“TO EVALUATE POST-OPERATIVE SHOULDER TIP PAIN IN LOW PRESSURE (10MMHG CO_2) VERSUS STANDARD PRESSURE (14MMHG CO_2) PNEUMOPERITONEUM IN LAPAROSCOPIC CHOLECYSTECTOMY, A ONE YEAR RANDOMISED CONTROLLED TRIAL, HOSPITAL BASED STUDY”

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ENDORSEMENT

This is to certify that the dissertation entitled **"TO EVALUATE POST-OPERATIVE SHOULDER TIP PAIN IN LOW PRESSURE (10MMHG CO2) VERSUS STANDARD PRESSURE (14MMHG CO2) PNEUMOPERITONEUM IN LAPAROSCOPIC CHOLECYSTECTOMY, A ONE YEAR RANDOMISED CONTROLLED TRIAL, HOSPITAL BASED STUDY"** is a bonafide research work done by **CANDIDATE REG NO. BH0114001**.

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LIST OF ABBREVIATIONS USED

^0C	-	Degree Centigrade
ACR	-	American College of Radiology
ALT	-	Alanine aminotransferase
AST	-	Aspartate aminotransferase
BP	-	Blood pressure
CBD	-	Common bile duct
cm	-	Centimeter
CO_2	-	Carbon dioxide
COPD	-	Chronic obstructive pulmonary disease
CT	-	Computed tomography
DIDA	-	Derivatives of iminodiacetic acid
DPQ	-	Dartmouth pain Questionnaire
ERCP	-	Endoscopic retrograde cholangiopancreatography
$ETCO_2$	-	Partial pressure concentration of carbon dioxide
EUS	-	Endoscopic Ultrasound
HBS	-	Hepatobiliary scintigraphy
HIDA	-	Hepatobiliary iminodiacetic acid scan
i.e.,	-	That is,
ICU	-	Intensive care unit
Kg	-	Kilogram
LC	-	Laparoscopic cholecystectomy
LFT	-	Liver function tests
LTI	-	Left thumb impression
min.	-	Minute

MIS	-	Minimally invasive surgery
mm	-	Millimeter
mmHg	-	Millimeters of mercury
MPQ	-	Mc Gill pain Questionnaire
MRCP	-	Magnetic resonance cholangiopancreatography
MRI	-	Magnetic resonance imaging
n	-	Total number
N_2O	-	Nitrous oxide
NMDA	-	N-methyl-D-aspartate receptor
p	-	Probability value
$PaCO_2$	-	Partial pressure of carbon dioxide
PR	-	Pulse rate
QOL	-	Quality of life
RCT	-	Randomised controlled trial
RR	-	Respiratory rate
SAGES	-	Society of American Gastrointestinal and Endoscopic Surgeons
SD	-	Standard deviation
SPECT	-	Single positron emission computed tomography
VAS	-	Visual analog scale
vs.	-	Versus
WDR	-	Wide dynamic range
WHYPQ	-	West Haven-Yale pain Questionnaire

ABSTRACT

Background and objectives

Improving post-operative pain has become an increasingly important issue. This study was aimed to compare postoperative shoulder tip pain and the use of analgesics postoperatively the use of the low pressure pneumoperitoneum with the use of standard pressure pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

Methodology

This one year Randomised Controlled Trial was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi from January 2015 to December 2015. A total of 80 patients undergoing elective laparoscopic cholecystectomy were enrolled. Based on 'Sequential Numbered Opaque Envelope Method' the patients were randomly divided into two groups of equal number as Group A (pneumoperitoneum with standard pressure of 14 mm Hg CO_2) and Group B Patients underwent (pneumoperitoneum with low pressure of 10 mm Hg CO_2).

Results

Most of the patients (67.50% each) in group A and Group B were females ($p=1.000$). The mean age of patients was almost equal in group A (46.93 ± 14.09 years) and (45.80 ± 13.07 years) in group B ($p=0.712$). The mean duration of surgery in group A and group B was comparable (71.43±18.43 vs 80.50±26.62 minutes; $p=0.081$). The mean pain scores at 1 (5.00±1.84 vs 2.20±1.22; $p<0.001$), 6 (4.10±1.57 vs 1.38±0.98; $p<0.001$), 12 (3.03±1.46 vs 0.68±0.83; $p<0.001$) and

24 (1.75±1.32 vs 0.35±0.48; $p<0.001$) hours were significantly low in group B compared to group A. The mean requirement of rescue analgesia was significantly high in group A compared to Group B at all the intervals ($p<0.050$).

Conclusion and interpretation

Low pressure pneumoperitoneum offers some benefit in terms of lower incidence and intensity of postoperative shoulder tip pain thereby results in lower consumption of rescue analgesia without altering the operative time.

Keywords

Gall stones; Laparoscopic cholecystectomy; Low pressure pneumoperitoneum; Shoulder tip pain; Standard pressure pneumoperitoneum;

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INTRODUCTION

Gall stone disease is one of the most common condition encountered in general surgical practice in today's adult population.[1] Laparoscopic cholecystectomy (LC) is the Gold standard treatment for symptomatic gallstone disease since the early 90's. Worldwide, it is one of the most common operations performed. The advantages of LC are less postoperative pain, shorter hospital stays, a rapid return to work, fewer intra-abdominal adhesions, better cosmetic outcome and a significant decrease in perioperative septic complications. This procedure is also being performed safely as a day care procedure at many centres.[2]

The role of ambulatory surgery is expanding and the need to facilitate an earlier hospital discharge along with improving postoperative pain control has become an increasingly important issue.[5]

As described by the international association for study of pain, it is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, and causes the individual to react to remove the noxious stimulus". Also, pain is a complex summation of nociceptive input, emotion, state of arousal, thought process and social influences.[6]

One of the main undesirable side effects of LC is shoulder tip pain. It is a frequent symptom.[7] Incidence of post-operative shoulder tip pain is in around 30-50% of operated patients.[8]

There are several proposed mechanisms for generation of pain following laparoscopy. They are;

- ruptured blood vessels caused by the rapid distension of the peritoneum
- traumatic traction on nerves
- release of inflammatory molecules
- instrument trauma to the abdominal wall
- abdominal wall stretching when gallbladder is removed from the abdomen
- pneumoperitoneum created by the use of carbon dioxide (CO_2)
- maintenance of high abdominal pressure
- irritation of the phrenic nerve
- and the use of cold CO_2.[9]

During the first 24 hours, the sites of most severe pain are the right upper quadrant and the port sites.[10] The severity of pain after laparoscopic procedure is influenced by many factors. They include; the type of gas used for pneumoperitoneum, the volume of the residual gas, the pressure created by pneumoperitoneum and the temperature of the insufflated gas.[11]

The reverse Trendelenburg position causes CO_2 to rise and get trapped in between the liver and the right diaphragm. This causes diaphragmatic irritation and results in post-operative shoulder tip pain.[12] Another factor is the overstretching of the fibres of the diaphragm from high CO_2 pressure and stimulation of the sympathetic nervous system leading to amplified local tissue inflammatory response. These directly cause shoulder tip pain.

Adequate working space is required in the abdomen for good exposure that contributes to satisfactory operative results and patient safety. Common methods to create working space in the abdomen are pneumoperitoneum and abdominal wall lifting methods such as the laparotensor and laparolift. Pneumoperitoneum is most often created by insufflation of the peritoneal cavity with carbon dioxide. It is held at constant pressure till the end of surgery and released at the time of removal of the ports. Standard pressure pneumoperitoneum employs a pressure range of 12-14 mmHg. However, over prolonged periods it has been associated with a few adverse effects. They are; decreased pulmonary compliance, altered blood gas parameters, impaired functioning of the circulatory system, raised liver enzymes and renal dysfunction, and increased intra-abdominal venous pressures.[13]

As a result of uncontrolled postoperative pain, a cascade of adverse effects follows. These include delayed resumption of normal pulmonary function, restriction of mobility (thus contributing to thromboembolic complications), nausea/vomiting, an increase in the systemic vascular resistance, increased cardiac contractility and increased myocardial oxygen consumption through a higher catecholamine release induced by the stress response.[14]

Pain control is pertinent for optimal care in surgical patients. Despite better understanding of pain pathophysiology, pharmacology of analgesics and development of newer more effective analgesic techniques, many patients still continue to experience considerable discomfort.

Numerous studies[13,15-18] have tested methods to reduce the incidence and severity of shoulder tip pain following LC. Techniques include warming and humidifying of CO_2, abdominal wall lift, intraperitoneal gas drain, intraperitoneal saline wash, nitrous oxide pneumoperitoneum and low pressure CO_2 insufflations.

An emerging trend has been the application of low pressures for pneumoperitoneum in the range of 7-10 mmHg. This method enables to lower the impact of pneumoperitoneum on human physiology while providing adequate working space. Low pressure pneumoperitoneum has fewer adverse effects on the cardiac and respiratory functions. It is also preferable in the elderly patients and for those with chronic cardiac or respiratory diseases. Another advantage of low pressures during pneumoperitoneum appears to be a reduced incidence and severity of shoulder tip pain in the postoperative period. This provides better quality of life following laparoscopic surgery.[13]

The need for this study arises with the thought that low pressure CO_2 insufflation will reduce the post-operative shoulder tip pain and enable for a faster recovery with less requirement for post-operative analgesia. We hypothesised that the low pressure CO_2 insufflation will cause less shoulder tip pain post-operatively as compared to standard pressure CO_2 insufflation.

Keeping this in mind, this study was designed to compare the use of the low pressure pneumoperitoneum (defined as 10 mmHg) with the use of standard pressure pneumoperitoneum (defined as 14 mmHg) in patients undergoing laparoscopic cholecystectomy in a prospective randomised manner.

OBJECTIVES

The objectives of present study were;

Primary objective

To study the intensity of post-operative shoulder tip pain in low pressure (10 mmHg CO_2) and standard pressure (14 mmHg CO_2) pneumoperitoneum during laparoscopic cholecystectomy

Secondary

Reducing the use of analgesics postoperatively

REVIEW OF LITERATURE

HISTORICAL REVIEW

Laparoscopic surgery is also known as minimally invasive surgery (MIS) or 'keyhole' surgery. It is a modern surgical technique to perform surgeries in the abdomen through cannulae (also known as ports) which are channels into the body through small incisions.[19]

For over 2000 years cholelithiasis has plagued mankind, as proven by archaeological excavations demonstrating the presence of gall stones in young Egyptian women.[20]

In 1881, German surgeon Carl Johann August Langebuch (1846-1901) described gall stone pathology[21] and then performed the first cholecystectomy.[44]He envisioned the path for further advanced and modified biliary surgeries[22] before his demise on June 9, 1901. The first laparoscopic cholecystectomy (LC) was performed in 1985, by German Professor Dr. Erich Mühe. He had performed 94 such surgeries after whom another surgeon from France, Phillipe Mouret of Lyon, performed his first laparoscopic cholecystectomy in 1987; followed by Francois Dubois of Paris, France, in 1988.

In 1998, Cadiere and colleagues reported the first successful clinical implementation of tele-robotics when they accomplished a laparoscopic cholecystectomy using a prototype of the Da Vinci robotic surgical system.[23]

The introduction of the computer chip television camera was a key event in the development of laparoscopy, as the procedure could then be conducted while viewing a projected image of the abdominal contents, as well as providing a better view of the internal structures. This also allowed free movement of the surgeon's hands, enabling an easier performance of more complex procedures.

The laparoscope had been used by gynaecologists for many years for diagnostic purposes before the general surgeon. Mühe initiated laparoscopic cholecystectomy in 1985.[24]

The other essential instruments used at that time were the haemoclip, namely the Weck-Reynolds pistol grip clip applier and the Weck-Reynolds pistol grip scissors, which were important for the ligation and cutting of the cystic duct and artery during laparoscopic cholecystectomy. Walker Reynolds Jr's interest in haemoclips began in 1970 when these devices were used for haemostasis of blood vessels in conjunction with staple surgery.[25]

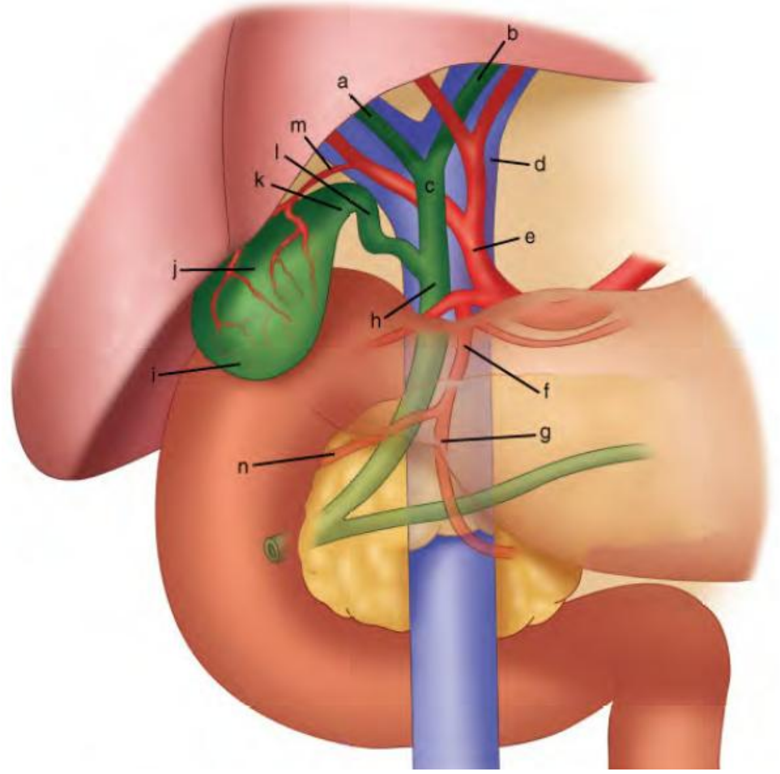
Surgical Anatomy

The gallbladder is reservoir for bile. It is a pyriform structure in the gall bladder fossa in the inferior surface of the right hepatic lobe. It extends forward from a point near the right end of the porta hepatic to the inferior hepatic border.[26] Its upper surface is attached to the liver by the connective tissue, elsewhere it is completely covered by the peritoneum and attached to the liver by a short mesentery.

It is 7 to 10 cm long, 3 cm broad at its widest and 30-50ml in capacity. Its parts are fundus, body and neck. The neck is narrow, curving up and forwards and then abruptly backwards and downwards, to become the cystic duct, at which there is a constricted part. The neck is attached to the liver by the areolar tissue containing the cystic artery. The mucosa of the neck is obliquely rigid forming a spiral valve, when the neck is distended this gives its surface a spiral grove.

From the right side of the neck a small recess may project down and back towards the duodenum, often termed Hartmann's pouch (originally described by Broca).

The cystic duct is 3 to 4 cm long, it passes back, down and to the left from the neck of the gall bladder, joining the common hepatic duct to form the common bile duct. Usually near the porta hepatis but sometimes lower, in which case the cystic duct lies along the lesser omentum's right edge. Its mucosa bears 5-10 concentric folds, they project obliquely in regular succession, like a spiral valve, which are referred to as the Valves of Heister.[26-29]



a = right hepatic duct; b = left hepatic duct; c = common hepatic duct; d = portal vein; e = hepatic artery; f = gastroduodenal artery; g = left gastric artery; h = common bile duct; i = fundus of the gallbladder; j = body of gallbladder; k = infundibulum; l = cystic duct; m = cystic artery; n = superior pancreatico-duodenal artery. Note: the situation of the hepatic bile duct confluence anterior to the right branch of the portal vein, the posterior course of the right hepatic artery behind the common hepatic duct.[28]

Figure1. Anterior aspect of the biliary anatomy

Arterial Supply of the Gallbladder:[26]

The cystic artery, which is a branch of right hepatic artery is the major vessel to the gall bladder. Small vessels from the hepatic bed also supply the gall bladder. The cystic artery generally passes behind the common hepatic and cystic ducts to the upper surface of the neck of the gall bladder, on which it runs downward forwards before dividing into superficial and deep branches. The cystic artery supplies branches to the hepatic ducts and to the upper part of the common bile duct. The lower part of the bile duct receives several branches from the posterior superior pancreatico-duodenal artery. The right hepatic artery gives branches to the middle part of the bile duct.

There may be anomalies in the artery's origin and are of surgical interest so as to enable damage free surgery. In 800 specimens Anson (1963) observed the following incidences, origin from the right hepatic artery 63.9%, the hepatic trunk 26.9%, left hepatic 5.5% gastroduodenal 2.6%, superior pancreatico-duodenal 0.3%, right gastric 0.1%, coelic trunk 0.3%, and superior mesenteric 0.8%. An accessory cystic artery may arise from the common hepatic or one of its branches, the cystic artery supplies the hepatic ducts and upper part of common bile duct. The cystic artery is an end artery and its occlusion is followed by the gangrene of the gall bladder.[30]

Venous Drainage of the Gallbladder:[26]

The veins draining the gall bladder vary considerably. In its upper surface they lie in the areolar tissue between the gallbladder and liver. These run directly into the liver through the fossa of the gallbladder to join the hepatic veins. From the rest of the gall bladder, the veins join to form one or more cystic veins on its neck. These commonly enter liver, either directly or after joining with the veins draining the hepatic ducts and upper part of the bile duct. Rarely a single or double cystic vein may drain directly in to the right branch of the portal vein. They do not accompany the cystic artery.

Lymphatic Drainage[26]

The lymphatics draining the gall bladder are of significant importance for both inflammatory and malignant disease of gall bladder. The lymphatics from the subserosal and sub-mucosal plexus drain into cystic lymph node of Lund. This sentinel lymph node lies in the fork created by the junction of cystic and common hepatic ducts. Lymph also drains to a node situated at the anterior border of epiploic foramen. Efferent vessels from the nodes pass in the free edge of the lesser omentum to the coeliac group of preaortic nodes.

The sentinel node when enlarged, may distort the normal anatomy in patients with acute cholecystitis or carcinoma. The subserosal lymphatic vessels of the gall bladder also have connection with the sub-capsular lymphatic channels of liver, and accounts for the frequent spread of carcinoma of gallbladder to the liver.

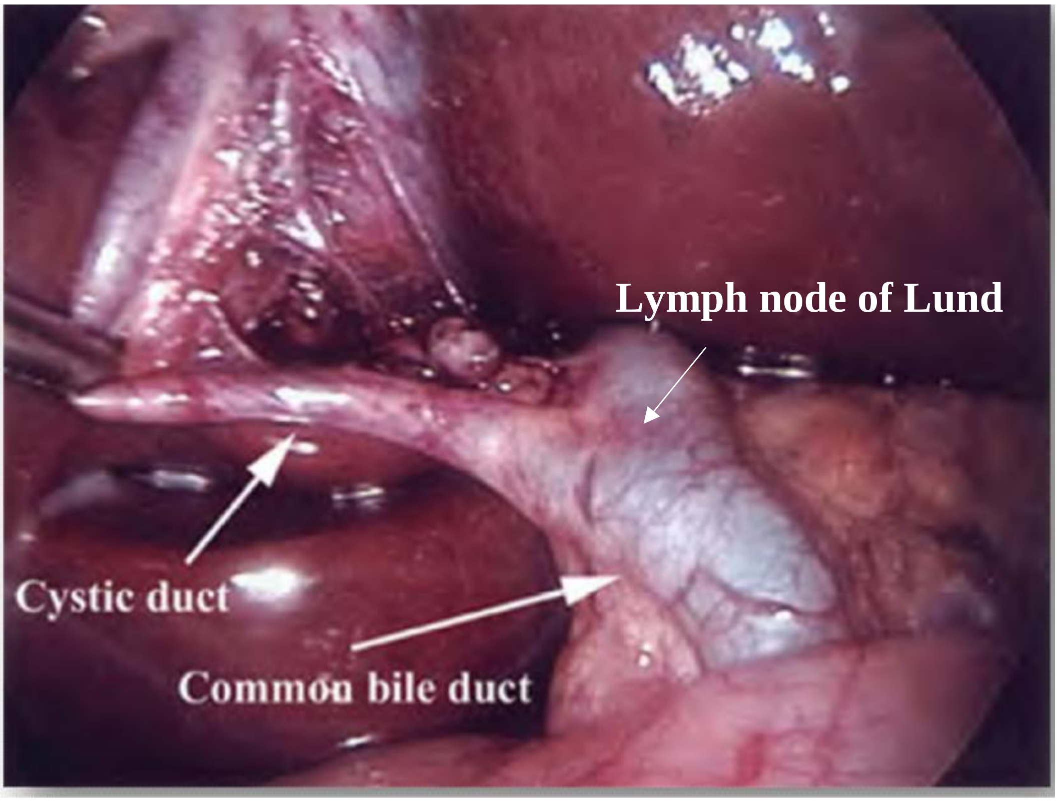


Figure 2. Calot’s triangle

Innervation[26]

There is rich innervation with both sympathetic and parasympathetic nerve fibres. They pass along the hepatic artery and its branches. Parasympathetic fibres, mainly from the hepatic branch of anterior vagal trunk, stimulate contraction of the gall bladder and relax the ampullary sphincter. Sympathetic fibres from the cell bodies in the coeliac ganglia, with the preganglionic cells in the lateral horn of the spinal cord segments, T7-T9 inhibits contraction. Autonomic plexus of the nerve exists in the muscular and sub-mucosal layers. Fibres from the right phrenic nerve, through communication between phrenic and coeliac plexus, appear to reach the gallbladder via the hepatic plexus. This explains the phenomenon of referred “shoulder pain” in gall bladder pathology. The biliary tract pain is usually felt in the right hypochondrium and epigastrium and may radiate round to the back in the infrascapular region, in the area of distribution of spinal nerve T7-T9.

