

Original Research Article

An observational study on effect of carbon dioxide pneumoperitoneum on liver function test in laparoscopic cholecystectomy

Anilkumar Bellad, Kartik Sahu*

Department of General Surgery, J.N. Medical College, KAHER, Belgaum, Karnataka, India

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*Correspondence:

Dr. Kartik Sahu,

E-mail: kartiksahu11@gmail.com

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ABSTRACT

Background: In many studies it was noticed that following a laparoscopic cholecystectomy (LC), liver function parameters were disturbed. The carbon dioxide pneumoperitoneum causes changes in the splanchnic microcirculation and can affect cardiac, pulmonary, liver and kidney physiology. Alterations in intracranial pressure, blood acid-base control and the immune system have also been seen. This study was done to know the effects of carbon dioxide pneumoperitoneum on liver function tests in LC. Aim of the study was to study the significance of alterations in Liver function tests and procedure's safety

Methods: Blood samples of 100 patients who underwent laparoscopic cholecystectomy preoperatively once and post operatively after 24 hours were collected. These blood samples were tested for LFT. The pre op and post op levels of these liver function test values were compared.

Results: The level of serum AST, ALT, bilirubin (total) and ALP were increased significantly during the first 24 hrs. Postoperatively after laparoscopic cholecystectomy as compared to baseline values and the levels of serum albumin and total proteins were decreased.

Conclusions: There may be a transient elevation of hepatic enzymes after LC and the major causative factor seemed to be CO₂ pneumoperitoneum.

Keywords: CO₂ pneumoperitoneum, Laparoscopic cholecystectomy, Liver function tests

INTRODUCTION

Laparoscopic cholecystectomy (LC) is the surgery of choice for cholecystectomy. It requires creation of pneumoperitoneum

To get proper visualization and exposure of the operative field the intra-abdominal pressure during laparoscopy is set at 15-14 mm Hg. The normal value intra-abdominal pressure of non-obese individuals is 5 mmHg or less.¹

Elevation in values of liver enzymes such as AST and ALT after an uneventful lap cholecystectomy has become a well-known finding which was once considered as

incidental in previous studies, transient hepatic malfunction was suspected. Although the clinical significance of these changes in enzyme levels has not been clarified.

The normal range of portal venous pressure is around 7-10 mmHg and approximately 50% of the hepatic blood flow is from the portal venous system, pneumoperitoneum with pressure of 14 mmHg with CO₂ is an important cause of transient hepatic ischemia in LC.

Halevy et al in their study showed increased intra-peritoneal pressure, compression of liver by retraction of gallbladder, cauterization of liver bed to achieve

hemostasis, handling of biliary tract and effects of general anaesthesia as a causative factor for elevation in levels of certain liver enzymes.² However, gall bladder retraction for better view, manipulation of biliary ducts for possibility of common duct stones, cauterization of the liver bed were usually performed in open cholecystectomy too.

Guven studied the changes in liver enzyme levels before and 24 hours after the operations in LC patients and compared these changes with the open cholecystectomy patients.³ AST, ALT, GGT and LDH levels were significantly raised 24 hours after the lap cholecystectomy. In lap cholecystectomy patients, the mean postoperative values of AST, ALT and LDH were above the upper limits of normal ranges. However, the enzyme levels postoperatively in open cholecystectomy patients were normal. When compared with the open cholecystectomy patients the changes in liver enzymes were significant for the Lap Cholecystectomy group. In addition to AST and ALT, GGT and LDH were also affected after Lap Cholecystectomy. Raised LDH can be because of high intraperitoneal pressure decreasing the mesenteric venous flow causing passive venous congestion.

Morino et al studied the duration of pneumoperitoneum at constant pressure and found that when the duration of operation exceeds 60 minutes, elevations in AST and ALT levels become more significant.⁴ Studies comparing alterations in enzymes in LC and other laparoscopic operations were also done to know effects of a pneumoperitoneum on liver enzymes excluding the other possible factors such as liver tissue damage and biliary tract manipulations that might interfere with results.

In a study comparing hepatic enzyme alterations in LC, gasless LC and LC under low pressure (below 10 mmHg) pneumoperitoneum, Giraudo et al found significant enzyme level rises after lap cholecystectomy that are not seen after gasless or low pressure lap cholecystectomy, underlining the absolute effect of intraperitoneal pressure on hepatic perfusion by means of enzyme level changes.

