	IV	3	4	4	3	4	4	4	180 min	75	none
19	Muttapa	50	M	IV	3	3	3	3	4	5	5	180 min	110	none
20	Kumar	42	M	IV	3	3	4	4	3	4	5	180 min	100	none
21	Roopa	45	F	IV	4	3	3	4	3	4	4	110 min	120	none
22	Sangappa	48	F	IV	4	3	4	3	3	4	4	120 min	150	none
23	Sanjay	23	M	IV	2	3	3	3	4	4	4	170 min	190	none
24	Satish	34	M	IV	3	4	4	3	4	4	4	180 min	200	none
25	Gopal	43	M	IV	4	4	3	3	4	4	5	110 min	100	none
26	Annappa	30	M	IV	3	3	4	3	4	4	5	180 min	110	none
27	Veeresh	53	M	IV	4	4	4	3	4	5	4	180 min	120	none
28	Kanchana	30	F	IV	4	3	4	3	3	5	4	280 min	75	none
29	Basamma	52	F	IV	3	3	4	3	3	4	4	110 min	75	none
30	Naveen	29	M	IV	4	3	4	4	3	4	4	110 min	75	none
31	Saraya	38	M	IV	3	4	4	4	3	5	5	240 min	75	none
32	Maha devi	44	F	IV	4	4	4	3	4	4	5	240 min	75	none
33	Shivamma	40	F	IV	4	4	4	3	4	4	5	240 min	75	none

MASTER CHART

INTRA PERITONEAL GROUP

Sl. No.	Name	Age in Year	Gender	Group	VAS(0.5 hrs	VAS (1 hr)	VAS (2hrs	VAS(4 hrs	VAS(6 hrs)	VAS (12hrs	VAS (24 hrs	rescue anage	ofenac con	complications
1	Suma patta	52	F	IP	2	4	4	4	3	4	4	100 min	100	none
2	Nanda goud	50	M	IP	3	3	4	3	3	3	3	100 min	100	none
3	Jagadish	29	M	IP	3	4	3	3	3	4	3	120 min	120	none
4	Vidya	50	F	IP	3	3	3	4	4	4	3	100 min	75	none
5	Saraswati	45	F	IP	3	3	3	4	3	4	3	100 min	180	none
6	Nagamma	33	F	IP	3	4	4	4	3	3	4	120 min	110	none
7	Ashok	43	M	IP	2	3	3	3	3	4	4	100 min	125	none
8	Govind	30	M	IP	2	3	4	4	4	3	3	90 min	90	none
9	Santosh	34	M	IP	3	4	3	3	3	4	3	100 min	75	none
10	Veeresh	45	M	IP	2	3	4	3	4	3	3	100 min	150	none
11	Basamma	57	F	IP	3	4	3	3	3	4	4	110 min	150	none
12	Savita	40	F	IP	2	3	4	4	3	4	4	110 min	100	none
13	Ramesh	39	M	IP	3	4	4	4	4	4	3	100 min	180	none
14	Yellappa	56	M	IP	2	3	3	3	4	3	3	100 min	120	none
15	Manju	45	M	IP	3	3	4	4	4	4	4	110 min	90	none
16	Sundaresh	38	M	IP	2	3	3	4	3	3	4	110 min	110	none
17	Anant	37	M	IP	2	4	3	4	4	3	4	120 min	100	none
18	Umesh	33	M	IP	2	3	4	4	3	3	3	100 min	150	none
19	Kasappa	56	M	IP	3	3	3	4	4	4	3	120 min	100	none
20	Rajashekha	40	M	IP	2	3	4	3	3	3	4	100 min	120	none
21	Nithin	29	M	IP	3	3	3	4	3	3	4	110 min	150	none
22	Chandrakal	35	F	IP	2	4	3	4	4	4	3	120 min	75	none
23	Suresh	48	M	IP	3	4	4	3	3	3	4	100min	100	none
24	Gopal	39	M	IP	3	3	3	3	3	3	4	110 min	140	none
25	Prakash	38	M	IP	2	3	3	4	3	3	4	100 min	150	none
26	omalingapp	58	M	IP	2	4	4	4	3	3	4	110 min	75	none
27	Somappa	40	M	IP	3	3	4	4	4	4	4	100 min	75	none
28	Nelavwa	50	F	IP	3	3	4	3	3	3	4	120 min	150	none
29	Shivayya	54	M	IP	2	4	3	3	4	3	3	100 min	100	none
30	Shivanand	44	M	IP	2	3	3	4	3	3	3	100 min	120	none
31	Prasad	29	M	IP	3	3	4	3	3	3	3	110 min	150	none
32	Laxmi	35	F	IP	3	3	4	3	4	3	3	100 min	75	none
33	Tara	53	F	IP	2	3	3	4	3	3	3	100 min	120	none