Triangles of Cholecystectomy

In 1891, Jean-François Calot defined a triangle of anatomical area formed by the common hepatic duct medially, the cystic duct laterally and the cystic artery superiorly. The previous concept of the triangle of cholecystectomy had for its upper limit not the cystic artery but the inferior surface of the liver which is now known as hepatocystic triangle.[31] This triangle is of surgical importance because a number of important structures pass through it. Therefore during cholecystectomy it is a need to identify all structures within the triangle to prevent complications.[32]

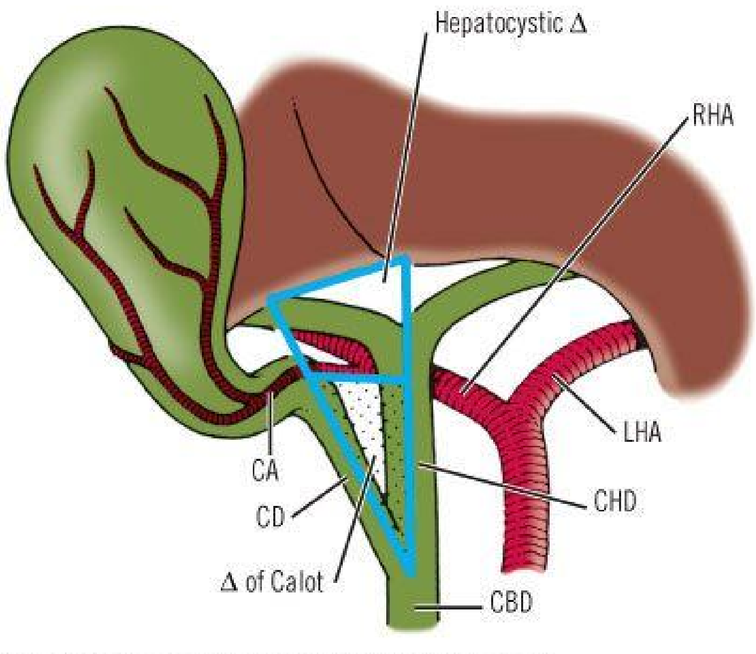


Figure 3. Triangles of cholecystectomy

Common anomalies and variations

1. Absent gall bladder – extremely rare, autopsy incidence of 0.03% have been reported.[26]

2. Variation in size and shape of gall bladder.
   a. Bilobed gall bladder.
   b. Fundal diverticulum.
   c. Phrygian cap.
   d. Hour glass gall bladder.

3. Variation in position left sided gall bladder, floating gall bladder.

4. Double gall bladder, duplication of gall bladder with two separate cavities and two separate cystic ducts has an incidence of approximately 1 in 4000.

Pathological process such as cholelithiasis and cholecystitis may involve one organ while the other is spared.[33]

5. Other anomalies related to gall bladder
    a. Persistence intrahepatic gall bladder
    b. Diverticulum's of body or neck of gall bladder
    c. Accessory peritoneal fold due to congenital adhesions.

Floating gall bladder occurs when there is increase in the peritoneal investment; this condition occurs in the 5% of patients and predisposes to torsion, resulting in gangrene or perforation of the viscus.[26]

Rarely, the cystic duct may be absent. Two or more cystic ducts may combine. The junction of the cystic duct and common hepatic ducts may vary in its level from the porta hepatis to behind or even below the first part of duodenum. When the junction is low the two ducts may be connected by fibrous tissue. Accessory hepatic ducts may emerge, more often from the right lobe to join the main hepatic ducts rarely, the gall bladder itself.[29]

Physiology of gall bladder[28,29,32]

The gall bladder concentrates bile by absorption of water and sodium to acquire greater strength and digestive power. The gallbladder and bile ducts are well adapted for the function of storing and secreting bile into the duodenum during digestion. The flow of bile in and out of the gallbladder is determined primarily by contraction and relaxation of the sphincter of Oddi and the storage in small bulk is made possible by the concentrating power of the gallbladder.

The healthy gallbladder is rarely static as a result of continuous cycle of partial emptying and refilling. This is governed by the intestinal migratory myoelectric complex between meals. During relaxation and refilling it intermittently contracts and expels pulses of bile into the duodenum. This constant fluctuation prevents stone formation.

Epidemiology

Cholecystitis is defined as inflammation of the gallbladder. This occurs most commonly because of cholelithiasis. Ninety percent of cases involve stones in the cystic duct (i.e., calculous cholecystitis), with the other 10% of cases representing acalculous cholecystitis.[34]

Common risk factors include the 5 F's: fat, female, fecundity, forty and family history. Gallstones constitute a significant health problem in developed societies, affecting 10% to 15% of the adult population, meaning 20 to 25 million Americans have (or will have) gallstones. Gallstone disease is a leading cause for hospital admissions related to gastrointestinal problems as seen with an estimated 1.8 million ambulatory care visits each year.[35]

Gallstone disease per se carries inherent risks. Prospective population-based surveys have shown an increased overall mortality, particularly from cardiovascular disease and cancer, as seen in Americans and Pima Indians with cholelithiasis.[35]

As the incidence of gallstone disease escalates, there is a further concomitant increase in complications like gallstone associated pancreatitis.[36]

Age distribution in cholecystitis

The incidence of cholecystitis increases with age. The physiologic explanation for the increasing incidence of gallstone disease in the elderly population is unclear. At least 10% of adults have gallstones. There is an increasing prevalence after the age of 60. About 10 to 15% of men and 20 to 40% of women have gallstones.[37]

Sex distribution for cholecystitis

Gallstones are two to three times more frequent in females than in males, resulting in a higher incidence of calculous cholecystitis in females. Elevated progesterone levels during pregnancy may cause biliary stasis, resulting in higher rates of gallbladder disease in pregnant females. Acalculous cholecystitis is observed more often in elderly men.[38]

Prevalence of cholecystitis by race and ethnicity

Cholelithiasis the major risk factor for cholecystitis, has an increased prevalence among people of Scandinavian descent, Pima Indians, and Hispanic populations, whereas cholelithiasis is less common among individuals from sub-Saharan Africa and Asia. In the United States, Caucasians have a higher prevalence than African-Americans.[39,40]

The prevalence of gallstones is especially high in the Scandinavian countries and Chile. Among Native Americans, Mexican Americans and American Indians, the Pima tribe are reported with an increased predisposition to gallstone formation.[39]

The epidemiology of gallstone disease in India

Research has been done by authors in India. In Western literature of Medicine and Gastroenterology, it is stated that India is a country with a low incidence of gallstones. The prevalence of gallstone disease varies in different parts of India.[41] In 1966, an epidemiological study in Indian Railway employees showed that North Indians had seven times higher prevalence of gallstones as compared the South Indian employees. Good epidemiological studies have been performed in Kashmir. There is a very high and increasing prevalence, as reported.[42-46] Khuroo from Kashmir reported a prevalence of 6.12% (men 3.07% and women 9.6%) the prevalence increasing progressively to reach a peak in the sixth decade.[47] Multiparous women have a higher prevalence rate.[45] There was no correlation with diet, obesity or socioeconomic status.[43]

South Indian data shows a different picture. Mixed and pigment stones were more common than cholesterol stones in Tamil Nadu as reported by Jayanthi et al.[47] They found no correlation with demographic features or social customs. An interesting observation is an association with high consumption of tamarind although yet there is no scientific explanation for this observation. The overall prevalence of gallstones in Tamil Nadu appears to be lower than in the Northern states. However cholecystectomy once an extremely uncommon surgery in south India has become frequent reflecting possibly a real increase in the prevalence of the disease or sooner diagnosis from the ease of detecting stones by abdominal ultrasound.[49]

Clinical Manifestations of Gallstones

Four types of gallbladder diseases are recognised:

1. Asymptomatic gallstone disease.
2. Symptomatic gallstone disease
3. Pain abdomen from another etiology such as peptic ulcer, with asymptomatic gallstones
4. Cholecystitis with no gallstones

The decision to do surgery is based on a careful understanding of the above.

<u>1. Asymptomatic Gallstones</u>

Most do not develop symptoms even after follow up periods for as long as 20 years. Around 20% of patients may develop symptoms by 15 years. Asymptomatic gallstone disease (in many Western countries) does not need surgery, although there are exceptions. The role of prophylactic cholecystectomy in young patients from various parts of India is emphasised in many recent papers, but criticised in one.[50]

<u>2. Symptomatic Gallstone Disease</u>

a. Biliary colic

Frequently characterised as post-prandial pain in the right side of the upper abdomen. Contrary to popular belief it may not necessarily occur only after fatty foods but after any mixed diet.[51]

b. Acute Cholecystitis

Patients will often have a history of biliary pain in acute cholecystitis; pain lasts for > 3 hours, associated with fever and tenderness in the right upper quadrant (Murphy's sign).[51]

c. Chronic Cholecystitis

Patients will have episodic epigastric, right upper quadrant pain lasting for more than 30 minutes. Patients, may present with complications of gallstones which are pancreatitis, choledocholithiasis and cholangitis.[51]

d. Choledocholithiasis

Patients may be asymptomatic or they present with biliary colic, acute cholangitis or pancreatitis.[51]

e. Acute Cholangitis

This is a medical emergency. Patients may present with Charcot's triad- right upper quadrant pain, fever and jaundice. With advances in clinical chemistry, imaging studies the diagnosis can be made before the classic triad develops.[51]

Diagnosis

<u>Diagnostic tests</u>[51]

- Abdominal Ultrasonography: Single most useful test to evaluate gallstones, CBD size and stones.

- Endoscopic Ultrasound (EUS): Excellent to evaluate CBD stone, size. Expensive. Not easily available.
- ERCP: As solely a diagnostic test it has lost its value. Can be used to do sphincterotomy, therapeutically
- HIDA, DIDA, Radioisotope Scans: Accurate identification of cystic duct obstruction. Diagnosis of acute cholecystitis.
- CT scan Abdomen: Not ideal due to high radiation. Not useful in pregnancy
- MRI/MRCP: MRCP does not require contrast. It can be safely used in 2nd/3rd trimester of pregnancy. Reduces the number of invasive ERCPs.

Delays in making the diagnosis of acute cholecystitis result in a higher incidence of morbidity and mortality. This is especially true for intensive care unit (ICU) patients who develop acalculous cholecystitis. The diagnosis should be considered and investigated promptly in order to prevent poor outcomes.[52]

Differential diagnosis[53,54]

- Cholelithiasis
- Choledocholithiasis
- Biliary Colic
- Biliary Disease
- Cholangitis

- Gallbladder Mucocele
- Gallbladder Cancer
- Gallbladder Tumours
- Acute Mesenteric Ischemia
- Abdominal Aortic Aneurysm
- Gastric Ulcers
- Gastritis, Acute
- Cholangiocarcinoma
- Appendicitis

Approach

The workup for cholecystitis may include laboratory tests (though these are not always reliable), radiography, ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), hepatobiliary scintigraphy (HBS), and endoscopy.

Laboratory investigations[55]

Although laboratory criteria are not reliable in identifying all patients with cholecystitis, the following findings may be useful in arriving at the diagnosis:

- Leucocytosis may be observed in cholecystitis.

- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels are used to evaluate the presence of hepatitis and may be elevated in cholecystitis or with common bile duct obstruction.

- Bilirubin and alkaline phosphatase assays are used to evaluate evidence of common duct obstruction.

- Amylase/lipase assays are used to evaluate the presence of pancreatitis. Amylase may also be elevated mildly in cholecystitis.

- An elevated alkaline phosphatase level is observed in 25% of patients with cholecystitis.

Imaging

The 2010 American College of Radiology (ACR) Appropriateness Criteria offers the following imaging recommendations:[56]

- Sonography is the preferred and gold-standard imaging test for the diagnosis of cholelithiasis, acute cholecystitis.

- CT is a secondary imaging test that can identify extrabiliary disorders and complications of cholecystitis, such as gangrene, gas formation, and perforation.

- CT with intravenous contrast is useful in diagnosing cholecystitis in patients with non-specific abdominal pain.

- MRI, often with intravenous gadolinium-based contrast medium, is also a possible secondary imaging modality useful in confirming a diagnosis of acute cholecystitis.

- MRI without contrast is useful to eliminate radiation exposure in pregnant women for whom sonograms have not indicated a clear diagnosis.

Radiography

Gallstones may be visualised on non-contrast radiography in 10-15% of cases. This finding only indicates cholelithiasis, with or without active cholecystitis.

Ultrasonography

Ultrasonography is 90-95% sensitive for cholecystitis and is 78-80% specific. It provides greater than 95% sensitivity and specificity for the diagnosis of gallstones more than 2 mm in diameter. Studies indicate that emergency clinicians require minimal training in order to use right upper quadrant ultrasonography in their practice.[57,58]

Ultrasonographic findings that are suggestive of acute cholecystitis include the following: pericholecystic fluid, gallbladder wall thickening greater than 4 mm, and sonographic Murphy sign. The presence of gallstones also helps to confirm the diagnosis.[59]

Ultrasonography is performed best following a fast of at least 8 hours because gallstones are visualised best in a distended bile-filled gallbladder.[60]

Computed tomography and magnetic resonance imaging

The sensitivity and specificity of CT scan and MRI for predicting acute cholecystitis have been reported to be greater than 95%.[61] Spiral CT scan and MRI (unlike endoscopic retrograde cholangiopancreatography [ERCP]) have the advantage of being non-invasive, but they have no therapeutic potential and are most appropriate in cases where stones are unlikely.

Findings suggestive of cholecystitis include wall thickening (>4 mm), pericholecystic fluid, subserosal oedema (in the absence of ascites), intramural gas, and sloughed mucosa. CT scan and MRI are also useful for viewing surrounding structures if the diagnosis is uncertain.

Hepatobiliary scintigraphy[55]

HBS has been found to be up to 95% accurate in diagnosing acute cholecystitis. The reported sensitivities and specificities of biliary scintigraphy are in the range of 90-100% and 85-95%.

In a typical study, the gallbladder, common bile duct, and small bowel fill within 30-45 minutes. If the gallbladder is not visualised, intravenous morphine administration can improve the accuracy of HBS by increasing resistance to flow through the sphincter of Oddi, resulting in filling of the gallbladder if the cystic duct is patent. The addition of morphine also reduces the number of false-positive scan results observed in patients who are critically ill and immobilised with viscous bile.

<u>Endoscopic retrograde cholangiopancreatography</u>

ERCP may be useful for visualizing the anatomy in patients at high risk for gallstones if signs of common bile duct obstruction are present. A study performed by Sahai *et al* found that ERCP was preferred over endoscopic ultrasonography and intraoperative cholangiography for patients at high risk for common bile duct stones undergoing laparoscopic cholecystectomy.[62]

Disadvantages of ERCP include the need for a skilled operator, high cost, and complications such as pancreatitis, which occurs in 3-5% of cases.

<u>Histologic findings</u>

Oedema and venous congestion are early acute changes. Acute cholecystitis is usually superimposed on a histologic picture of chronic cholecystitis. Specific findings include fibrosis, flattening of the mucosa, and chronic inflammatory cells. Mucosal herniations known as Rokitansky-Aschoff sinuses are related to increased hydrostatic pressure and are present in 56% of cases. Focal necrosis and an influx of neutrophils may also be present. Advanced cases may show gangrene or perforation.[63]

Treatment

Treatment of cholecystitis depends on the severity of the condition and the presence or absence of complications. Uncomplicated cases can often be treated on an outpatient basis; complicated cases may necessitate a surgical approach. Antibiotics may be given to manage infection.

Surgical Treatment

Surgical treatment, if required, typically involves cholecystectomy, preferably laparoscopic. Percutaneous drainage may be considered in patients at high surgical risk.[64]

Cholecystectomy

Laparoscopic cholecystectomy is the gold standard for the surgical treatment of cholecystitis. Studies have indicated that early laparoscopic cholecystectomy resulted in shorter total hospital stays with no significant difference in conversion rates or complications.[65] The ACR 2010 criteria state that laparoscopic cholecystectomy is the primary mode of treatment for cholecystitis.[56]

The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) issued guidelines for the clinical application of laparoscopic biliary tract surgery in 2010. The guidelines include detailed recommendations for making the decision to operate, performing the procedure, and managing post-operative care, with the patient's safety always the primary consideration. Recommendations are as follows:[66]

- Pre-operative antibiotics should be considered only to reduce the possibility of wound infection in high-risk patients, and then limited to one pre-operative dose.
- Intraoperative cholangiography may improve injury recognition and decrease the risk of bile duct injury.

- If bile duct injury occurs, the patient should be referred to an experienced hepatobiliary specialist before any repair is undertaken, unless the primary surgeon has experience with biliary reconstruction.

Early operation within 72 hours of admission has both medical and socioeconomic benefits and is the preferred approach for patients treated by surgeons with adequate experience in laparoscopic cholecystectomy.[67] Immediate cholecystectomy or cholecystostomy is usually reserved for complicated cases in which the patient has gangrene or perforation.

One study suggests that when CT scanning is performed as long as 72 hours prior to surgery, it may better detect acute gangrenous cholecystitis. Acute gangrenous cholecystitis was significantly correlated with perfusion defect of the gallbladder wall, pericholecystic stranding, and no-gallstone condition, which can be better observed through CT scanning when compared with ultrasonography.[68]

For elective laparoscopic cholecystectomy, the rate of conversion from a laparoscopic procedure to an open surgical procedure is approximately 5%. The conversion rate for emergency cholecystectomy where perforation or gangrene is present may be as high as 30%.[65]

Although laparoscopic cholecystectomy performed in pregnant women is considered safest during the second trimester, it has been performed successfully during all trimesters.

LAPAROSCOPIC CHOLECYSTECTOMY

Laparoscopic cholecystectomy has received universal acceptance and is currently considered the gold standard for the treatment of symptomatic cholelithiasis. Many centres worldwide have special “short-stay” units or “24-hour admissions” for post-operative observation following this procedure.[69]

With more than 500,000 cases performed annually laparoscopic cholecystectomy (LC) is one of the world’s most common surgical procedures. Laparoscopic cholecystectomy offers many advantages compared to open cholecystectomy. The conversion rate and complications associated with LC depend on the experience of the surgeon and the degree of difficulty faced during surgery. Different centres have reported widely varying rates of conversion to open operation (range: 1.5% to 6%). The reported incidence of bile duct injury is in between 0% to 1% in LC.

Because of these distinct advantages, the procedure has gained worldwide popularity and has now become one of the most common operations performed in general surgical practice. LC is essentially a safe procedure with low morbidity and mortality rate.

Laparoscopic cholecystectomy has the advantages of less scar size compared to open cholecystectomy. The laparoscopic surgeries have the advantages of reduction in number of emergency operations and decreased morbidity, fewer CBD exploration, shortened hospital stay, reduced total costs in expert hands and for cosmetic purposes.

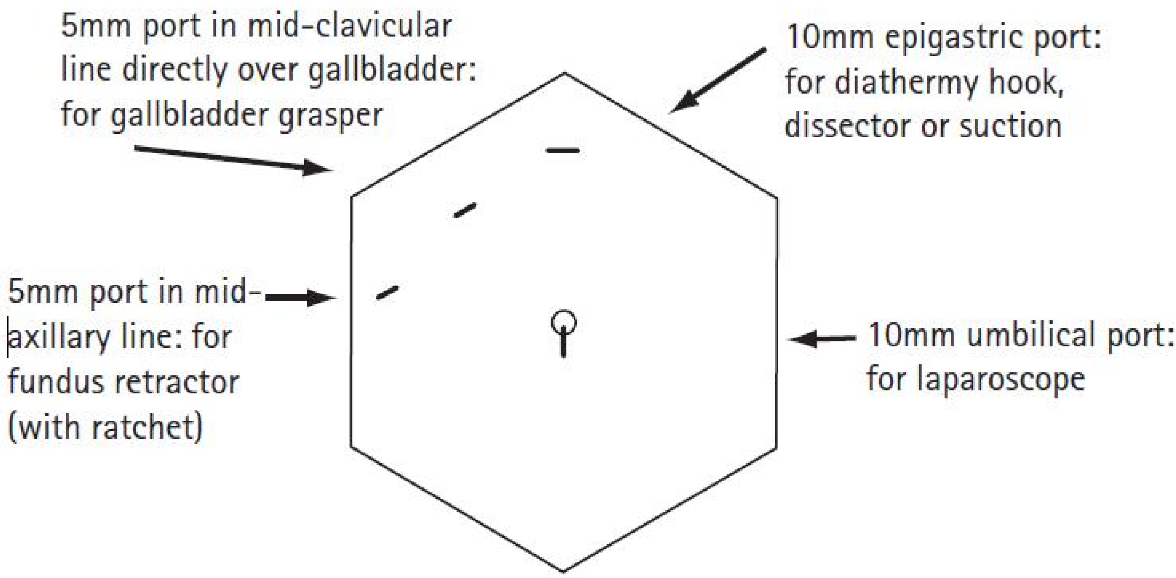


Figure 4. Common port placement in laparoscopic cholecystectomy

PNEUMOPERITONEUM

Pneumoperitoneum is needed for safe and effective surgery. It also enables for space to perform diagnostic and therapeutic procedures. This visual clarity is achieved by filling the abdominal cavity with a gas.