Hasukic et al, in their randomized study comparing the effects of low and high pressure pneumoperitoneum on liver functions, stated that AST and ALT elevations were significantly higher in patients operated under high pressure (14 mmHg) pneumoperitoneum than those under low pressure (7 mmHg).⁵

The same significant enzyme level elevations were also observed in laparoscopic colectomy patients suggesting that a pneumoperitoneum plays the key role in transient hepatic ischemia causing enzyme elevations.^{4,6} Preoperative and postoperative levels of AST, ALT, GGT, ALP, LDH, prothrombin time and bilirubin have been investigated in various studies to determine the physiological basis of hepatic malfunction.⁷⁻⁹ However significant elevations after lap cholecystectomy compared with open cholecystectomy have been defined

for only AST and ALT levels. Time controlled studies have shown that these enzyme elevations last for about 3 days postoperatively and the significance between lap cholecystectomy and open cholecystectomy values fade away after 2 days.

Tan tested the liver function of patients who underwent lap cholecystectomy or open cholecystectomy.⁶ Author suggested that transient postoperative hypertransaminases in lap cholecystectomy patients might be attributed to the following possible factors. The first factor of consideration was CO₂ pneumoperitoneum. A second possible mechanism for alterations of serum liver enzymes after LC is the "squeeze" pressure effect on the liver. The traction of the gallbladder may free these enzymes into the blood stream. The third possibility may be the local effect of prolonged use of diathermy to the liver surface and spread of heat to liver parenchyma. In addition, transient liver dysfunction occurs in patients after some general anesthesia. Another possible mechanism of alterations of serum liver enzymes that had been considered was the inadvertent clipping of the right branch of the hepatic artery or any other aberrant arterial branch supplying blood to the liver.

According to Halevy, the mechanism for alter enzymatic changes is unclear.² However, he postulate several possible explanations for this:

- Increase in Intra-abdominal pressure leads to decrease in portal vein and hepatic artery flow which results in decreased hepatic perfusion leading to increased LFT.
- The compressive effect on liver while retraction of gall bladder can result in release of enzymes in the blood.⁹
- Retraction of gall bladder while operation causes temporary kink of the extrahepatic ducts resulting in increased pressure in lumen causing release of these enzymes.
- There can be damage to liver parenchyma as a result of lateral spread of diathermy.⁷
- In cases of abnormal anatomy there can be accidental clipping of supplying artery or even hepatic artery's right branch.
- Presence of one or more causes.

This study aims to investigate the alterations in the serum levels of liver enzymes after LC performed under constant intraperitoneal pressure (14 mmHg) at KLES Prabhakar Kore Hospital, Belgaum, Karnataka, India.

Aim of the study is to study the significance of alterations in Liver function tests and procedure's safety.

METHODS

Study design: Prospective observational study.

Study period: January 2013 – December 2013.

Sample size: 100 patients.

Sampling procedure: Applying thumb rule, 100 cases of cholelithiasis who underwent elective laparoscopic cholecystectomy were taken up for study.

Informed consent: Those patients who fulfilled selection criteria were explained about the nature of study and a written informed consent and ethical clearance was obtained prior to the enrolment.

Source of data: All symptomatic patients getting admitted to the surgery wards, in KLES Dr. Prabhakar Kore Hospital and scheduled for LC.

Inclusion criteria

Inclusion criteria were all patients undergoing elective laparoscopic cholecystectomy; all the patients who gave written consent for the procedure; all the patients chosen had values of LFT under normal limits previous to operation.

Exclusion criteria

Exclusion criteria were any patient with altered liver enzyme level before operation; suspected or coexisting chronic liver diseases; CBD pathology; conversion to open cholecystectomy; intra-operative complication – bile duct injury.

Study procedures

All patients who gave consent for study underwent a standard clinical and laboratory evaluation including USG. Pre-operative investigations included liver function tests i.e. bilirubin (total), alanine transaminase, aspartate transaminase, alkaline phosphatase, total proteins and serum albumin.

The subjects under inclusion and the exclusion criteria were taken up for the study. All such patients underwent lap cholecystectomy. The liver function tests were repeated 24 hours after the operation and compared.