MASTER CHART

CONTROL GROUP

Sl. No.	Name	Age in Year	Gender	Group	VAS(0.5 hrs	VAS (1 hr)	VAS (2hrs	VAS(4 hrs	VAS(6 hrs)	VAS (12hrs	VAS (24 hrs	scue anage	ofenac con	none
1	Rajesh	39	M	CONTROL	6	5	5	5	5	5	4	60 min	200	none
2	Sherkhan	43	M	CONTROL	6	5	5	5	5	5	4	60 min	250	none
3	Kashmitai	30	F	CONTROL	6	5	5	5	4	4	3	65 min	220	none
4	Mahadevi	55	F	CONTROL	6	5	5	5	4	4	3	60 min	200	none
5	Rajesh	40	M	CONTROL	6	5	5	5	4	4	3	60 min	240	none
6	Malakappa	52	M	CONTROL	6	5	5	5	4	4	4	50 min	220	none
7	Mahadev	58	M	CONTROL	6	5	5	5	4	4	4	45 min	250	none
8	Sayabanna	50	M	CONTROL	6	5	5	5	4	4	4	45 min	260	none
9	Mallawad	38	M	CONTROL	6	5	5	5	4	4	4	50 min	260	none
10	Lakshman	39	M	CONTROL	6	5	5	5	4	4	4	60 min	280	none
11	Chandasab	46	M	CONTROL	6	5	5	5	4	4	4	65 min	300	none
12	Mallappa	50	M	CONTROL	6	5	4	4	4	4	4	60 min	220	none
13	Sangeeta	29	F	CONTROL	6	5	4	4	4	4	4	65 min	220	none
14	Padma	45	F	CONTROL	5	5	4	4	4	4	4	60 min	240	none
15	Nanda	59	M	CONTROL	5	5	4	4	4	4	4	60 min	300	none
16	Sudha	45	F	CONTROL	5	5	4	4	4	4	4	60 min	200	none
17	Shakuntala	37	F	CONTROL	5	5	4	4	4	3	4	65 min	210	none
18	Parashuram	25	M	CONTROL	6	6	5	4	4	3	4	45 min	260	none
19	Bhimaraya	55	M	CONTROL	6	6	5	4	4	3	4	50 min	220	none
20	Veena	44	F	CONTROL	6	6	5	5	5	5	4	55 min	240	none
21	Saraswathi	45	F	CONTROL	6	6	5	4	4	4	4	45 min	240	none
22	Ashok	40	M	CONTROL	6	6	5	5	5	4	4	50 min	220	none
23	Govind	47	M	CONTROL	5	5	5	4	4	4	4	45 min	200	none
24	Bhagirathi	33	F	CONTROL	5	5	5	4	4	4	4	50 min	210	none
25	Mallikarjur	45	M	CONTROL	4	5	5	4	4	4	4	55 min	260	none
26	Laxmi	50	F	CONTROL	5	5	4	4	4	4	4	50 min	300	none
27	Siddanna	34	M	CONTROL	4	5	4	4	4	4	4	55 min	300	none
28	Aditya	40	M	CONTROL	5	4	4	4	4	4	4	50 min	220	none
29	Santosh	40	M	CONTROL	5	5	4	4	4	4	4	60 min	220	none
30	Gaddenna	43	M	CONTROL	5	5	5	5	5	4	3	65 min	240	none
31	Raju	32	M	CONTROL	5	5	4	4	4	3	3	45 min	260	none
32	Bouramma	55	F	CONTROL	5	5	5	5	4	3	3	55 min	260	none
33	Janabai	51	F	CONTROL	6	6	5	4	4	3	3	50 min	260	none