The ideal qualities of an appropriate gas are determined by:

- type of anaesthesia
- non-combustibility
- physiologic compatibility
- toxicity
- method of delivery
- ease of use
- safety, and cost.

Gases like carbon dioxide (CO_2), air, oxygen, nitrous oxide (N_2O), argon, helium and mixtures of these gases are used for pneumoperitoneum. However, CO_2 gas insufflation is the most preferred because it has:

- A high diffusion coefficient
- It is a normal metabolic end product
- It is rapidly cleared from the body
- Non-combustible
- The risk of gas embolism is lowest with CO_2

Pneumoperitoneum with CO_2 has been used in clinical practice since the introduction of laparoscopic cholecystectomy in the late 1980s. It is initiated by use of a needle (Veress or Tuhoy) or a trocar device to transverse the abdominal wall and then distend the peritoneal cavity.[70]

The physiologic effects of pneumoperitoneum are:

1) Systemic absorption of CO_2

2) Hemodynamic and physiologic alteration in a variety of organs as a result of the increased intra-abdominal pressure.

There are other methods for creation of a working space. A technique is abdominal wall lift. This may be performed without gas insufflation (laparotenser) but is reported with increased post-operative pain. Low-pressure insufflation (8-10 mmHg) is an alternative and studies report reduced intensity of post-operative pain.[13]

EFFECTS OF CARBON DIOXIDE ABSORPTION DURING PNEUMOPERITONEUM

CO_2 is absorbed via the peritoneum during pneumoperitoneum. It may cause systemic absorption of CO_2whichaltersthe acid-base balance. In some cases where intraoperative ventilation is impaired CO_2 absorption can result in hypercapnia and acidosis.[71]

The adverse effects of acidosis associated with hypercapnia are serious. There may be stimulation of the autonomic nervous system. This leads to tachycardia and increased myocardial contractility. Hypercapnia can also cause cardiac arrhythmias, vasoconstriction of the pulmonary vessels, hypertension and seizures. It is essential for the surgeon and the anaesthetist to monitor end-tidal CO_2 ($ETCO_2$) or arterial partial pressure of CO_2 ($PaCO_2$). This would help to prevent hypercapnia.

During pneumoperitoneum, the anaesthetist adjusts the minute ventilation and makes ventilatory changes. These interventions eliminate the increased CO_2 load and therefore prevent systemic acidosis.

EFFECTS OF INCREASED INTRA-ABDOMINAL PRESSURE DURING PNEUMOPERITONEUM

To provide adequate visualisation and exposure of the operative field, the intra-abdominal pressure during laparoscopy is usually set at 14 mmHg. The normal intra-abdominal pressure of non-obese individuals is 5 mmHg or less.[72]

DURATION AND FREQUENCY OF PNEUMOPERITONEUM

The duration of pneumoperitoneum was directly related to the volume of air seen on the initial chest radiograph in the first 24 hours. In 1961, Bevan reported that 77% of his patients had pneumoperitoneum after a variety of abdominal operations. He found that after laparotomy pneumoperitoneum generally resolved by 10 days but could last significantly longer. Keiser and Lemmertz[21] found that 50% of their patients had pneumoperitoneum after open cholecystectomy and that the pneumoperitoneum lasted for 4.9 days on an average.

In a study by Lemay et al.[73] 10 patients were evaluated in whom laparoscopic tubal ligation was performed. All of these patients had post-operative pneumoperitoneum that was resorbed in the majority at day 3. Two patients had residual intraperitoneal gas as late as post-operative day 9.

In a study by Millitz,[74] the frequency of pneumoperitoneum after laparoscopic cholecystectomy was 46%. The pneumoperitoneum was graded as trace in 74% of these patients and mild (<1 cm) in the remaining 26%. The author found all but one patient showed resorption of the pneumoperitoneum in the first week after surgery, with the remaining case resolving in the second week after surgery.

In a study by Gayer et al,[75] post-operative pneumoperitoneum was seen less frequently in obese patients. They also reported that when present, it was less extensive and it would resorb faster as compared to average and thin individuals. 33% of obese patients had pneumoperitoneum post-operatively; in comparison, 62% of patients who were thin or of average weight had this condition.[22, 23] In asthenic patients, it is thought that more air is trapped beneath the lower part of the rib cage (partial roof of the peritoneal cavity) when the abdominal muscles are relaxed and the peritoneum is pulled up to close the incision.

Pain after laparoscopy

Pain is much less after laparoscopic surgery as compared to the same surgery performed through laparotomy. However, there still is pain. The reduction in pain has made early discharge from the hospital possible.[76]

Pain may be felt in the upper abdomen, lower abdomen, back, or shoulders. The greatest incidence of pain is in the upper abdomen.

Pain after laparoscopy may be transient or it may persist for 48 hours. In laparoscopic cholecystectomy, during the first 24 hours, visceral pain was predominant. Shoulder pain is reported to increase over the first day and it becomes significant on the following day.[77]

Pain

Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage” by the International Association for the Study of Pain. This definition recognises the interplay between the objective, physiologic aspects of pain and its subjective, emotional and psychological components.[78]

Clinically, pain is of two types- acute and chronic. Acute pain is primarily due to nociception. Chronic pain, may also be due to nociception, but include psychological and behavioural factors. Post-operative pain is a type of acute pain. It is further differentiated based on the origin and feature, into somatic and visceral pain. Somatic pain is due to nociceptive input arising from skin, subcutaneous tissues, and mucous membranes. It is characterised by being well-localised. It is described as sharp, pricking, throbbing or burning sensation. On the other hand, visceral pain is due to nociceptive input from the internal organs or one of its covering. It is described as a dull, diffuse pain. There is association of abnormal sympathetic or parasympathetic activity which causes nausea, vomiting, sweating and /or changes in blood pressure or heart rate.[79]

Magnitude of the problem

Multiple variables of post-operative pain like the occurrence, intensity, quality, and duration are related to the site, nature & duration of surgery, type of incision (thoracic and upper abdominal operations are associated with the most severe pain), the pre-operative psychological, physical and pharmacological preparation of the patient, and lastly the anaesthetic management and the quality of post-operative care.[79]

NEURO-PHYSIOLOGY OF PAIN

Nociceptors

Sensation is described as either protopathic (noxious) or epicritic (non-noxious). Epicritic sensation (light touch, pressure, proprioception, and temperature discrimination) is characterised by low-threshold receptors (specialised endorgans on the afferent neurons) and conducted by large myelinated nerve fibres while; protopathic sensation (pain) is sub-served by high-threshold receptors (free nerve endings).[80]

Noxious sensations have two components: “first pain” is a fast, sharp, and well-localised sensation. This is conducted by Aδ fibres. “Second pain” is a dull, slow onset, and poorly localised sensation. This is conducted by C fibres. This protopathic pain is transmitted mainly by free nerve endings that sense mechanical or chemical tissue damage.[81-83]

Several types of this pain is recognised

1. Mechano-nociceptors, which respond to pinprick.
2. Silent nociceptors, which respond only on the presence of inflammation
3. Polygonal mechano-heat receptors which is more prevalent and respond to excessive pressure, extreme of temperature, and pain producing substances.[6]

Nociceptors are of two types:

- Somatic- located in skin and deep tissues (muscle, tendons, joints),
- Visceral- located in internal organs.[81-83]

Pain pathway

Pain is conducted along three neuron pathways; from the peripheral nerve endings up to the cerebral cortex.[81-83]

First order neuron

Cells of these neurons are located in the dorsal root ganglia (for the body) and specific cranial nerve ganglia (for the head and neck) for example, Gasserian ganglion for trigeminal nerve. The Proximal end of their axons reach spinal cord via the dorsal sensory root of cervical, thoracic, lumbar, and sacral level (for the body) and through the cranial nerves (for head and neck).[81-83]

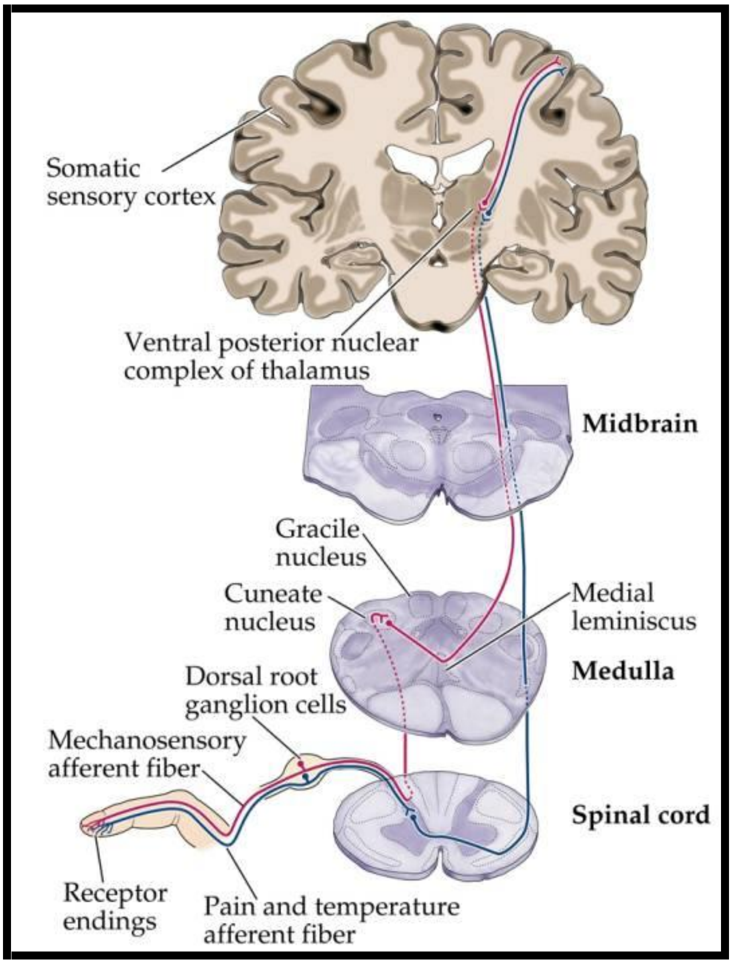


Figure 5. Pain pathway[81-83]

Second order neurons

Pain fibres may ascend or descend three spinal cord segments in the Lissauer's tract before synapsing with the second order neuron in the grey matter of the ipsilateral dorsal horn, this synapsing may be through interneurons. Second order neurons are either; nociceptive specific which serves only noxious stimuli and are normally silent or wide dynamic range (WDR) neurons that can receive also non-noxious afferent input. WDR neurons are more prevalent in the dorsal horn and are responsible for the increased intensity of firing in response to same stimulus "wind-up".[82,83]

Lamina II of the gray matter of the dorsal horn of the spinal cord, (also called the substantia gelatenosa) contains many interneurons and is believed to play a role in processing and modulating nociceptive input. [82,83]

Axons of most of the second order neurons cross the midline to the contra-lateral side of the spinal cord forming the lateral spinothalamic tract that send its fibres to the thalamus, the reticular formation, nucleus raphe and periaquiductal gray.[82,83]

Third order neurons

Those are located in the thalamus and send their fibres to the somato-sensory area I and II in the cerebral cortex.[83-85]

Pre-emptive analgesia

Pre-emptive analgesia is defined as what is administered to the patient before surgical incision; that would prevent the development of central sensitisation from incisional injury and inflammatory injuries (during intraoperative and post-operative periods). As reported by experimental data and positive clinical trials, there is a strong suggestion that pre-emptiveanalgesia is a clinically relevant phenomenon. Complete blockade of noxious stimuli provides maximum benefit.[86]

Mechanism of pain in laparoscopy

Pain results from trauma caused to the abdominal wall and the visceral organs by the endoscope and the surgical instruments.There are other mechanisms responsible for pain after laparoscopy as well. The rapid distension of peritoneum with high flow of gas is associated with tearing of blood vessels, traumatic traction of the nerves and release of inflammatory mediators. Peritoneal inflammation is probably also the origin of the upper abdominal pain after lower abdominal surgery or after diagnostic laparoscopy. This can persist for at least three days. Peritoneal biopsy performed two to three days after laparoscopy showed peritoneal inflammation and neuronal rupture. A linear inverse relationship between abdominal compliance at the time of laparoscopy and severity of post-operative pain was seen.[87]

Therefore, abdominal distention should be slow with a low flow rate of gas. Adequate muscle relaxation is essential. The prolonged presence of shoulder tip pain suggests excitation of the phrenic nerve that is caused by the persistence of gas in the abdomen (pneumoperitoneum). This pain can be reduced by the active gas or drain suction of the gas under the diaphragm.[87]

a. Factors associated with pneumoperitoneum

1. Neuropraxia of the phrenic nerve

It is suggested that distention of the diaphragm during gas insufflationcauses phrenic nerve neuropraxia. This could contribute to post-operative pain through stimuli via the C4 dermatome.[88]

2. The type of insufflated gas and intraabdominal pH

The phrenic nerves may be damaged by the acid milieu created by the dissolution of CO_2. The intraperitoneal pH when CO_2 gas is insufflated has been measured at 6.0 immediately post-operatively. On the first post-operative day, the pH rises to 6.4 to 6.7, and on the second post-operative day to 6.8 to 6.9. Thereafter it normalizes to above 7.0.[89] Similar values were found when argon gas was substituted.

3. Residual intraabdominal gas

Several reports have indicated that residual intra-abdominal gas after laparoscopy causes pain. Factors like CO_2 dissolution, intra-abdominal acidosis, and consequently peritoneal irritation occurs for an increased duration if the gas is not evacuated at the end of the laparoscopic surgery. Residual gas also may result in a loss of peritoneal surface tension and support to the abdominal viscera, thus contributing to post-operative pain.[90]

4. Temperature of gas

The effect of gas temperature on post-operative pain after gynaecologic laparoscopic procedures has been investigated. In a prospective randomised study of standard insufflation gas (20^0C) versus gas at body temperature, they found that pain was less in the warm gas group. This was especially with respect to diaphragmatic and shoulder tip pain, with the lasting effect of three days.[88] Semm, et al.[91] reported that heating the CO_2 gas to 37°C will reduce intraoperative hypothermia, the occurrence of tachycardia, CO_2 consumption, shoulder pain, and post-operative pain medication requirements by 31%.

5. Humidity of gas

A prospective randomised controlled trial[85] of 40 patients at Queen Elizabeth Hospital, Adelaide. They investigated the outcome when humidified gas was insufflated during laparoscopic cholecystectomy instead of standard dry gas. Results demonstrated statistically significant reduction in post-operative pain in those patients who underwent humidified gas insufflation. These patients also required less post-operative analgesia, shorter hospital stay and were quicker to return to daily work. The mean time to return to normal activities was significantly less 5.9 days, as compared to 10.9 days in the control group. The exact relation between dry gas and post-operative pain is not yet determined, but it is observed that dry gas insufflation causes ultra-structural damage to exposed membranes. This effect is not seen with the use of humidified gas.

b. Operational factors

1. Wound pain

The number of incisions,the location and the size of the incisions made are partly responsible for the effect of pain. Administering local anaesthesiato the surgical wound is recommended by many authors. There is documented reduction in pain with respect to both open[92] and laparoscopic surgeries.[93] For laparoscopic procedures, only small amounts of local anaesthesia are needed as the incisions are small. This in turn has minimal side effects, and infiltration of local anaesthetic into the wound is recommended.[94]

2. Wound drainage

Wound drains after laparoscopic surgery is preferred to be sited over the lateral aspect of the abdomen, traversing the muscle layers. The umbilical incision is not preferred as there is a greater incidence of pain, infection, and potential incisional herniation at this site if the defect is not formally closed.

c. Socio-cultural and individual factors

Hospital stay and recovery time are influenced by the socio-cultural environment. This variable was effectively demonstrated in a study comparing the course after laparoscopic cholecystectomy in French and American patients. Within two weeks in 73% of the French and in 93% of the Americans, post-operative discomfort had resolved. More Americans returned to daily work in a given period when compared to French patients.[95]

A multitude of factors like an individual's threshold and previous pain experience, influence the individual's post-operative pain perception and recovery time.

There is a substantial variation in the incidence and intensity of pain in different patients after laparoscopic cholecystectomy. The intensity peaks within the first four to eight hours. It has been reported to be unbearable up to the first post-operative morning in one third of the patients. It involves three different components: incisional pain (parietal pain component); deep intra-abdominal pain (visceral pain component) and shoulder tip pain (presumed referred visceral pain). The intensity of visceral pain dominates in the immediate post-operative period after laparoscopic cholecystectomy.

Effects of post-operative pain

Moderate to severe acute pain, regardless of its site, can affect nearly every organ function. It may be responsible for post-operative morbidity or mortality, if any.

The neuroendocrine stress response which ensues following acute pain is proportional to the intensity of pain. It has been hypothesised that a reduction in surgical stress response (endocrine, metabolic and inflammatory) will lead to a reduced incidence of post-operative organ dysfunction, thereby leading to an improved outcome.[96]

a. Cardiovascular effects

Cardiac morbidity is a major cause of peri-operative death. It is important to realise that in high risk populations, peri-operative myocardial ischemia is most likely to occur after surgery (from day one to day three post-operatively). This has led to treatment strategies designed to prevent its occurence.[97]

A variety of factors may contribute to the development of post-operative myocardial. They are ischemia, hypothermia, anaemia, anxiety, tracheal intubation/suctioning. The intrinsic response to poorly controlled pain plays a prominent role. This leads to the activation of sympathoadrenal, and neuroendocrine axes which may have a major impact on myocardial oxygen supply and demand. Catecholamine-induced tachycardia, increased contractility, increased preload and after load from hypervolemia caused by enhanced release of arginine vasopressin and aldosterone, are well characterised aetiologies of increased oxygen demand. The increased oxygen demand in addition to hypervolemia, may precipitate ischemia and acute cardiac failure. Especially in patients who have pre-existing compromised coronary arteries or valvular heart disease.[98]

Pulmonary dysfunction may lead to diminished myocardial oxygen delivery.Atelectasis resulting from pain-induced hypoventilation and pulmonary oedema resulting from stress-induced hypervolemia are mainly responsible for this. Other causes are as follows:

- Coronary artery constriction secondary to high circulatory levels of catecholamine and increased coronary sympathetic tone
- Stress-induced increase in plasma viscosity and platelet-induced occlusion;
- Serotonin induced coronary vasospasm secondary to platelet aggregation.[99]

b. Pulmonary effects

Pulmonary function may be substantially altered by surgically induced pain. The classical pulmonary response to upper abdominal surgery is increased respiratory rate with decreased tidal volume. There is also increased vital capacity, forced expiratory volume and functional residual capacity. Suchpathophysiologic alterations are characteristic of acute restrictive pulmonary disease and may be associated with clinically significant hypoxia and hypercarbia.[99]

Pain causes a higher total body oxygen consumption and increased carbon dioxide production at the cellular level. This in turn necessitates an increase in the breathing efforts. Patients with poor pain control (especially in upper abdominal and thoracic procedures) have shallow breathing. They also have inadequate cough due to the pain. This leads to further reduction in the tidal volume and functional residual capacity which in turn may cause atelectasis, intra-pulmonary shunting and hypoxemia.[97]

c. Gastrointesinal effects

Pain causes sympathetic hyperactivity which leads to an increase in sphincter tone and decreased motility of intestine. Thereby causing intestinal ileus.Pain is also known to increasegastric acid secretion and lead to stress ulceration.[100]

d. Endocrinal effects

The dominant neuroendocrine responses to pain involve hypothalamic-pitutary-adrenocortical interactions. As a result, there is increased release of catecholamine and catabolic hormones. This effect causes retention of sodium and water, and increased levels of blood glucose, free fatty acids and lactate. The negative nitrogen balance and protein catabolism may impede the patient's recuperation.[101]

e. Haematological effects

Pain and the cascade of stress response causes a reduction in the levels of natural anticoagulants, inhibition of fibrinolysis and increase in platelet reactivity. This leads to a post-operative hypercoagulable state. Hypercoagulability causes a series of other events such as deep venous thrombosis and myocardial ischemia.[102]

f. Immunological effects

The stress response potentiatesimmunosuppression in the post-operative period.The extent of immunosuppression correlates with the extent of surgery. Stress response has been reported to depress the reticulo-endothelial system which predisposes to infection.[80]

g. Psychogenic effects

Intense anxiety, fear, and the loss of control that accompany severe tissue injury may have profound impact on the hypothalamic-pituitary axis. Poorly controlled pain can lead to some behavioural responses like sleep deprivation and a reduced morale.[103]

Uncontrolled post-operative pain can produce a series of long-term emotional disturbances in some patients.This could impair the patient’s health and cause undue fear/anxiety if there is a need for subsequent surgery. Post-operative cognitive dysfunction occurs in up to 20% of patients after major non-cardiac surgery and may persist in about 10% of patients 3 months after surgery.[96]

h. Development of chronic pain

Recently, it is accepted that neuropathic pain can develop after surgery, be persistent, and be the basis for ongoing suffering for the patient. The diagnosis of neuropathic pain can be obtained from the presenting features of burning, stinging or shooting pain, despite apparent tissue healing with a relative lack of response to doses of opioids used in the post-operative period.[104]

Lastly, the optimum treatment of acute post-operative pain can definitely improve health-related quality of life, (QOL) while sub-standardpost-operative pain management may negatively interfere with patient’s activities of daily life.