Statistical analysis

Demographic data were collected and presented as mean and SD.

All liver function tests parameter (alanine transaminase, aspartate transaminase, alkaline phosphatase, total proteins, serum albumin, and bilirubin (total) was presented in mean and SD.

Paired 't' test was applied to all liver function tests parameter to measure the significant change in liver function.

Appropriate statistical analysis was applied for comparing the incidences of adverse events and other complications. Additional exploratory (parametric and non-parametric) analysis of data was done as felt essential by using various appropriate statistical tests.

RESULTS

Table 1 shows the mean age of patients of study was approx. 48 years. Table 2 shows female preponderance was seen and 54% of them were females and 46% being males. In Table 3, while comparing pre op and post op values of serum bilirubin levels there was mean difference of 0.51 and p value was <0.0001. In Table 4 On comparison of pre and post op values of serum ALP levels, postoperatively ALP levels increased by mean difference of 41.8 with p value being <0.0001.

Table 1: Mean age of the study group.

Parameter	Mean±SD
Age (in years)	47.8±10.80

Table 2: Sex distribution amongst the samples.

Sex	Frequency	Percentage (%)
Female	54	54
Male	46	46
Total	100	100

Table 3: Serum total bilirubin levels paired sample statistics.

Serum total bilirubin	N	Mean (mg/dl)	SD	Mean diff.	T	P value
Preoperative	100	0.66	0.18	-0.51	-18.086	<0.0001
Postoperative	100	1.18	0.29			

Table 4: Serum ALP levels paired sample statistic.

Alkaline phosphatase	N	Mean (U/l)	SD	Mean diff.	T	P value
Preoperative	100	112.50	38.11	-41.8	-11.787	<0.0001
Postoperative	100	154.3	39.15			

Table 5: Serum AST levels paired sample statistics.

Serum AST	N	Mean (U/l)	SD	Mean diff.	T	P value
Preoperative	100	24.58	8.76	-16.4	-14.110	<0.0001
Postoperative	100	40.9	10.34			

Table 6: Serum ALT levels paired sample statistics.

Serum ALT	N	Mean (U/l)	SD	Mean diff.	T	P value
Preoperative	100	30.9	7.63	-22.6	-12.96	<0.0001
Postoperative	100	53.5	17.13			

Table 7: Total proteins levels paired sample statistics.

Total proteins	N	Mean (g/dl)	SD	Mean diff.	T	P
Preoperative	100	6.85	0.55	-0.88	-17.030	<0.0001
Postoperative	100	5.96	0.49			

Table 8: Serum albumin levels paired sample statistics.

Serum albumin	N	Mean (g/dl)	SD	Mean diff.	T	P value
Preoperative	100	4.04	0.39	-0.85	-18.030	<0.0001
Postoperative	100	3.19	0.38			

Table 5 shows postoperatively serum AST levels increased by mean difference of 16.4 with $p < 0.0001$. Table 6 shows postoperatively there was increase in serum ALT levels by 22.6 and p value came out to be < 0.0001 . Table 7 shows postoperatively the total protein levels decreased by 0.88 with $p < 0.0001$. Table 8 shows post operatively serum albumin levels decreased by a mean difference of 0.85 with $p < 0.0001$.

DISCUSSION

Within the last 25 years, the open cholecystectomy has been taken over by laparoscopic cholecystectomy in benign gallbladder conditions and has been labelled as gold standard in cases of cholelithiasis. Muhe in 1985 did the first laparoscopic cholecystectomy.^{10,11}

The main advantage of laparoscopic cholecystectomy includes the reduction of tissue trauma due to small skin incisions, reduction in adhesion formation, reduction in patient morbidity, shortening in hospital stay and early return to normal daily activity. Many hospitals are now doing lap cholecystectomy as a day care procedure and discharging patients in 24 hours.¹²

The basis for choosing the ideal gas for pneumoperitoneum are the type of anaesthesia, non-combustibility, toxicity, delivery method, usability, safety, and cost. Gases preferred for creating pneumoperitoneum are carbon dioxide (CO₂), air, oxygen, nitrous oxide (N₂O), argon, helium and mixtures of these gases. CO₂ is the gas of choice because it has:

- A high diffusion coefficient, is a normal metabolic end product rapidly cleared from the body.
- CO₂ is high solubility in blood and tissues and is not combustible.
- Fewer chances of gas embolism.