Measurement of pain

Pain measurement is done by two methods;

1. Type I methods

Theseare objective methods, done by the physician as he/she assigns numbers about the patient's condition. They include the following variables:

Physiological indices

- Endocrinal (increase in serum cortisol and catecholamine).
- Cardiovascular (increase in blood pressure and heart rate)
- Respiratory (increase in respiratory rate and decrease in tidal volume)

Neuro-pharmacological

- Correlation with beta endorphin (decreased in acute painful conditions)
- Thermography (hypo-emission in chronic pain)

Neurological

- Nerve conduction velocity
- Evoked potentials
- Single positron emission tomography (SPET).

Behavioural

- Sighing, crying, shouting, trembling.

2. Type II methods

Broadly, type II methods consist of:

Single dimension methods

- Category scale (verbal rating scale)
- Numerical rating scale
- Visual analogue scale (VAS)
- Graphic rating scale

Multi-dimensional methods

- Mc Gill pain Questionnaire, MPQ
- Dartmouth pain Questionnaire, DPQ
- West Haven-Yale pain Questionnaire, WHYPQ.[97]

Measurement of pain in clinical practice is dependent on verbal dialogue between the patient and the doctor or nurse. In research projects and in case of processing clinical data, a rating scale is mandatory.

A number of differences between individual patients makes the comparison of pain measurement tricky. For example,positive or negative experiences in the past influence the patient's present perception of pain. Also, demographic factors such as gender, age, and ethnic background influence the individual's perception of pain. Clinically depressed and anxious patients naturally tend to report increased pain intensity.

Even though pain is a mostly a subjective experience, great attention has been paid to the quantification of this experience. As pain is a subjective experience, everyone has different perceptions of that experience. Differences are found in how individuals quantify pain. For example, some individuals would never say that their pain was a (10) on a scale from (0) to (10). On the other hand, other individuals report their pain as a constant (10) despite looking calm and relaxed. Also, all visual and numerical scales used to measure pain have ‘floor and ceiling’ effect. If the patient describeshis/her pain to be a (10), there is no way to report a subsequent increase in pain intensity.

From most of the methods available to score pain, Visual Analogue Scale (VAS) is most commonly used in the single dimension method.

Visual analogue scale (VAS)

The visual analogue scale uses a straight line with extremities of pain intensity on either end. The line is typically 10 cm long with one end defined as “no pain” and the other end being “excruciating unbearable pain”. The line can be either vertical or horizontal. The patient is asked to place a mark on that line to describe the amount of pain that he/she is currently experiencing. The distance between the end labelled “no pain” and the mark placed by the patient is measured and rounded to the nearest centimetre. To assist in describing the intensity of pain, words can be placed along the scale (for example, mild, moderate, or severe). Such descriptors can help to orient the patient for the degree of pain; this particular variation of the VAS has been known as a graphic rating scale. Occasionally, the patient may be confused about the line, perceiving it to represent time of degree of relief rather than degree of pain intensity. Hence, good explanation towards the patient is required by the clinician when using the VAS.[80]

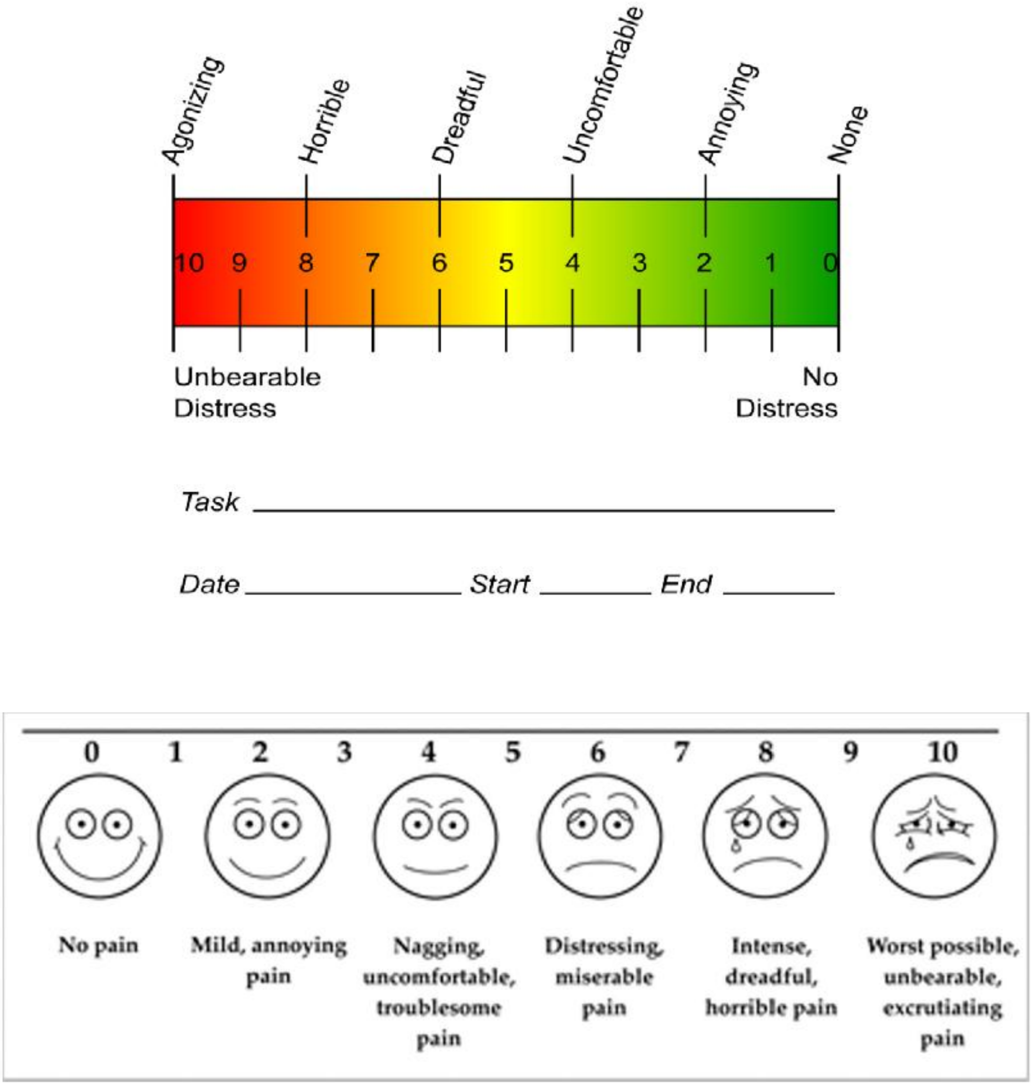


Figure 6. Visual Analog Scale

MANAGEMENT OF POST-OPERATIVE PAIN

Prophylactic measures

The incidence, severity, duration of pain and suffering during the post-operative period can be reduced by good pre-operative and post-operative surgical and psychological care. Although the accepted definition of pain emphasises the cognitive, emotional response to tissue damage, the role of psychological techniques in the relief of acute pain has been minimised. Psycho-educational care has beneficial effects on recovery, post-operative pain and in psychological distress post-surgery.

Psycho-educational care was classed as health-care information (information in preparation for surgery, timing of procedures, function and roles of health-care providers, self-care actions, and pain and discomfort information); skills teaching (coughing, breathing and bed exercises, relaxation, hypnosis); and psychosocial support (identifying and alleviating concerns, reassurance, problems solving, and encouraging questions).

Good surgical technique helps decrease the severity of post-operative pain. Skilled gentle handling of tissues, carrying out the operation under observance of good surgical principles promote minimal trauma. Proper post-operative care help to decrease the magnitude of post-operative pain. This involves provision of psychological support, proper care of wounds, early ambulation, and good nursing care.

ACTIVE MEASURES

Post-operative pain can be partially or completely eliminated by one of the following methods:

1. Systemic analgesics and adjuvants

- Narcotics
- Non-steroidal anti-inflammatory drugs

- Intravenous paracetamol
- NMDA antagonists
- Alpha-2 adrenergic agonists
- Miscellaneous non-opioid compounds

2. Local infiltration and field block - Regional analgesia with local anaesthetics

- Continuous segmental epidural block
- Interpleural analgesia
- Intraperitoneal analgesia

3. Regional analgesics with neuro-axial opioids

4. Regional analgesia with combined local anaesthetics and opioids

5. Electrical analgesia achieved with transcutaneous electrical stimulation or electroacupuncture.[81]

PNEUMOPERITONEUM AND PAIN

Post-laparoscopic pain syndrome is well recognised and characterised by abdominal and particularly shoulder tip pain; it occurs frequently following laparoscopic cholecystectomy. The etiology of post-laparoscopic pain can be classified into three aspects:

- Visceral
- Incisional

- Shoulder.

The origin of shoulder pain is thought to be due one of many possible factors, most commonly due to the overstretching of the diaphragmatic muscle fibres from high CO_2 pressure. The stimulation of the sympathetic nervous system leads to an amplified local tissue inflammatory response. Another factor is the reverse Trendelenburg position. This causes CO_2 to rise and get trapped in between the liver and the right diaphragm causing diaphragmatic irritation and hence post-operative shoulder tip pain.[12]

A pneumoperitoneum of 12 to 16 mmHg is generally used in laparoscopic cholecystectomy. Lower pressures are claimed to be safe and effective in decreasing cardiopulmonary complications and pain.[105]

Post-operative shoulder tip pain due to pneumoperitoneum most commonly affects the right shoulder but the left shoulder can be affected as well.[106] A number of studies have looked at methods to reduce the incidence and severity of shoulder tip pain following laparoscopic cholecystectomy; such as warming and humidifying of CO_2, abdominal wall lift, intraperitoneal gas drain, intraperitoneal saline wash, nitrous oxide pneumoperitoneum and low pressure CO_2 insufflations.

Abdominal wall lift although has an advantage of not causing any haemodynamic changes, but it provides sub-optimal visualisation of the intra-abdominal cavity. It also needs special instrument setup as well as the additional cost of equipment. NO_2 gas insufflation is not preferred as it is a combustible gas. Intra-abdominal drain placement to drain residual CO_2 gas is a possible source of entry for infections. Drains are also reported to increase the intensity of posoperative pain. The cardio-pulmonary effects induced by pneumoperitoneum are secondary to CO_2 insufflation and the increased intraabdominal pressure. Carbon dioxide insufflation is also associated with altered blood gas parameters like hypercarbia and acidosis, both of which are proven direct myocardial depressants.[108]

It was earlier believed that the higher the pressure, the better the view and exposure for laparoscopic procedures. However, the maintenance of elevated intra-abdominal pneumoperitoneum pressure during the surgery is associated with numerous undesirable consequences- hemodynamic changes, decreased pulmonary compliance, decreased kidney and liver perfusion, decreased venous blood return from the lower extremities, and even increased risk of arrhythmias and cardiac events.[108]

The need for this study arises with the thought that low pressure CO_2 insufflation will reduce the post-operative shoulder tip pain and enable for a faster recovery with less need for post-operative analgesia.

With the expanding role of ambulatory surgeries and the need to facilitate an early discharge, improving post-operative pain has become an increasingly important issue. Keeping this in mind, this study has been planned. This would lead to early discharge from hospitals, early recovery and patients can soon get back to their routine activities, as pain post-operatively is a major discomfort for the patient.

Studies have shown that the incidence and intensity of post-operative shoulder tip pain is significantly less in the low-pressure pneumoperitoneum (10 mm Hg of CO_2) group when compared with standard-pressure pneumoperitoneum (14 mm Hg CO_2) groups.[108,109]

METHODOLOGY

This study was done at the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, Karnataka.

Study Design

The study design was a Randomised Controlled Trial (RCT).

Study Period and Duration

This study was done for a period of one year from 1st January 2015 to 31st December 2015.

Place

This study was conducted under the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi a tertiary care teaching hospital attached to KLE University's Jawaharlal Nehru Medical College, Belagavi.

Source of Data

Patients undergoing elective laparoscopic cholecystectomy for cholelithiasis during the study period were enlisted.

Sample Size

The study comprised of 80 patients with cholelithiasis who were categorised into two groups of 40 patients each.

Sampling Procedure

The sample size was calculated based on the following equation,

$$n = \frac{2(Z_{\alpha}+Z_{\beta})^2 (S_1^2+S_2^2)}{(x_1-x_2)^2}$$

where, n = sample size

$Z_{\alpha} = 1.96$

$Z_{\beta} = 0.84$

S_1, S_2 = Standard deviation = 0.45, 0.74

x_1-x_2 = Effect size = 0.2-0.64

According to data from published articles, sample size suggested for each group is calculated to be 62 patients each in group A and B.

However, on the basis of data collection over the past three years in this institute, it was anticipated that approximately 80 such surgical procedures would be performed during the study period. Hence, the total sample size of 80 patients; divided into two groups of 40 patients each in group A and B was finalised.

Randomisation

The patients undergoing laparoscopic cholecystectomy and those who fulfilled the selection criteria were randomly divided into two groups of equal number by a ‘Sequential Numbered Opaque Envelope Method’ as below.

- Group A: Laparoscopic Cholecystectomy with standard pressure of 14 mmHg CO_2 pneumoperitoneum.

- Group B: Laparoscopic Cholecystectomy with low pressure of 10 mmHg CO_2 pneumoperitoneum

Selection Criteria

Inclusion

- Patients aged 18 years to 65 years.
- Elective surgery for gall stone disease.
- Patients who give written and informed consent for participation.

Exclusion

- Conversion to open cholecystectomy.
- Acute inflammation or any other complication of gall stone disease.
- Choledocholithiasis.
- Co-existent liver disease.
- Any intra-operative or post-operative complication such as bile duct injury, bile duct obstruction, intra-operative discovery of bile duct anomalies, infection and high fever.
- Uncontrolled medical diseases like hypertension, coronary artery disease, diabetes mellitus, COPD or asthma.
- Patients with significant portal hypertension, coagulopathies, suspected gallbladder carcinoma, cirrhosis or generalised peritonitis.
- Patients undergoing any additional surgical procedure in the same sitting.

- Failure to obtain consent.

Ethical Clearance

Prior to the commencement, the study was approved from the Institutional Ethical Committee, Jawaharlal Nehru Medical College, Belagavi.

Informed Consent

The patients fulfilling this selection criteria were briefed regarding the purpose of this research study. A written informed consent was then obtained, prior to the surgery, from the patient and/or next of kin (Annexure I).

Method of Collection of Data

Demographic data including age and gender were noted. Patients were questioned about their presenting complaints, past history regarding comorbid conditions, treatment history and surgical history. Clinical presentation and symptoms of abdominal pain, vomiting and fever were recorded. Further these patients were subjected to clinical examination for vitals and systemic examination including abdominal examination. These findings were recorded on a predesigned pro forma (Annexure II).

Investigations

Patients were subjected to the following investigations.

- Complete blood count
- Liver function tests (LFT)
- Urine routine & microscopy,

- Serum Urea & Serum Creatinine
- Coagulation profile

Radiological assessment

Patients underwent ultrasound of abdomen and CT scan (as & when required) to conclude the diagnosis.

Procedure

Laparoscopic cholecystectomy at our hospital is performed by experienced consultant surgeons.

Pre-operative work-up

Pre-operative work up is done for all patients from the day of admission. These include routine investigations like complete haemogram, liver function tests, renal and urinary profile, coagulation profile. Also, pre-operative abdominal ultrasound was done to confirm diagnosis, to look at the site of calculi, to record gall bladder wall thickness, and to look for evidence of inflammation. All the patients were assessed pre-operatively by physicians and anaesthetists to evaluate co-morbidities and document fitness for surgery.

Laparoscopic Cholecystectomy

Procedure of laparoscopic cholecystectomy

Position: Classical supine position with the patient in 30^0 reverse Trendelenburg tilt.

Nasogastric tube was used to ensure complete gastric deflation during the procedure. This is because a distended stomach and duodenal cap can obscure the view of the operative field. The urinary bladder was catheterised so as to prevent any Veress needle injury to a distended urinary bladder.

Part-preparation and draping done was in the standard manner.

Access to peritoneal cavity

1. Closed peritoneal insufflation
2. Open laparoscopy using the modified Hasson's cannula.

Closed pneumoperitoneum

This technique entails the initial creation of a carbon dioxide pneumoperitoneum using Veress needle and electronic insufflators. Veress needle most often inserted at the infra-umbilical site

A 10 mm port is inserted at the infra-umbilical region, through which the camera (30^0) is introduced. Following this the abdomen is inspected. After inspection, three more ports inserted under vision. 10mm left upper paramedian, placed 1cm lateral to linea alba and 3 cm below the left costal margin (to avoid the Falciform ligament), 5 mm right upper midclavicular, 5 mm right lower axillary.

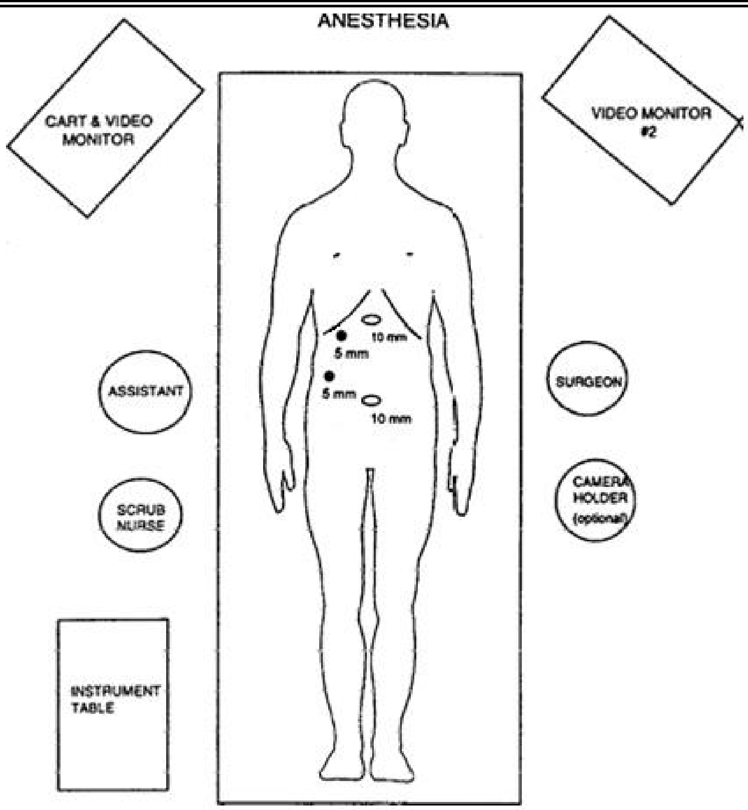


Figure 7. Laparoscopic Cholecystectomy Trocar Placement & OT Setup

Intervention

Group A

Patients in this group underwent Laparoscopic Cholecystectomy under pneumoperitoneum with standard pressure that is, 14 mmHg CO_2.

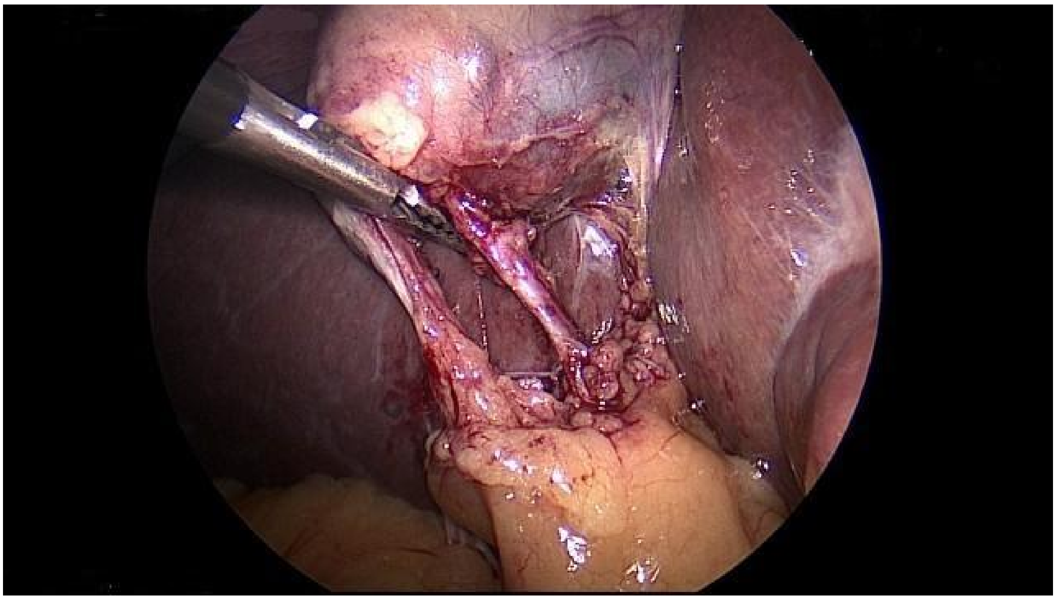
Group B

Patients in this group underwent Laparoscopic Cholecystectomy under pneumoperitoneum with standard pressure that is, 10 mmHg CO_2.

Photograph 1. CO_2 Insufflators Showing Selected Pressure of Pneumoperitoneum

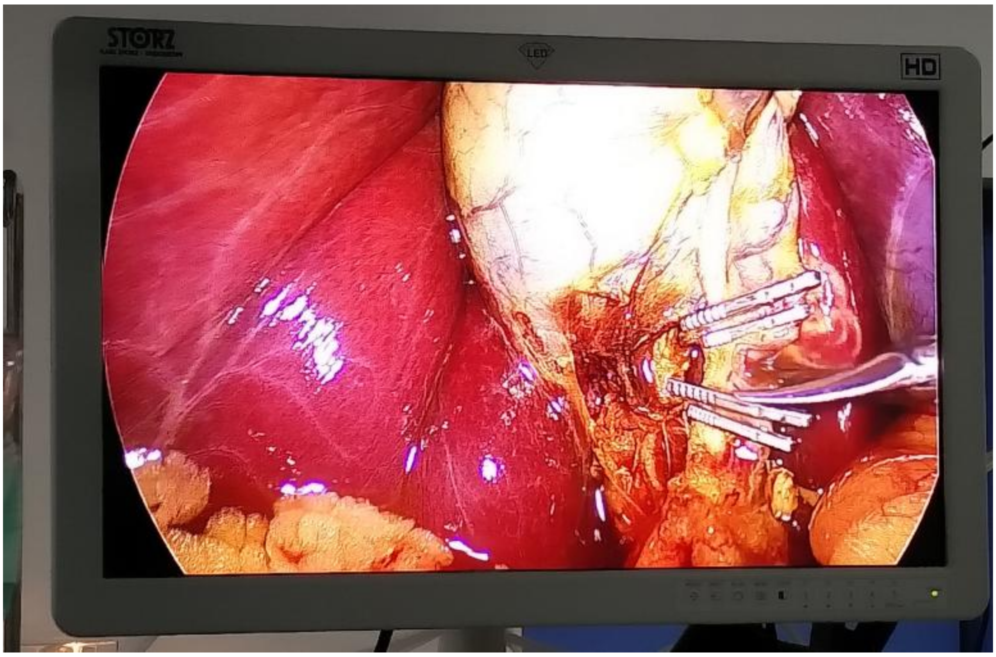
Surgical Procedure:

The cystic pedicle was exposed by grasping the fundus of the gallbladder. This was then retracted in the direction of the right shoulder, enabling to view the sub-hepatic anatomy. An atraumatic grasper was used to hold the neck and then directed upwards and anteriorly. The Calot’s triangle was visualised after skeletonising the cystic duct (usually runs anteriorly), the cystic artery (above and behind the duct) and the lymph node of Lund which is found attached to the neck of the gallbladder in between the duct and artery. The dissection of the pedicle was performed with monopolar/bipolar forceps, scissors, or J-hook instruments. Once the cystic duct and artery were adequately exposed and the confluence of the cystic duct with the common hepatic duct was identified, the critical view of safety was established. When the Calot's triangle is dissected, except cystic duct and artery and the base of the liver bed is exposed 'the two structures entering the gall bladder can only be cystic duct and cystic artery.



Photograph 2. The Critical View of Safety

The cystic duct was milked towards the gall bladder to ensure no calculi remained in the duct. Titanium clips were applied nearer to the gallbladder end and duct was transected in between clips. The same was followed for the cystic artery. The dissection was carried out in the loose fibrous layer of the cystohepatic plate to separate the gallbladder from the liver bed. Once separation of gallbladder was complete, it was grasped with claw forceps and retrieved in an endo-bag through the epigastric 10 mm port. Care was taken to avoid spillage of contents into the peritoneal cavity. After this, final inspection was done to look for any ooze (blood and bile). All ports were removed under vision after decompressing the abdominal cavity to evacuate the carbon dioxide. Ports were closed using Vicyl™ for the rectus sheath and skin sutured with Ethilon™. Sterile dressing was applied. The patient was extubated and subsequently monitored in the OT recovery.



Photograph 3. Cystic Duct Transected In between Clips

Photograph 4. Typical Gall Bladder Specimen

Post-operative assessment

At the first hour post-surgery, the VAS for shoulder tip pain was documented as stated by the patient. Later the patient was shifted to his/her ward or Surgical ICU as per the condition.

Outcome variables

Post-operative shoulder tip pain

Post-operative shoulder tip pain was assessed at 1, 6, 12 and 24 hours after operation by the Numerical Rating Scale of Pain. A 100 mm horizontal line with scores from 0 (no pain) to 10 (agonizing pain) at 10 mm intervals was used, allowing patients to mark a point along the scale that best represents their shoulder tip pain at that particular time.

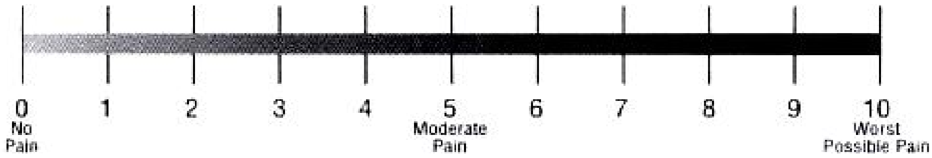


Figure 8. Numerical rating scale

<u>Management of pain</u>

If Numerical Analogue score was 3 or more, an intramuscular injection of Diclofenac Sodium (75 mg) was given as rescue analgesia and the time and quantity given was noted.

The data regarding these variables was documented by the operating surgeon.

Statistical analysis

The data obtained was coded and entered in Microsoft Excel™ Spreadsheet (Annexure III). The categorical data was expressed as rates, ratios and percentages and comparison was done using chi-square test or Fisher's exact test. Continuous data was expressed as mean ± standard deviation. A 'p' value of less than or equal to 0.05 at 95% confidence interval was considered as statistically significant.

RESULTS

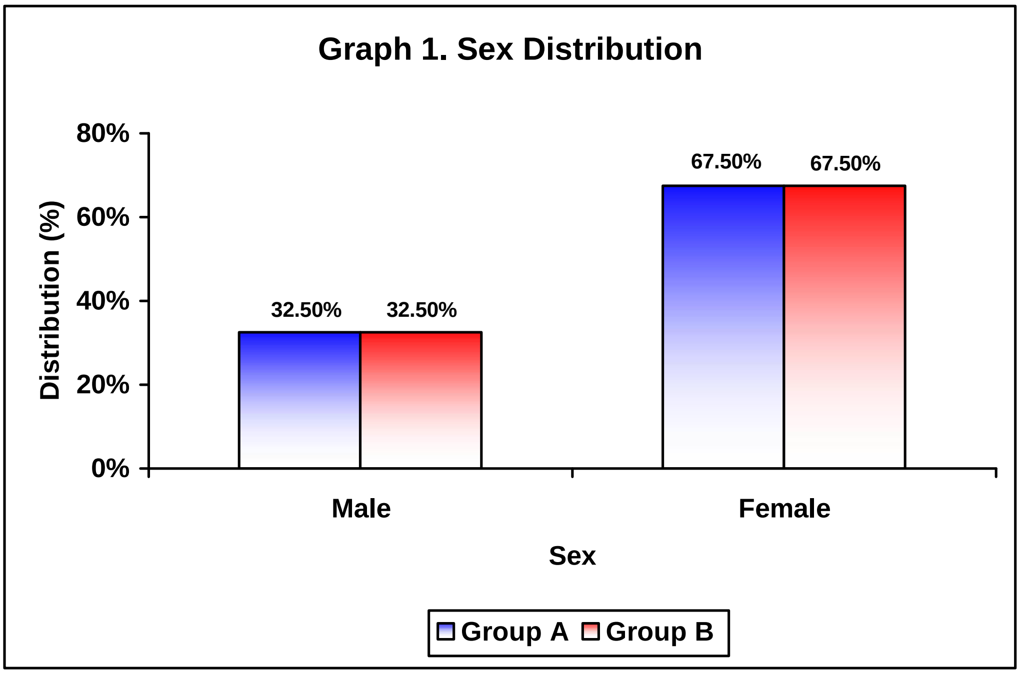
This one year Randomised Controlled Trial was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, during 1st January 2015 to 31st December 2015. A total of 80 patients undergoing elective laparoscopic cholecystectomy were selected. These patients were randomly divided into two groups of equal number by a ‘Sequential Numbered Opaque Envelope Method’. Group A (Patients underwent Laparoscopic Cholecystectomy under standard pressure pneumoperitoneum of 14 mmHg CO_2) and Group B Patients underwent Laparoscopic Cholecystectomy under low pressure pneumoperitoneum of 10 mmHg CO_2).

The data was analysed and the final results and observations were tabulated as follows:

Table 1. Sex Distribution

Sex	Group A (n=40)		Group B (n=40)	
	Number	Percentage	Number	Percentage
Male	13	32.50	13	32.50
Female	27	67.50	27	67.50
Total	**40**	**100.00**	**40**	**100.00**

p = 1.000

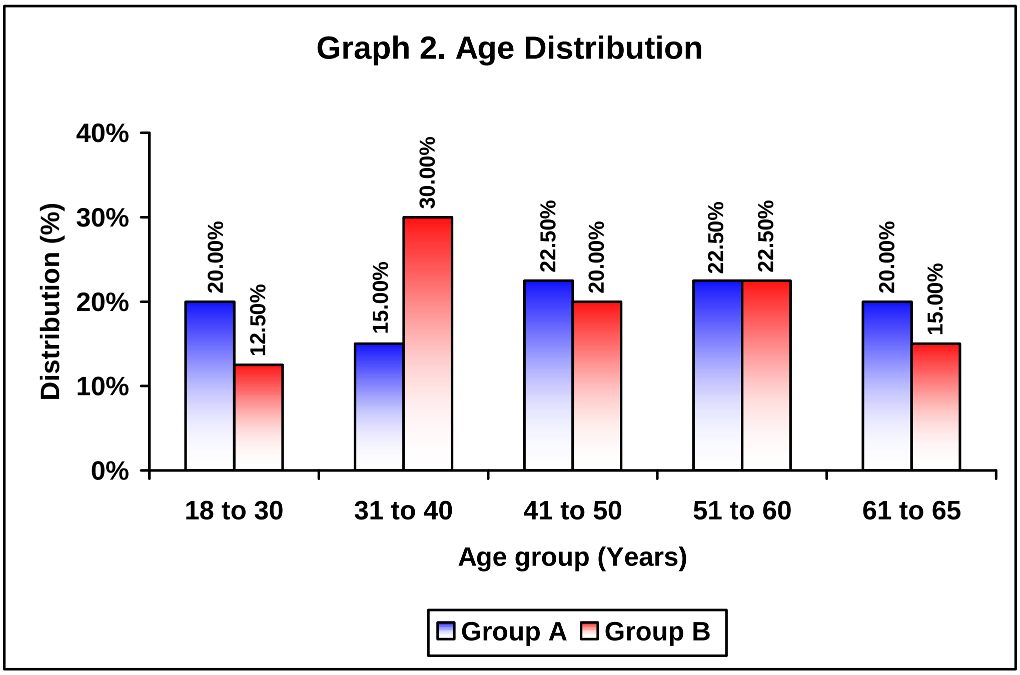


In the present study 67.50% of the patients each in group A and Group B were females with male to female ratio of 1:2.07 in each group. However sex distribution in Group A and B was comparable (p=1.000).

Table 2. Age Distribution

Age Group (Years)	Group A (n=40)		Group B (n=40)	
	Number	Percentage	Number	Percentage
18 to 30	8	20.00	5	12.50
31 to 40	6	15.00	12	30.00
41 to 50	9	22.50	8	20.00
51 to 60	9	22.50	9	22.50
61 to 65	8	20.00	6	15.00
Total	**40**	**100.00**	**40**	**100.00**

p = 0.552



In this study most of the patients were aged between 31 to 40 years (30.00%) in group B, while in group A, 22.50% of the patients each were aged 41 to 50 years and 51 to 60 years. However this difference was statistically not significant (p=0.552).

Table 3. Mean age

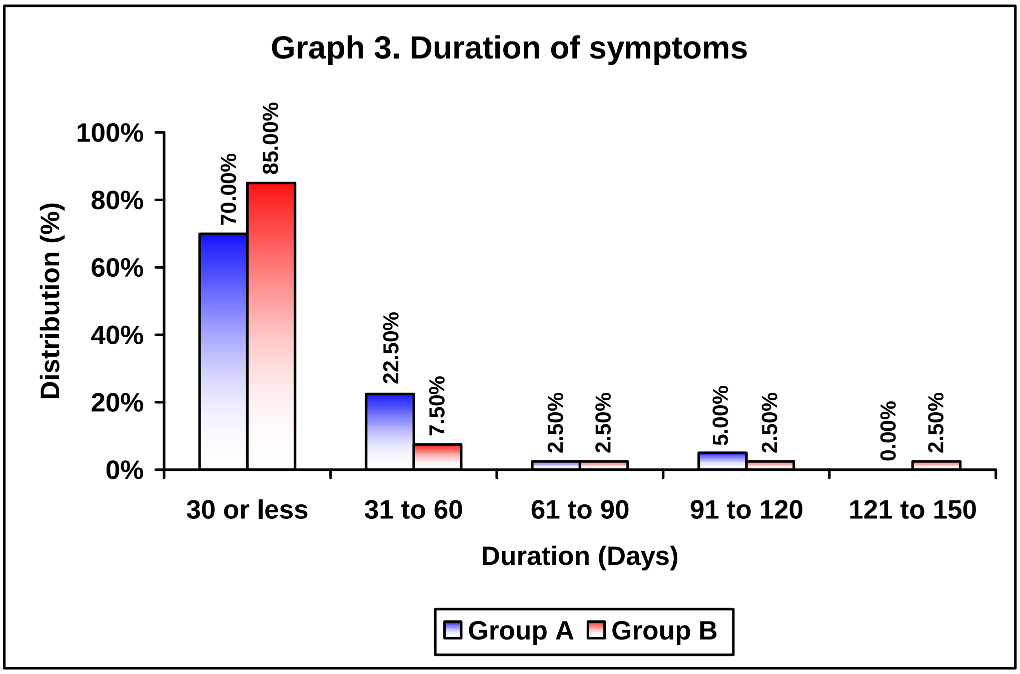
Variables	Group A (n=40)		Group B (n=40)		p Value
	Mean	SD	Mean	SD	
Age (Years)	46.93	14.09	45.80	13.07	0.712

In the present study mean age of patients was almost equal in group A (46.93 ± 14.09 years) and in group B (45.80 ± 13.07 years) (p=0.712).

Table 4. Duration of symptoms

Duration (Days)	Group A (n=40)		Group B (n=40)	
	Number	Percentage	Number	Percentage
30 or less	28	70.00	34	85.00
31 to 60	9	22.50	3	7.50
61 to 90	1	2.50	1	2.50
91 to 120	2	5.00	1	2.50
121 to 150	0	0.00	1	2.50
Total	**40**	**100.00**	**40**	**100.00**

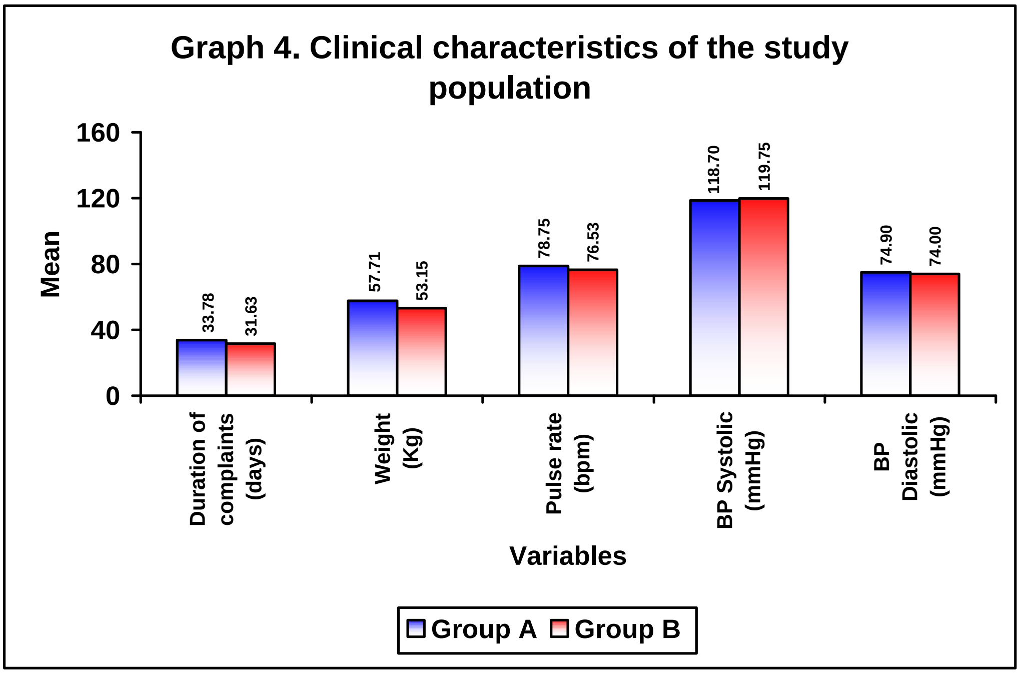
p = 0.296



In the present study the duration of symptoms among 85% of the patients in group B was ≤30 days compared to 70% in group A. However this difference was statistically not significant (p=0.296).

Table 5. Clinical characteristics of the study population

Variables	Group A (n=40)		Group B (n=40)		p Value
	Mean	SD	Mean	SD	
Duration of complaints (days)	33.78	28.31	31.63	29.32	0.740
Weight(Kg.)	57.71	12.21	53.15	8.02	0.052
Pulse rate (bpm)	78.75	5.14	76.53	5.34	0.061
BP Systolic (mmHg)	118.70	7.45	119.75	9.74	0.590
BP Diastolic (mmHg)	74.90	6.34	74.00	5.91	0.513

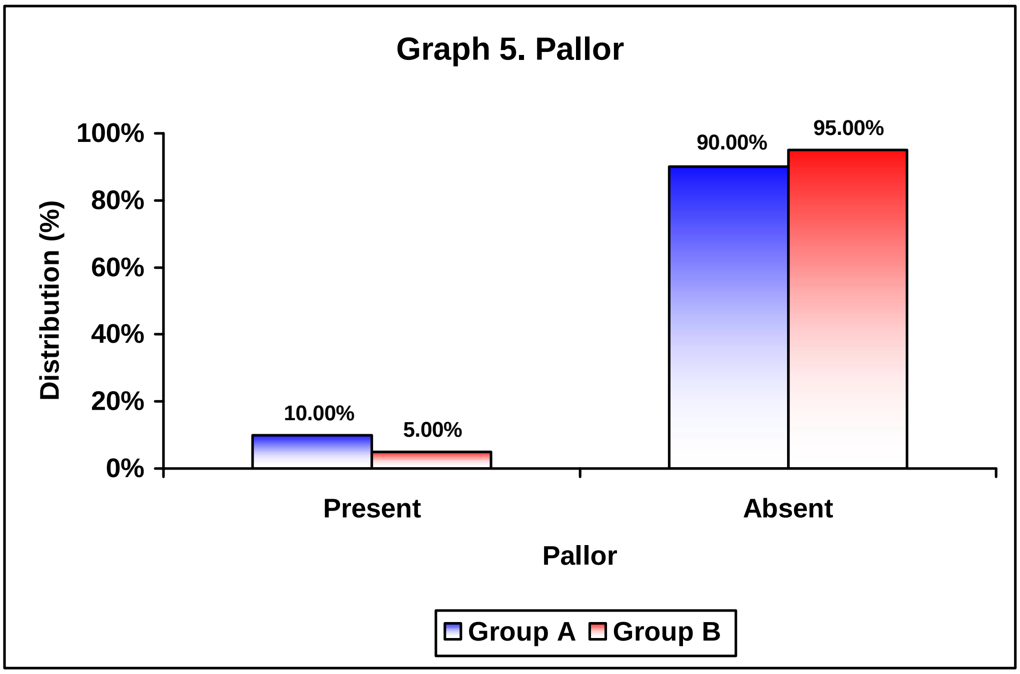


The comparison of clinical characteristics is as shown in Table 5 and graph 4. It was observed that, the mean duration of complaints, weight, pulse rate, systolic and diastolic blood pressure were comparable in group A and B (p>0.050).

Table 6. Pallor

Pallor	Group A (n=40)		Group B (n=40)	
	Number	Percentage	Number	Percentage
Present	4	10.00	2	5.00
Absent	36	90.00	38	95.00
Total	**40**	**100.00**	**40**	**100.00**

p = 0.396

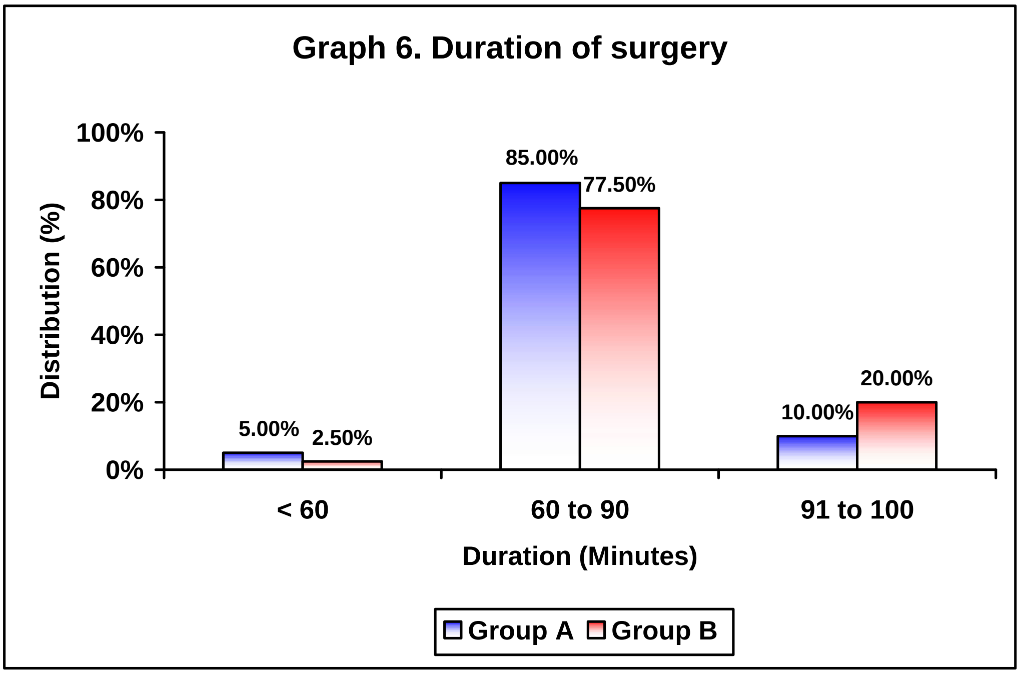


In the present study pallor was noted in 10.00% of the patients in group A compared to 5% in group B. However, this difference was statistically not significant (p=0.396).

Table 7. Duration of surgery

Duration (Minutes)	Group A (n=40)		Group B (n=40)	
	Number	Percentage	Number	Percentage
< 60	2	5.00	1	2.50
60 to 90	34	85.00	31	77.50
91 to 120	4	10.00	8	20.00
Total	**40**	**100.00**	**40**	**100.00**

p = 0.406

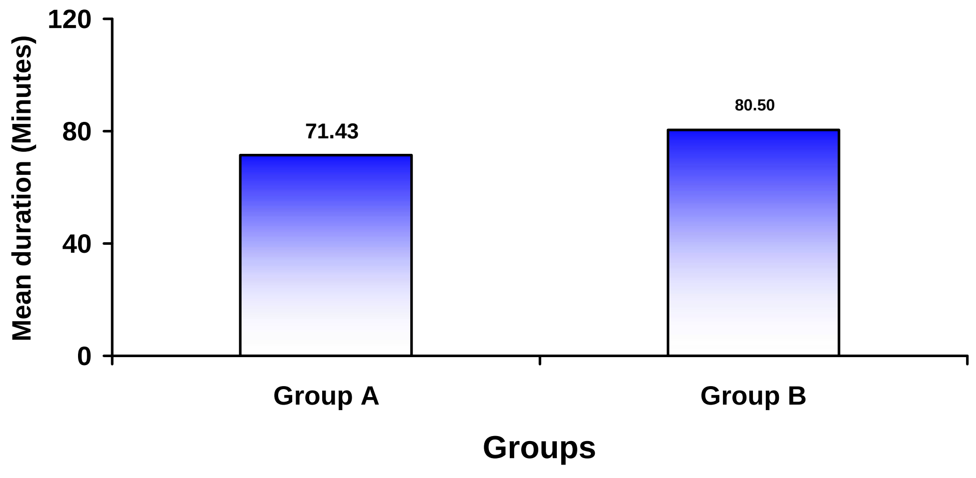


In this study most of the patients in group A and group B had 60 to 90 minutes duration of surgery (85.00% vs. 77.50%; p=0.406)

Table 8. Comparison of mean duration of surgery

Variables	Group A (n=40)		Group B (n=40)		p value
	Mean	SD	Mean	SD	
Duration of Surgery (minutes)	71.43	18.43	80.50	26.62	0.081

Graph 7. Comparison of mean duration of surgery

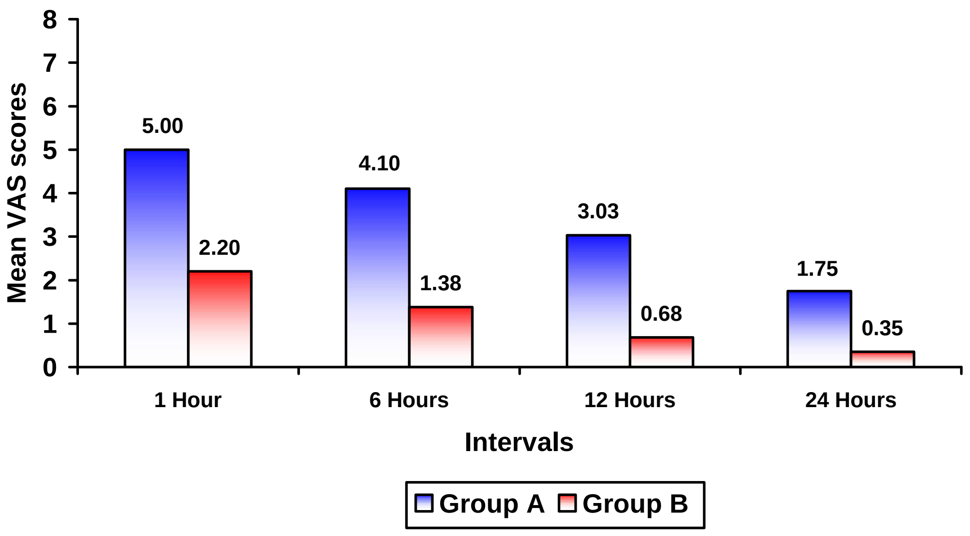


In the present study mean duration of surgery in group A and group B was comparable (71.43 ± 18.43 vs 80.50 ± 26.62 minutes; p=0.081).

Table 9. Comparison of pain

Intervals	Group A (n=40)		Group B (n=40)		p Value
	Mean	SD	Mean	SD	
1 Hour	5.00	1.84	2.20	1.22	**<0.001**
6 Hours	4.10	1.57	1.38	0.98	**<0.001**
12 Hours	3.03	1.46	0.68	0.83	**<0.001**
24 Hours	1.75	1.32	0.35	0.48	**<0.001**

Graph 8. Comparison of pain

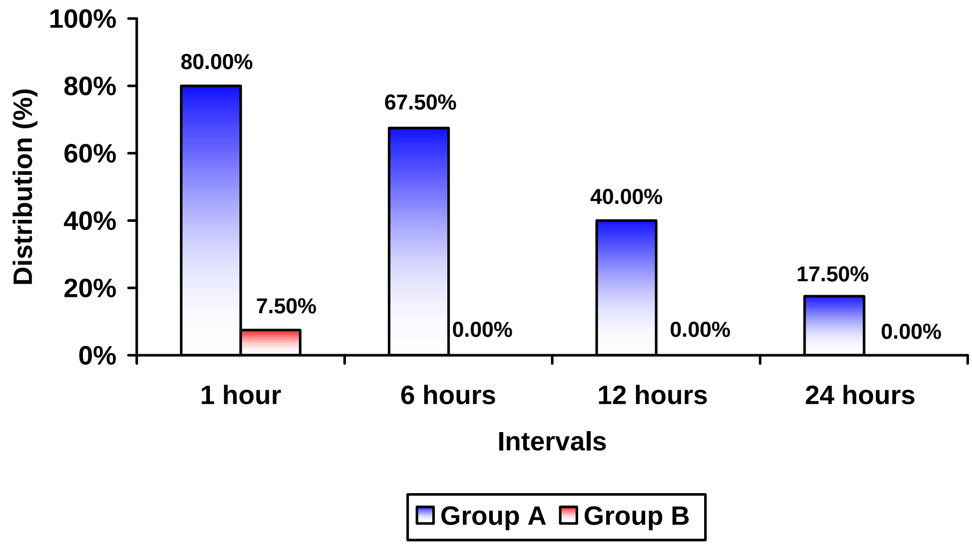


In the present study the mean pain scores at 1 (5.00 ±1.84 vs 2.20 ± 1.22; p<0.001), 6 (4.10 ±1.57 vs 1.38 ± 0.98; p<0.001), 12 (3.03 ±1.46 vs 0.68 ± 0.83; p<0.001) and 24 (1.75 ± 1.32 vs 0.35 ± 0.48; p<0.001) hours were significantly low in group B compared to group A.

Table 10. Requirement of rescue analgesia

Intervals (hours)	Rescue analgesia	Group A (n=40)		Group B (n=40)		p Value
		Number	Percentage	Number	Percentage	
1 hour	Required	32	80.00	3	7.50	**<0.001**
	Not required	8	20.00	37	92.50	
	Total	**40**	**100.00**	**40**	**100.00**	
6 hours	Required	27	67.50	0	0.00	**<0.001**
	Not required	13	32.50	40	100.00	
	Total	**40**	**100.00**	**40**	**100.00**	
12 hours	Required	16	40.00	0	0.00	**<0.001**
	Not required	24	60.00	40	100.00	
	Total	**40**	**100.00**	**40**	**100.00**	
24 hours	Required	7	17.50	0	0.00	**0.006**
	Not required	33	82.50	40	100.00	
	Total	**40**	**100.00**	**40**	**100.00**	

Graph 9. Requirement of rescue analgesia

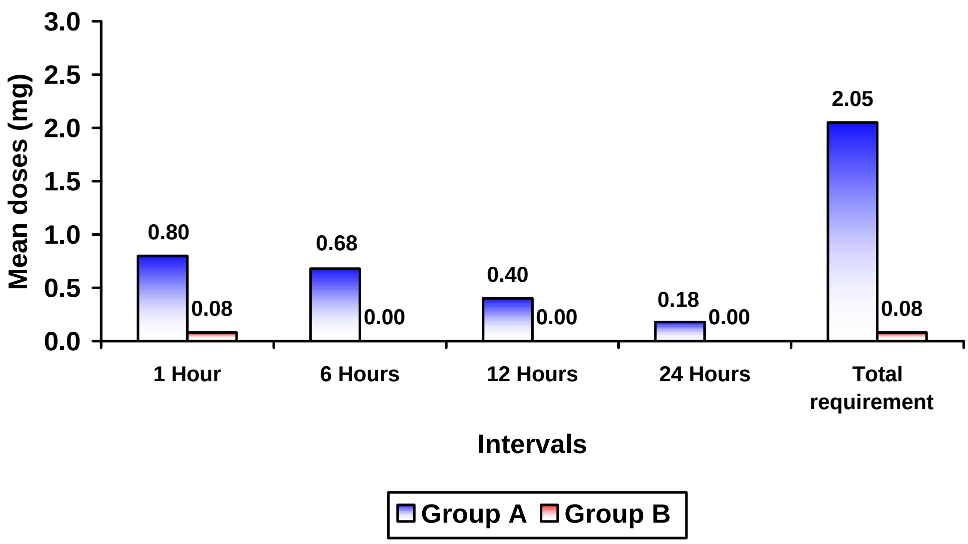


In this study the requirement of analgesia was significantly high in patients with group A compared to group B at 1,6, 12 and 24 hours interval (p<0.050).

Table 11. Requirement of mean rescue analgesia

Intervals	Group A (n=40)		Group B (n=40)		p value
	Mean	SD	Mean	SD	
1 Hour	0.80	0.41	0.08	0.27	**<0.001**
6 Hours	0.68	0.47	0.00	0.00	**<0.001**
12 Hours	0.40	0.50	0.00	0.00	**<0.001**
24 Hours	0.18	0.38	0.00	0.00	**0.006**
Total requirement	2.05	1.38	0.08	0.27	**<0.001**

Graph 10. Requirement of mean rescue analgesia



In the present study the mean requirement of rescue analgesia was significantly high in group A compared to group B at all the intervals (p<0.050). Also mean total requirement was high in group A compared to group B (p<0.001).

DISCUSSION

Laparoscopic cholecystectomy has substituted open surgery in the surgical management of cholecystolithiasis. It is now the gold standard in the treatment of benign gallstone disease.[110] Laparoscopic surgery requires pneumoperitoneum for adequate visualisation and operative manipulation.

During laparoscopic cholecystectomy, adequate working space is required in the abdomen for good visualisation. This contributes to good operative results and patient safety. Common methods to create working space in the abdomen are pneumoperitoneum and abdominal wall lifting methods such as the laparotensor and laparolift. Pneumoperitoneum for laparoscopic cholecystectomy is most often created by insufflating carbon dioxide gas into the peritoneal cavity and then holding it at constant pressure till the end of surgery when it is released at the time of removal of the ports. Standard pressure pneumoperitoneum employs a pressure range of 12-14 mmHg. But, over prolonged periods it has been associated with adverse effects such as decreased pulmonary compliance, altered blood gas parameters, impaired function of the circulatory system, raised liver enzymes, renal dysfunction, and elevated intra-abdominal venous pressures.[13]

Carbon dioxide is the most used gas used to create pneumoperitoneum because of high diffusibility and quick absorption and excretion.[13] The use of CO_2 in laparoscopy evokes local and systemic effects.[14] Peritoneal insufflation of CO_2 may alter the acid-base balance, affect cardiovascular and pulmonary physiology, and in high risk patients it may elevate the post-surgical complications.[7]

Nowadays, there is an emerging trend utilising low pressures for pneumoperitoneum in the range of 7-10 mmHg instead of the standard pressure pneumoperitoneum. This is in an attempt to lower the impact of pneumoperitoneum on human physiology while providing adequate working space· Other advantages of low pressure pneumoperitoneum appear to be lower incidence and severity of shoulder tip pain in the post-operative period and also better quality of life in the week following surgery.[16,17,111,112]

This study proposes to compare the use of the low pressure pneumoperitoneum (10mm Hg) with the use of standard pressure pneumoperitoneum (14mm Hg) in patients undergoing laparoscopic cholecystectomy in a prospective randomised manner. The main areas of interest were post-operative course shoulder pain scores.

This one year Randomised Controlled trial was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 80 patients undergoing elective laparoscopic cholecystectomy from 1st January 2015 to 31st December 2015 were selected. These patients were randomly divided into two groups of equal number by a ‘Sequential Numbered Opaque Envelope Method’ as Group A where patients underwent Laparoscopic Cholecystectomy under pneumoperitoneum with standard pressure of 14 mmHg CO_2 and Group B where patients underwent laparoscopic cholecystectomy under pneumoperitoneum with low pressure of 10 mmHg CO_2.

In the present study the majority of the patients were females, that is 67.50% of the patients each in Group A and Group B were females. The male to female ratio was 1:2.07 in each group and the sex distribution in Group A and Group B were almost same (p=1.000).

In this study most common age group was 31 to 40 years (30.00%) in Group B, compared to 22.50% of the patients each who were aged between 41 to 50 years and 51 to 60 years in Group A. However this difference was not statistically significant (p=0.552). Also the mean age of patients was almost equal in Group A (46.93 ± 14.09 years) and (45.80 ± 13.07 years) in Group B (p=0.712).

The above findings suggest that the demographic characteristics were comparable in both the groups (p>0.050).

In this study, among the 85% of the patients in Group A, the duration of symptoms was ≤30 days compared to 70% in Group B. However this difference was not statistically significant. (p=0.296). The clinical characteristics including mean duration of complaints, weight, pulse rate, systolic and diastolic blood pressure were comparable in Group A and B (p>0.050). On physical examination, the findings revealed pallor in 10.00% of the patients in Group A compared to 5% in Group B. However this difference was not statistically significant (p=0.396). These findings suggest that the clinical characteristics of the study population were comparable in Group A and Group B (p>0.050).

Overall the demographic and clinical profile of the study population in Group A and Group B were comparable ruling out the possible bias in the study results.

In this study with regard to operative time, 85% of the patients in Group A and had duration of surgery between 60 to 90 minutes compared to 77.50% in Group

B. However this difference was not statistically significant (p=0.406). The mean duration of surgery was slightly less in Group A (71.43 ± 18.43 minutes) compared to Group B (80.50 ± 26.62 minutes) but, statistically this difference was not significant suggesting comparable operative time with low or standard pressure (p=0.081). These findings suggest that, pneumoperitoneum with low pressure of 10 mmHg CO_2 does not significantly affect the surgical time.

These findings were consistent with a randomised controlled trial by Kanwer DB et al.[13] in Chandigarh to compare the use of low pressure pneumoperitoneum with the use of standard pressure pneumoperitoneum where authors reported that, laparoscopic cholecystectomy with standard pressure pneumoperitoneum took an average of 46.4 ± 6.9 minutes with a minimum of 35 minutes and a maximum of 65 minutes. Laparoscopic cholecystectomy with low pressure pneumoperitoneum took an average of 49.1 ± 5.7 minutes with a minimum of 40 minutes and a maximum of 60 minutes. Low pressure laparoscopic cholecystectomy took on average three minutes more than standard pressure laparoscopic cholecystectomy but this difference was not statistically significant (p=0.1). The operating surgeons had noted that there was little difference in the exposure at 10mmHg as compared to that at 14 mmHg. Similar observations were noted by Singla S. et al.[113] where authors reported duration of 39.16 ± 5.14 minutes in low pressure group compared to 39.36 ± 5.43 minutes in standard pressure group (p=0.851).

A major benefit of laparoscopic cholecystectomy is the avoidance of a large, traumatic upper abdominal incision. This results in less post-operative pain and early recovery. But even laparoscopic cholecystectomy is not entirely free from discomfort and pain. Patients complain of abdominal pain and shoulder tip pain after laparoscopic cholecystectomy. Various causes of this pain are peritoneal stretching and diaphragmatic irritation by high intra-abdominal pressure caused by pneumoperitoneum or by CO_2 absorption from the peritoneal cavity.[114,115] Several research studies are done to find out the strategies to reduce frequency and intensity of post-operative pain after laparoscopic cholecystectomy.[15,16,174,111,112,113,114,115]

In the present study based on numerical rating scale, the mean post-operative shoulder tip pain scores at all the intervals were significantly high in Group A compared to Group B, i.e., at 1 hour (5.00 ±1.84 vs 2.20 ± 1.22; p<0.001), 6 hours (4.10 ±1.57 vs 1.38 ± 0.98; p<0.001), 12 hours (3.03 ±1.46 vs 0.68 ± 0.83; p<0.001) and 24 hours (1.75 ± 1.32 vs 0.35 ± 0.48; p<0.001). These findings suggest that, pneumoperitoneum with low pressure of 10 mmHg CO_2 lowers the intensity of pain compared to pneumoperitoneum with standard pressure of 14 mmHg $CO_{2.}$ These findings were consistent with a similar study by Singla S. et al.[117] who reported higher pain intensity among patients who underwent laparoscopic cholecystectomy with standard pressure (Group B) pneumoperitoneum of 14 mmHg CO_2 at 1, 2, 4, 8 and 12 hrs. interval compared to those who underwent laparoscopic cholecystectomy with low pressure (Group A) pneumoperitoneum of 10 mmHg CO_2 with (p< 0.05). At 24 hours, no patient from Group A complained of pain. But in Group B, 16 patients complained of pain. Furthermore, the intensity of pain was assessed by VAS score at specified interval. At all the intervals, mean VAS score was lower in patients who underwent pneumoperitoneum with low pressure of 10 mmHg CO_2 as compared to patients who had pneumoperitoneum with standard pressure of 14 mmHg CO_2 with statistically significant difference. Mean of total VAS score of Group A was 1.42 and of Group B was 7.88 with p-value of 0.001. This shows that the intensity of pain measured by VAS was significantly higher in standard pressure pneumoperitoneum.

Another study by Kanwer DB et al.[13] reported that, one (3.7%) of the 27 patients who underwent low pressure laparoscopic cholecystectomy and two (7.1%) of the 28 patients who underwent standard pressure laparoscopic cholecystectomy had post-operative pain referred to the tip of the right shoulder. This difference was not statistically significant (p = 1.0). The average pain score at 6 hours for patients who underwent low pressure laparoscopic cholecystectomy was 62.2 ± 11.7 with a minimum of 36 and a maximum of 82. The pain score at 6 hours for standard pressure laparoscopic cholecystectomy was 59.1 ± 18.0 with a minimum of 35 and a maximum of 100. This difference was not statistically significant (p = 0.4). The average pain score at 12 hours for patients who underwent low pressure laparoscopic cholecystectomy was 54.2 ± 8.5 with a minimum of 38 and a maximum of 69. The average pain score at 12 hours for patients who underwent standard pressure laparoscopic cholecystectomy was 62.2 ± 12.0 with a minimum of 35 and maximum of 100. This difference was statistically significant. The average pain score at 24 hours for patients who underwent standard pressure laparoscopic cholecystectomy was 5.2 ± 0.8 with a minimum of 3.5 and a maximum of 10. Average pain score at 24 hours for patients who underwent low pressure laparoscopic cholecystectomy was 4.60 ± .81 with a minimum of 3.6 and a maximum of 8.2. This difference was not statistically significant. Despite the methodological differences, the findings of the present study are in agreement with the studies by Kanwer DB et al.[13] and Singla S. et al.[113]

Studies have been done to compare the effect of different intra-abdominal pressures on post-laparoscopic cholecystectomy pain.[116-117] It has been shown that low pressure pneumoperitoneum reduces pain intensity after laparoscopic cholecystectomy.[118] Analgesia requirement is also less in the low pressure group. In this study at 1 (80% vs 7.5%; $p<0.001$) hour interval significantly higher requirement of rescue analgesia was noted in patients with Group A compared to Group B ($p<0.001$). At 6, 12 and 24 hours none of the patient in Group B required rescue analgesia while in Group A 67.5%, 40%, 17.50% of the patients requested for rescue analgesia ($p<0.001$). Furthermore, the mean requirement of rescue analgesia was significantly high in Group A compared to Group B at all 1 hour (0.80 ± 0.41 vs 0.08 ± 0.27; $p<0.001$), 6 hours (0.68 ± 0.47 vs Nil; $p<0.001$), 12 hours (0.40 ± 0.50 vs Nil; $p<0.001$) and at 24 hours (0.18 ± 0.18 vs 1.38 ± 0.27; $p<0.001$). Also mean total requirement was high in Group A compared to Group B (2.05 ± 1.38 vs 0.08 ± 0.27; $p<0.001$). These findings suggest that, creation of pneumoperitoneum with low pressure of 10 mmHg CO_2 is beneficial not only in terms of lower pain scores but also results in significantly lower consumption of rescue analgesia as compared to patients who had pneumoperitoneum with standard pressure of 14 mmHg CO_2. Singla S. et al.[117] in their study also reported that, only four patients in Group A and sixteen patients in Group B were given rescue analgesia. Maximum demand of rescue analgesia was during 3rd and 4th hour with mean demand of 30 mg in low pressure group and 45 mg in standard pressure group. The difference was statistically significant with p-value of 0.045. During the rest of the intervals, rescue analgesia demand was higher in standard pressure group but it was not statistically significant. Overall analgesia consumption was higher in standard pressure group.

Pain following pneumoperitoneum in laparoscopic cholecystectomy is related to a number of factors. Whilst tissue injury at port insertion sites and gall bladder bed are probably the most important contributing factors, other factors that have been proposed are stretching of the peritoneum & diaphragm, chemical irritation of the peritoneum by carbon dioxide & carbonic acid formation, and stimulation of the sympathetic nervous system by hypercarbia.[113]

Overall the present study showed that, the use of the low pressure pneumoperitoneum (10 mmHg) offers lower post-operative shoulder tip pain and thereby results in lower consumption of rescue analgesia without altering the operative time as compared to laparoscopic cholecystectomy with standard pressure pneumoperitoneum (14 mmHg). Other studies by Barczyñski M et al.,[15,16] Davidas D et al.,[16] Vezakis A et al.,[17] Wallace DH et al.,[121] Perrakis E et al.,[122] Dexter SP et al.,[123] a meta-analysis by Gurusamy et al,[124] and Sarli L et al,[125] also reported lower incidence and intensity of postoperative pain in low pressure pneumoperitoneum groups with fewer requirements of analgesics in the postoperative period.

The increased intra-abdominal pressure due to the pneumoperitoneum causes several cardiopulmonary changes. The increased intra-abdominal pressure increases the absorption of CO_2, causing hypercapnia and acidosis, which has to be avoided by hyperventilation. It pushes the diaphragm upwards decreasing the pulmonary compliance and increases the peak airway pressure. Pneumoperitoneum increases the systemic vascular resistance and pulmonary vascular resistance. Carbon-dioxide pneumoperitoneum also predisposes to cardiac arrhythmias. During the early phase of pneumoperitoneum, there is a reduction in the cardiac output by decreasing the venous return. While these cardio-respiratory changes may be tolerated by healthy adults with adequate cardiopulmonary reserve, people with cardiopulmonary diseases may not tolerate these cardiopulmonary changes.

It has been proposed that in comparison to standard pressure pneumoperitoneum, low pressure pneumoperitoneum results in lesser hemodynamic changes with regard to cardiac output, heart rates and blood pressure.[13] Furthermore, The method with low pressure pneumoperitoneum appears to have little adverse effect on the cardiac and respiratory functions and is suitable for the elderly and for those with chronic cardiac or respiratory diseases.[13]

However, the present study did not consider the haemodynamic profile which was limitation of the study. One reason was that the actual difference of 4 mmHg in the intraperitoneal pressures in low pressure pneumoperitoneum and standard pressure pneumoperitoneum groups was not sufficient to influence the hemodynamic status. Also low pressure pneumoperitoneum group had intraperitoneal pressure maintained at 10 mmHg which is close to what some investigators describe as standard pressure in their own studies. The comparatively lower pressure of 10 mm Hg in our study might have been sufficiently high to produce the adverse effects of pneumoperitoneum to the same degree as standard pressure pneumoperitoneum at 14 mm Hg. A study by Kanwer DB et al.[13] failed to show any statistically significant difference between the two groups with regard to blood pressure changes and heart rate changes. In one study it was found that there was no statistical difference in change in blood pressure and heart rate in low pressure pneumoperitoneum (defined as 7 mmHg) and standard pressure pneumoperitoneum (defined as 15 mmHg) groups.[126] They also noted that cardiac output fell to the same level in both groups though it recovered earlier in the low pressure pneumoperitoneum group. In another study, both low pressure pneumoperitoneum and standard pressure pneumoperitoneum caused a decrease in heart rate and mean arterial BP but this was not statistically significant.[11] In our study none of the patients had any major intra-operative or postoperative complications. The post-operative course was by and large uneventful in all patients.

Hence, the findings in this study needs to be examined through a more complex set up and probably a larger sample size that includes a significant numbers of patients with cardiovascular comorbid conditions.

CONCLUSION

Based on the results of this study we conclude that, low pressure pneumoperitoneum with 10 mmHg is beneficial as it results in lower incidence and intensity of post-operative shoulder tip pain. This thereby results in less need for rescue analgesia; without significantly altering the operative time when compared to laparoscopic cholecystectomy with standard pressure pneumoperitoneum (14 mmHg).

SUMMARY

Improving post-operative pain has become an increasingly important issue. The present study was aimed to compare the use of the low pressure pneumoperitoneum (defined as 10 mm Hg) with the use of standard pressure pneumoperitoneum (defined as 14 mm Hg) in patients undergoing laparoscopic cholecystectomy with respect to postoperative shoulder tip pain and the use of analgesics postoperatively.

This one year Randomised Controlled trial was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. from January 2015 to December 2015. A total of 80 patients undergoing elective laparoscopic cholecystectomy were enrolled. These patients were randomly divided into two groups of equal number by a 'Sequential Numbered Opaque Envelope Method' as Group A (Patients underwent Laparoscopic Cholecystectomy under pneumoperitoneum with standard pressure of 14 mm Hg CO_2) and Group B Patients underwent Laparoscopic Cholecystectomy under pneumoperitoneum with low pressure of 10 mmHg CO_2).

Most of the patients (67.50% each) in group A and Group B were females ($p=1.000$). The mean age of patients was almost equal in group A (46.93 ± 14.09 years) and (45.80 ± 13.07 years) in group B ($p=0.712$). The duration of symptoms among 85% of the patients with group A was ≤30 days compared to 70% in group B. However this difference was statistically not significant. ($p=0.296$). It was observed that, the mean duration of complaints, weight, pulse rate, systolic and diastolic blood pressure were comparable in group A and B ($p>0.050$). Pallor was noted in 10.00%

of the patients in group A Compared to 5% in group B (p=0.396). Most of the patients in group A and group B had 60 to 90 minutes duration of surgery (85.00% vs. 77.50%; p=0.406) The mean duration of surgery in group A and group B was comparable (71.43 ± 18.43 vs 80.50 ± 26.62 minutes; p=0.081). The mean pain scores at 1 (5.00 ±1.84 vs 2.20 ± 1.22; p<0.001), 6 (4.10 ±1.57 vs 1.38 ± 0.98; p<0.001), 12 (3.03 ±1.46 vs 0.68 ± 0.83; p<0.001) and 24 (1.75 ± 1.32 vs 0.35 ± 0.48; p<0.001) hours were significantly low in group B compared to group A. The requirement of analgesia was noted significantly higher number of patients in group A compared to group B at 1,6, 12 and 24 hours interval (p<0.050). The mean requirement of rescue analgesia was significantly high in group A compared to Group B at all the intervals (p<0.050). Also mean total requirement was high in Group A compared to group B (p<0.001).

Low pressure pneumoperitoneum with 10 mm Hg does result in some benefit in the form of lower incidence and intensity of postoperative shoulder tip pain thereby results in lower consumption of rescue analgesia without altering the operative time as compared to laparoscopic cholecystectomy with standard pressure pneumoperitoneum (14 mm Hg).

BIBLIOGRAPHY

1. Abbasi SA, Azami R, Haleem A, Tariq GR, Iqbal A, Almas D, et al. An audit of laparoscopic cholecystectomies performed at PNS Shifa. Pak Armed Forces Med J 2003;53:51–8.

2. Mehraj A, Naqvi MA, Feroz SH, ur Rasheed H. Laparoscopic cholecystectomy:an audit of 500 patients. J Ayub Med Coll Abbottabad 2011;23(4):88-90.

3. Yeh CN, Chen MF, Jan YY. Laparoscopic cholecystectomy in 226 cirrhotic patients. Experience of a single center in Taiwan. Surg Endosc 2002;16:1583–7.

4. Yeh CN, Chen MF, Jan YY. Laparoscopic cholecystectomy for 58 end stage renal disease patients. Surg Endosc 2005;19:915–8.

5. Paul FW. The changing role of non-opioid analgesic techniques in the management of postoperative pain. Anesth Analg 2005;101:5-22.

6. Miller RD. Miller’s anaesthesia. 6th ed., Philadelphia: Elsevier, Churchill Livingstone; 2005.

7. Russel RCG, Williams NS, Bulstrode CJK. Bailey & Love’s Short Practise of Surgery. 25th edition. Hodder Arnold; 2008.

8. Bisgaard T, Kehlet H, Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. Eur J Surg. 2001;167:84-96.

9. Inan A, Sen M, Dener C. Local anesthesia use for laparoscopic cholecystectomy. World J Surg 2004;28:741-4.

10. Ure BM, Troidl H, Spangenberger W, Neugebauer E, Lefering R, Ullmann K, et al. Preincisional local anaesthesia with bupivacaine and pain after laparoscopic cholecystectomy:a double-blind randomized clinical trial. SurgEndosc 1993;7:482-8.

11. Aitola P, Airo I, Kaukinen S, Ylitalo P. Comparison of N2O and CO2 pneumoperitoneums during laparoscopic cholecystectomy with special reference to postoperative pain. Surg Laparosc Endosc 1998;8:140-4.

12. Esmat ME, Elsebae MM, Nasr MA, Elsebae SB. Combined Low Pressure Pneumoperitoneum and Intraperitoneal Infusion of Normal Saline for Reducing Shoulder Tip Pain Following Laparoscopic Cholecystectomy. World J Surg 2006;30:1969-73

13. Kanwer DB, Kaman L, Nedounsejiane M, Medhi B, Verma GR, Bala I. Comparative study of low pressure versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy - A randomised controlled trial. Tropical Gastroenterol 2009;30(3):171–4.

14. Rawal N, Allvin R, Amilon A. Postoperative analgesia at home after ambulatory hand surgery: A controlled comparison of tramadol, metamizol and paracetamol. Anesth Analg 2001;92:347-51.

15. Barczyñski M, Herman RM. A prospective randomized trial on comparison of low pressure and standard pressure pneumoperitoneum for laparoscopic cholecystectomy. Surg Endosc. 2003;17:533–8.

16. Davidas D, Birbs K, Vezakis A, Mcmohan MJ. Routine low pressure pneumoperitoneum during laparoscopic cholecystectomy. Surg Endosc 1999:13:87–9.

17. Vezakis A, Davides D, Gibson JS, Moore MR, Shah H, Larvin M,et al. Randomized comparison between laparoscopic cholecystectomy and gasless laparoscopic cholecystectomy. Surg Endosc. 1999;13:890–3.

18. Wallace DH, Serpell MG, Baxter JN, O'Dwyer PJ. Randomized trial of different insufflation pressures for laparoscopic cholecystectomy. Br J Surg. 1997;84:455–8

19. History of laparoscopic surgery, surgical innovation ltd. Oct 2014

20. Karan JA, Rose GJ. Cholelethiasis and cholecystectomy. In:Zynnel MJ, Schwartz SI, ellis H eds. Manigots abdominal operation. 10th ed. New York: McGraw Hill Publishers; p. 1717-38.

21. Russell JC, Walsh SJ, Reed-Fourquet L, Mattie A, Lynch J. Symptomatic Cholelithiasis: A different disease in Men. Ann Surg 1998;227:195-200.

22. Servetus M. Christianismi Restitutio and Other Writings. Birmingham: The Classics of Medicine Library; 1989. Servetus M. Christianismi Restitutio and Other Writings. Birmingham: The Classics of Medicine Library; 1989.

23. Olsen DO. Laparoscopic Cholecystectomy In:MacJadyer BV eds. Laparascopic surgery of abdomen. New York:Springer Publication;2004.

24. Mehraj A, Naqvi MA, Feroz SH, ur Rasheed H. Laparoscopic cholecystectomy:an audit of 500 patients. J Ayub Med Coll Abbottabad 2011;23(4):88-90

25. Keiser d, l.k., ueber die dauer des postoperative pneumoperitoneums. Chirurg, 1947.260:: p. 17-18.

26. Bannister LH. Bile duct and gallbladder In: Bannister LH. Grey's anatomy. 38th ed., Martin Berry; 2000. p. 1809-12.

27. Linder HH, Green RB. Embryology and surgical anatomy of the extra hepatic biliary tract. Surg Clin North Am 1964;44:1273

28. Oddsdottir M, Phaas TH, Hunter JG. Gallbladder and extrahepatic biliary system. In: Brucardi CF Eds. Schwartz's Principles of Surgery. 9th ed. USA: McGraw Hill Companies Inc; 2009. p. 1135-66.

29. Chari RS, Shah SA. Biliary system In: Townsend CM Eds. Sabiston Textbook of Surgery. 18th ed. India: Elsevier Publication; 2009. p. 1517-88.

30. Gordon KCD. A comparative anatomical study of the distribution of the cystic artery in man and other species. J Anat 1967;101(Pt 2):351-9.

31. Rocko JM, Swan KG, DiGioia JM. Calots triangle revisited. Surg Gynecol Obstetrics 1981;153:410.

32. Specint MJ. Calots triangle. JAMA 1967;200:1186.

33. Mincsev M. Bilocular gallbladder. Orvoskepzes 1967;42;286-98.

34. Huffman JL, Schenker S. Acute acalculous cholecystitis - a review. Clin Gastroenterol Hepatol 2010;8(1):15-22.

35. Stinton LM, Shaffer EA. Epidemiology of Gallbladder Disease: Cholelithiasis and Cancer. Gut Liver 2012;6(2):172-87.

36. Lindkvist B, Appelros S, Manjer J, Borgström A. Trends in incidence of acute pancreatitis in a Swedish population: is there really an increase? Clin Gastroenterol Hepatol. 2004;2:831-7.

37. Blumgart LH. Gallstones and gallbladder. In: Blumgart LH, Fong Y eds. Text book of Surgery of liver and biliary tract. Vol 1. London: Harcourt Publishers; 2002. p. 617-791.

38. Torgerson JS, Lindross AK, Naslund I, Peltonen M. Gallstones, Gallbladder disease and Pancreatitis; Cross-Sectional and 2-Year data from the Swedish Obese Subjects (SOS) and SOS Reference Studies. Am J Gastroenterol 2003;98:1032-41.

39. Huang J, Chang CH, Wang JL, Kuo HK, Lin JW, Shau WY, et al. Nationwide epidemiological study of severe gallstone disease in Taiwan. BMC Gastroenterol. Aug 22 2009; 9: 63.

40. Lee SW, Yang SS, Chang CS, Yeh HJ. Impact of the Tokyo guidelines on the management of patients with acute calculous cholecystitis. J Gastroenterol Hepatol. 2009; 24(12): 1857-61.

41. Pichumoni CS. Increasing prevalence of gallstones: Diagnostic and therapeutic options. API India update. Available from: URL: www. apiindia.org/pdf/medicine_update.../ge_and_hepatology_05b.pdf Access Date:18.06.2014.

42. Sarin SK, Negi VS, Dewan R, Sasan S, Saraya A. High family prevalence of gallstones in the first degree relatives of gallstone patients. Hepatology 1995; 22:138-41.

43. Tandon, RK, Saraya A, Paul S, Kapur BM. Dietary habits of gallstone patients in Northern India. J Clin Gastroenterol 1996;22:23-7.

44. Sharma MP, Duphare HV, Nijhawan S, Dasarathy S. Gallstone disease in north India: Clinical and ultrasound profile in a referral hospital. J Clin Gastroenterol 1990;12:547-9.

45. Khuroo MS, Mahajan R, Zargar SA, Javid G, Munshi S. Prevalence of peptic ulcer in India:an endoscopic and epidemiological study in urban Kashmir. Gut 1989;30:930-4.

46. Kapoor VK, McMichael AJ. Gallbladder cancer: An Indian disease. Natl Med J India 2003;16:209-13.

47. Jayanthi V, Anand L, Ashok L, Srinivasan V. Dietary factors in pathogenesis of gallstone disease in southern India – A hospital based case-control study. Indian J Gastroenterol 2005;24:97-9

48. Lee SW, Yang SS, Chang CS, Yeh HJ. Impact of the Tokyo guidelines on the management of patients with acute calculous cholecystitis. J Gastroenterol Hepatol 2009;24(12):1857-61.

49. Pichumoni CS. Increasing prevalence of gallstones: Diagnostic and therapeutic options. API India update. Available from: URL: www. apiindia.org/pdf/medicine_update.../ge_and_hepatology_05b.pdf Access Date:18.06.2014.

50. Kapoor VK. Cholecystectomy in patients with asymptomatic gallstones to prevent gall bladder cancer-the case against. Indian J Gastroenterol 2006;25:152-4

51. Pichumoni CS. Increasing prevalence of gallstones: Diagnostic and therapeutic options. API India update. Available from: URL: www. apiindia.org/pdf/medicine_update.../ge_and_hepatology_05b.pdf Access Date:18.06.2014.

52. Blumgart LH. Gallstones and gallbladder. In: Blumgart LH, Fong Y eds Text book of Surgery of liver and biliary tract. Vol 1. London: Harcourt Publishers; 2002. p. 617-791.

53. Oddsdottir M, Phaas TH, Hunter JG. Gallbladder and extrahepatic biliary system. In:Brucardi CF Eds. Schwartz's Principles of Surgery. 9th ed. USA:McGraw Hill Companies Inc;2009. p. 1135-66.

54. Chari RS, Shah SA. Biliary system In:Townsend CM Eds. Sabiston Textbook of Surgery. 18th ed. India:Elsevier Publication;2009. p. 1517-88.

55. Singer AJ, McCracken G, Henry MC, Thode HC Jr, Cabahug CJ. Correlation among clinical, laboratory, and hepatobiliary scanning findings in patients with suspected acute cholecystitis. Ann Emerg Med 1996;28(3):267-72.

56. Katz DS, Rosen MP, Blake MA, and Expert Panel on Gastrointestinal Imaging. ACR Appropriateness Criteria right upper quadrant pain. [online publication]. Reston (VA):American College of Radiology (ACR);2010:

57. Bingener J, Schwesinger WH, Chopra S, Richards ML, Sirinek KR. Does the correlation of acute cholecystitis on ultrasound and at surgery reflect a mirror image? Am J Surg 2004;188(6):703-7.

58. Rubens DJ. Hepatobiliary imaging and its pitfalls. Radiol Clin North Am 2004;42(2):257-78.

59. Rosen CL, Brown DF, Chang Y, Moore C, Averill NJ, Arkoff LJ, et al. Ultrasonography by emergency physicians in patients with suspected cholecystitis. Am J Emerg Med 2001;19(1):32-6.

60. Shah K, Wolfe RE. Hepatobiliary ultrasound. Emerg Med Clin North Am 2004;22(3):661-73 viii.

61. Kim YK, Kwak HS, Kim CS, Han YM, Jeong TO, Kim IH, et al. CT findings of mild forms or early manifestations of acute cholecystitis. Clin Imaging 2009;33(4):274-80.

62. Sahai AV, Mauldin PD, Marsi V, Hawes RH, Hoffman BJ. Bile duct stones and laparoscopic cholecystectomy:a decision analysis to assess the roles of

intraoperative cholangiography, EUS, and ERCP. Gastrointest Endosc 1999;49(3 Pt 1):334-43.

63. Linder HH, Green RB. Embryology and surgical anatomy of the extra hepatic biliary tract. Surg Clin North Am 1964;44:1273.

64. Greenwald JA, McMullen HF, Coppa GF, Newman RM. Standardization of surgeon-controlled variables: impact on outcome in patients with acute cholecystitis. Ann Surg. 2000; 231(3):339-44.

65. Siddiqui T, MacDonald A, Chong PS, Jenkins JT. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis:a meta-analysis of randomized clinical trials. Am J Surg 2008;195(1):40-7.

66. Overby DW, Apelgren KN, Richardson W, Fanelli R. SAGES guidelines for the clinical application of laparoscopic biliary tract surgery. Surg Endosc 2010;24(10):2368-86.

67. Binenbaum SJ, Teixeira JA, Forrester GJ, Harvey EJ, Afthinos J, Kim GJ, et al. Single-incision laparoscopic cholecystectomy using a flexible endoscope. Arch Surg 2009;144(8):734-8.

68. Wu CH, Chen CC, Wang CJ, Wong YC, Wang LJ, Huang CC, et al. Discrimination of gangrenous from uncomplicated acute cholecystitis: Accuracy of CT findings. Abdom Imaging 2011;36(2):174-8.

69. Bryant, l.r., j.f. Wiot, and r.j. Kloecker, a study of the factors affecting the incidence and duration of postoperative pneumoperitoneum. Surg Gynecol Obstet, 1963. 117:145-150.

70. Douglas EJ Laparoscopic hysterectomy - Pneumoperitoneum: production, management, effects and consequences

71. Ninh T. Nguyen, md, facs and bruce m. Wolfe, md, facs, the physiologic effects of pneumoperitoneum in the morbidly obese, ann of surg, feb 2005 241 (2), 219-226

72. Bryant, l.r., j.f. Wiot, and r.j. Kloecker, a study of the factors affecting the incidence and duration of postoperative pneumoperitoneum.surggynecolobstet, 1963. 117:145-150.

73. Lemay m, l.m., pugere p, letter to the editor. Clin invest med, 1978. 1: p. 211-212

74. Millitz K, Moote DJ, Sparrow RK, Girotti MJ, Holliday RL, et al. Pneumoperitoneum after laparoscopic cholecystectomy: frequency and duration as seen on upright chest radiographs. AJR Am J Roentgenol 1994;163(4):837-9.

75. Gayer G, Jonas T, Apter S, Amitai M, Shabtai M, Hertz M. Postoperative pneumoperitoneum as detected by CT: prevalence, duration, and relevant factors affecting its possible significance. Abdom Imaging. 2000;25(3):301-5.

76. Joris J, Thiry E, Paris P, Weerts J, Lamy M. Pain after laparoscopic cholecystectomy:characteristics and effect of intraperitoneal bupivacaine. Anaesth Analg 1995;81:379-84.

77. Alexander JI. Pain after laparoscopy. British Journal of Anesthesia 1997;79:369.

78. Merskey H, Bogduk N. Classification of chronic pain - Descriptions of chronic pain syndromes and definitions of pain terms, 2nd ed. Seattle:IASP press;1994.

79. Macintyre PE, Ready LB. Acute Pain Management:A Practical Guide. 2nd ed., New York:Churchill Livingstone;2001.

80. Morgan GE, Mikhail MS, Murray MJ. Clinical Anesthesiology. 4th ed., USA:McGraw Hill;2006.

81. Miller RD. Miller's anaesthesia. 6th ed., Philadelphia: Elsevier, Churchill Livingstone; 2005.

82. Carr DB, Goudas LC. Acute pain. Lancet 1999;353:2051-62.

83. Kelly DJ, Ahmad, Mahmoud, Brull, Sorin J. Preemptive analgesia:physiological pathways and pharmacological modalities. Can J Anesth 2001;48 (10):1000-10.

84. Hollmann MW, Durieux ME. Local anaesthetic and inflammatory response: Anesthesiology 2000;93:858.

85. Grubb BD. Peripheral and central mechanisms of pain. Br J Anaesth 1998;81:8.

86. Moiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief:the role of timing of analgesia. Anesthesiology 2002;96:725-41.

87. Alexander JI. Pain after laparoscopy. Br J Anesth 1997;79:369.

88. Korell M, Schmaus F. Pain intensity following laparoscopy. Surg Lapar Endos 1996;6:375-9.

89. Sharp JR, Pierson WP. Comparison of CO2 and N2O induced discomfort during peritoneoscopy under local anaesthesia. Gastroenterology 1982;82:453-6.

90. Alexander JI, Hull MGR. Abdominal pain after laproscopy:the value of a gas drain. Br J Obstet Gynaecol 1987;94:267-9.

91. Semm K, Arp WD, Trappe M, Kube D. Schmerzreduzierung nach pelvi-/laparoskopischen Eingriffen durch Einblasen von körperwarmem CO_2-Gas (Flow-Therme) [Pain reduction after pelvi/-laparoscopic interventions by insufflation of CO_2 gas at body temperature (Flow-Therme)]. Geburtshilfe Frauenheilkd 1994;54:300-4.

92. Gibbs P, Purushottam A, Cushieri RJ Continuous wound perfusion with bupivacaine for postoperative pain. Br J Surg 1988;75:923-4

93. Murrat SA, Baykan N.The effect and timing of local anaesthesia in laparoscopic cholecystectomy. Surg Lap Endos 1996;6:362-6.

94. Glaser F, Buhr HJ. General stress response to conventional and laparoscopic cholecystectomy. Ann Surg 1995;221:372-80.

95. Vitale GC, Collet D, Miller FB. Interruption of professional and home activity after laparoscopic cholecystectomy among French and American patients. Am J Surg 1991;161:396-8.

96. Kehlet H, Holte K. The effect of postoperative analgesia on surgical outcome. British Journal of Anaesthesia 2001;87:62-72.

97. Kehlet H. Acute pain control and accelerated postoperative surgical recovery. Surg Clin N Am 1999;79:431-45.

98. Warltier DC, Pagel PS, Kersten JR. Approaches to the prevention of perioperative myocardial ischemia. Anesthesiology 2000;92:253.

99. Ballanyne JC, Carr DB, DeFerranti S. The comparative effect of postoperative analgesic therapies on pulmonary outcome: Cumulative metaanalyses of randomized, controlled trials. Anesth Analg 1998;86:598.

100. Holte K, Kehlet H. Postoperative ileus- a preventable event. Br J Anesth 2000;87:1480-9.

101. Desborough JP. The stress response to trauma and surgery. Br J Anesth 2000;85:109.

102. White PF. The role of non-opioid analgesic techniques in the management of pain after ambulatory surgery. Anesth Analg 2002;94:577-85.

103. Eccleston C. Role of psychology in pain management. Br J Anesth 2001;87:144-52.

104. Macrae WA. Chronic pain after surgery. Br J Anesth 2001;87:88.

105. Low pressure pneumoperitoneum versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy. Cochrane Database of Systematic Reviews: Plain Language Summaries [Internet]. Available from

URL: http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0014231/ Access Date 18.06.2016

106. Donatsky AM, Bjerrum F, Gogenur I. Surgical techniques to minimize shoulder pain after laparoscopic cholecystectomy. A systematic review. Surgical Endoscopy. Springer. 2013;27:2275-82

107. Brunicardi F, Anderson D, Billiar T, Dunn D, Hunter J, Pollock R. Schwartz's Manual of Surgery. 8th edition. McGraw Hill Professional; 2006.

108. Hua J, Gong J, Yao L, Zhou B, Song Z. Low-pressure versus standard-pressure pneumoperitoneum for laparoscopic cholecystectomy: a systematic review and meta-analysis. The Am J Surg 2014;208:143-50.

109. Berberoglu M, Dilek ON, Ercan F, Kati I, Ozmen M. The effect of CO_2 insufflation rate on the postlaparoscopic shoulder pain. Journal of Laparoendoscopic & Advanced Surgical Techniques. 1998;8:273-7

110. Tacchino R, Greco F, Matera D. Single-incision laparoscopic cholecystectomy: surgery without a visible scar. Surg Endosc 2009; 23: 896-9.

111. Barczyñski M, Herman RM. The usefulness of low pressure pneumoperitoneum in laparoscopic surgery. Folia Med Cracow 2002;43:43–50.

112. Wallace DH, Serpell MG, Baxter JN, O'Dwyer PJ. Randomized trial of different insufflation pressures for laparoscopic cholecystectomy. Br J Surg. 1997;84:455-8.

113. Singla S, Mittal G, Raghav Mittal RK. Pain Management after Laparoscopic Cholecystectomy-A Randomized Prospective Trial of Low Pressure and Standard Pressure Pneumoperitoneum. Journal of Clinical and Diagnostic Research. 2014;8(2):92-4.

114. Uen YH, Chen Y, Kuo CY, Wen KC, Koay LB. Randomized trial of low pressure carbon dioxide elicited pneumoperitoneum versus abdominal wall lifting for laparoscopic cholecystectomy. J Chin Med Assoc 2007; 70:324-30.

115. Chok KS, Yuen WK, Lau H, Fan ST. Prospective randomized trial on low pressure versus standard pressure pneumoperitoneum in out patient laparoscopic cholecystectomy. Surg Laparosc Endosc Percutan Tech 2006;16:383-6.

116. Gurusamy KS, Samraj K, Davidson BR. Low pressure versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy. The Cochrane Database of systemic Reviews 2009;2:CD006930.

117. Yasir M, Mehta KS, Banday VH, Aiman A, Masood I, Iqbal B. Evaluation of post-operative shoulder tip pain in low pressure versus standard pressure pneumoperitoneum during laparoscopic cholecystectomy Surgeon 2012;2:71-4.

118. Sarli L, Costi R, Sansebastiano CG, Trivelli M, Roncoroni L. Prospective randomized trial of low-pressure pneumoperitoneum for reduction of shoulder tip pain following laparoscopy. Br J Surg 2000;87:1161-5.

119. Barczynski M, Herman RM. Low pressure pneumoperitoneum combined with intraperitoneal saline washout for reduction of pain after laparoscopy cholecystectomy. Surg Endosc 2004;18:1368-73.

120. Barczyñski M, Herman RM. The usefulness of low pressure pneumoperitoneum in laparoscopic surgery. Folia Med Cracow. 2002;43:43-50

121. Wallace DH, Serpell MG, Baxter JN, O'Dwyer PJ. Randomized trial of different insufflation pressures for laparoscopic cholecystectomy. Br J Surg 1997;84:455-8

122. Perrakis E, Vezakis A, Velimexis G, Savanis G, Deverakis S, Antoniades J, et al. Randomized comparison between different insufflation pressure for laparoscopic cholecystectomy. Surg Laparo Endosc Percutan Tech 2003;13:245-9.

123. Dexter SP, Vucevic M, Gibson J, McMahon MJ. Hemodynamic consequences of high and low pressure capnoperitoneum during laparoscopic cholecystectomy. Surg Endosc 1999;13:376-81

124. Gurusamy KS, Samraj K, Davidson BR. Low pressure versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy (Review). The Cochrane Database of systemic Reviews. 2009;2:CD006930.

125. Sarli L, Costi R, Sansebastiano G, Trivelli M, Roncoroni L. Prospective randomized trial of low pressure pneumoperitoneum for the reduction of shoulder tip pain following laparoscopy. Br J Surg. 2000;87:1161–5.

126. Genton B, Berger JP. Cerebrospinal fluid lactates in 78 cases of adult meningitis. Intensive Care Med 1990; 16:196-200.

ANNEXURE I- CONSENT FORM

TITLE OF THE RESEARCH STUDY: TO EVALUATE POST-OPERATIVE SHOULDER TIP PAIN IN LOW PRESSURE (10MMHG CO2) VERSUS STANDARD PRESSURE (14MMHG CO2) PNEUMOPERITONEUM IN LAPAROSCOPIC CHOLECYSTECTOMY, A ONE YEAR RANDOMISED CONTROLLED TRIAL, HOSPITAL BASED STUDY.

Investigator:

DR. ** ***** ******
Post Graduate Student,
Department of General Surgery,
Jawaharlal Nehru Medical College,
Belagavi – 590 010

Introduction

Dear Mr./Mrs./Miss. ______________________________, you are kindly requested to participate in a research study titled "To Evaluate Post-Operative Shoulder Tip Pain in Low Pressure (10mmHg CO_2) versus Standard Pressure (14mmHg CO_2) Pneumoperitoneum in Laparoscopic Cholecystectomy, A one year Randomised Controlled Trial, Hospital Based Study" conducted by Dr. **** ***** *******, post graduate student in M.S. General Surgery in Jawaharlal Nehru Medical College, Belagavi, under the direct supervision and guidance of Dr. **** ******, Professor, Department of Surgery, Jawaharlal Nehru Medical College, Belagavi.

Objective/purpose of the study

Laparoscopic cholecystectomy is the treatment of choice for gallbladder stone disease.

Postoperative pain is a common problem in any surgical setup having a significant effect on the rate of recovery of a patient following surgery.

Laparoscopic cholecystectomy has the advantage of less postoperative pain and earlier ambulation with return of normal activities. Although it has some undesirable side effects, of which shoulder tip pain is a frequent symptom. Incidence of post-operative shoulder tip pain is in around 30-50% of operated patients. Through this study, by using low pressure pneumoperitoneum of 10mmHg CO_2, we aim to further improve pain relief after laparoscopic cholecystectomy by reducing the post-operative residual effects of CO_2 gas causing shoulder tip pain and lesser stretching of diaphragmatic muscle fibres as compared to that seen in standard pressure pneumoperitoneum of 14mmHg CO_2 gas.

The investigator/author of this study is Dr. **** ****** ******, a postgraduate student in the Department of General Surgery, Jawaharlal Nehru Medical College under the direct supervision of Dr. **** ******, Professor, Department of General Surgery, and Jawaharlal Nehru Medical College. The study is self-funded by the author the study.

You need to be eligible, meeting all the selection criteria to participate in this study. You should be willing to provide information about yourself. 80 subjects will be enrolled in this study who will then be randomised in either of 2 groups (details below).

Procedure

If you agree to participate in this study, you will be randomly allotted into a group (A or B) with the help of ‘sequentially numbered opaque envelope’ and accordingly undergo either the low pressure pneumoperitoneum (10mmHg CO_2) laparoscopic cholecystectomy or standard pressure pneumoperitoneum (14mmHg CO_2) laparoscopic cholecystectomy. In the 24 hours following surgery, you will be assessed at fixed intervals at 1hour, 6 hours, 12 hours and 24 hours by the help of a

Numerical Rating Scale for post-operative pain. You will be given an intramuscular injection of the analgesic if pain scores exceed a certain limit or on request for rescue analgesia.

Benefits

The benefits of the procedure under study are improved post-operative pain relief and lesser analgesic usage due to reduced post-operative shoulder tip pain sensation as a result of low pressure pneumoperitoneum, early recovery time, better cosmesis & minimum complications.

Risks

There is no additional risk as compared to the standard treatment.

Voluntary participation / withdrawal

Taking part in this study is voluntary; you may choose not to enrol in this study. Your decision will not change the present or future health care services offered to you at KLES Dr. Prabhakar Hospital, Belagavi. You would simply be excluded from the study and all your details shall be kept confidential. The alternative that you have is to undergo the traditional procedure that is carried out in KLES Hospital.

Privacy & confidentiality

Every effort will be made to protect the confidentiality of the information you provide. This means that the researchers will not let anyone, not a part of the study, see the information you provide. Only Dr. **** **** ****** and Dr. *** ******* **** will have access to the information collected. Results of this study may be published but your name will not be revealed.

Authorization to publish results

The results of the study may be used to publish an article. When the results of research published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information obtained in connection with this study and that can be identified with you will remain confidential.

Financial incentives for participation

No additional costs shall be incurred upon you for the purpose of this study. It is purely being done with the idea of research and all the cost of study will be borne by the investigator.

Compensation

In the event that you become injured as a result of taking part in this study, treatment will be offered to you at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, or you will be given information about where to receive medical care in which case you/your insurance company will be responsible for the costs. However, no reimbursement, compensation or free medical care will be given. There is no compensation or payment for such medical treatment by law.

Contact details

If you have any queries about the study, you may contact Dr. **** ***** ***** (Mobile No. +91 **** *****) or Dr. ***** ***** (Mobile No.: +91 **** *****) If you need any further information regarding your rights as a study participant, you may also contact Dr. **** ***** (Mobile no. 91 **** *****) Chairman of Institutional Ethics Committee, Jawaharlal Nehru Medical College, KLE University, Belagavi.

Dr.*** ****** ********
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CONSENT STATEMENT

I the undersigned Mr./Mrs./Miss/_________________________ do hereby give consent for my participation in this research study after being explained in-depth about the important elements of this study in own my vernacular language.

I voluntarily agree to participate in this study by signing up this form below. I understand that I may withdraw at any time from this study. I have been given adequate time to clarify my doubts about the study and my rights as a study participant.

My signature / left thumb impression below indicates that I have read or information in the consent been read to me including the risks and benefits and have cleared my doubts.

I do hereby also give consent for publication of this article in any media / journal and have no objections whatsoever.

Signature or left thumb impression of participant or legally authorised representative

Participant's name___________________________

Signature/LTI__________________

Investigator's name________________________

Signature/LTI___________________

Witness' name_____________________________

Signature/LTI___________________

Date ___/___/____ Time: am/pm Place:

ANNEXURE II- PROFORMA

The proposed pro forma / questionnaire to be used for data collection for the study titled **"TO EVALUATE POST-OPERATIVE SHOULDER TIP PAIN IN LOW PRESSURE (10MMHG CO2) VERSUS STANDARD PRESSURE (14MMHG CO2) PNEUMOPERITONEUM IN LAPAROSCOPIC CHOLECYSTECTOMY, A ONE YEAR RANDOMISED CONTROLLED TRIAL, HOSPITAL BASED STUDY."** is as follows:

1. PATIENT IDENTIFICIATION DATA

Group:	Ward:
Name:	In Patient Number:
Age:	
Sex:	Date of Admission:
Address:	Date of Surgery:
	Date of Discharge:
Education:	
Religion:	Marital Status:
Occupation:	Socio-Economic Status:

2. Chief Complaints

3. History of Presenting Complaints

4. Past History and history (if any) of surgeries in the past

5. Personal History

6. Family History

7. **General physical examination**

Built and Nourishment:

Weight: Pallor:

Icterus : Cyanosis:

Clubbing: Oedema:

Lymphadenopathy:

Vital Signs

PR: /min; Blood Pressure: mmHg;

RR: /min; Temp: °C

8. Systemic Examination

I) Abdomen

Inspection:

Palpation:

Percussion:

Auscultation:

II) Cardio Vascular System

III) Respiratory System

9. Clinical Impression

10. Investigations:

Blood - Routine :

Haemoglobin :

Total Leucocyte Count :

Platelet count :

Random blood sugar :

Blood urea. :

Serum Creatinine. :

LFT’s :

Bleeding time :

Clotting time :

Urine routine and microscopy:

11. Operation Details

Date of Surgery:

Name of Surgery

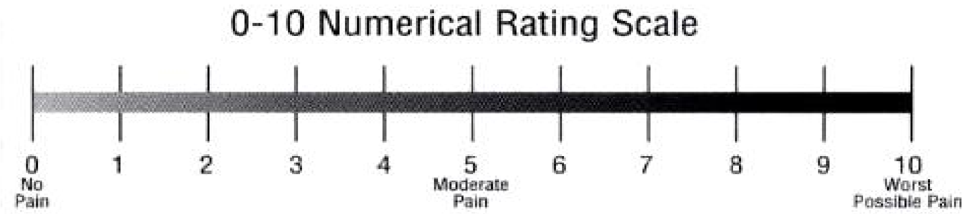
Laparoscopic Cholecystectomy

Anaesthesia

General Anaesthesia

Duration of Surgery

12. Assessment of Post-Operative Shoulder Tip Pain- Numerical Analogue Scale



0 – No Pain

1-3 – Mild Pain

4-7 – Moderate Pain

8-10 – Severe Pain

Numerical Rating Scale Time↓	0	1	2	3	4	5	6	7	8	9	10
1 hour											
6 hours											
12 hours											
24 hours											

ANNEXURE III _ KEY TO MASTER CHART

BP	-	Blood pressure
BPM	-	Beats per minute
F	-	Female
IP number	-	In patient number
Kg	-	Kilogram
M	-	Male
mmHg	-	Millimeters of mercury
N	-	No
S. No.	-	Serial number
Y	-	Yes