Pneumoperitoneum can be created by a needle (Veress or Tuohy) or a trocar to go through the abdominal wall and distend the peritoneal cavity.¹³

CO₂ is being used in clinical practice for creating pneumoperitoneum from the starting days of lap cholecystectomy. Hypercarbia and eventual systemic acidosis can occur by the CO₂ is absorbed from the peritoneal surface and then goes into the systemic circulation. The increased intra-abdominal pressure due to pneumoperitoneum results in hemodynamic alteration and changes are seen in femoral venous flow and renal, hepatic, and cardio respiratory function.^{14,15}

With the advent of laparoscopic cholecystectomy and its evolution over the years has made it as the treatment of choice for uncomplicated cholelithiasis.

Although LC offered many advantages over laparotomy, new concerns arose regarding the effects of a pneumoperitoneum on the cardiovascular and respiratory system.¹⁶ LC has been accepted as an alternative to laparotomy, but there is still controversy regarding the effects of pneumoperitoneum on splanchnic and hepatic perfusion.¹⁷

However, the application of carbon dioxide pneumoperitoneum in high-risk patients may induce undesirable consequences in critically ill patients with cardiovascular, respiratory or renal insufficiency due to either hypercapnia or increased intraabdominal pressure.¹⁸

The use of diathermy which may induce thermal damage to hepatic parenchyma, or the use of anaesthetic medications some of which might influence visceral blood flow have been addressed for these enzymatic changes. However, their effect is debatable, since both factors are used in the same manner in laparoscopic as well as in open cholecystectomy.

The occurring pathophysiological changes may be due to both carbon dioxide insufflation and increased intra-abdominal pressure. Carbon dioxide, has high solubility in the blood and may cause hypercapnia with respiratory acidosis resulting in increased heart rate, arterial pressure and systemic peripheral resistances.⁶ The increased intraabdominal pressure on the other hand, affects the cardiovascular system by compressing inferior vena cava and pericardium, and thus decreasing directly the venous blood return to the right atrium and the cardiac output. The usual level of intraabdominal pressure (12-14 mmHg) is higher than that of portal vein system (7-10 mmHg); consequently, it may lead to reduction of portal blood flow and abnormalities in liver.^{5,19}

Alterations in liver enzymes after laparoscopic cholecystectomy were first noticed and analysed by Halevy et al in 1994. The main reasons concluded were:-

- Increase in intra-abdominal pressure,
- Compressive effect on liver while retraction,
- Lateral spread of diathermy and gall bladder retraction,
- Spill of small calculi in CBD.

According to Tan et al, the serum levels of alanine transaminase and aspartate transaminase increased to significant extent during the initial 48 hours after the surgery in laparoscopic cholecystectomy patients. However, the changes in serum level liver enzymes was not significant in open cholecystectomy patients. Normal values of both enzymes was seen on 7th post-operative day.⁶

Jakimowicz et al noticed 53% decrease in portal blood flow when intra-abdominal pressure was increased to 14 mmHg.¹⁴

Hasukic et al, compared the levels alanine transaminase and aspartate transaminase in settings of low and high pressure creation of pneumoperitoneum on the liver functions, and noticed significant increase in alanine transaminase and aspartate transaminase levels in patients operated under high pressure (14 mmHg) pneumo-

peritoneum in comparison to those who underwent procedure under low pressure (7 mmHg).⁵

Moustafa et al, showed that disturbances of liver function tests following laparoscopic cholecystectomy had been previously reported although their etiology still remained uncertain. Electrocautery, general anaesthesia, and the vasoconstrictive effect of CO₂ also cause reduced visceral blood flow may also have a role. In this study, it was found that all liver function tests which include AST, ALT, GGT, alkaline phosphatase, and bilirubin showed a transient rise in their values and in majority of cases these values went back to normal level in 48 to 72 hours following surgery.

Many studies tried to find the physiological reasons of hepatic malfunction.^{8,20,21} But when comparing LC and OCs for changes in liver enzyme levels, significant increase after laparoscopic cholecystectomy has been seen for alanine transaminase and aspartate transaminase levels only. Studies show that these increase in enzyme level remains for about 3 days postoperatively and the significance between LC and OC values goes off after further 2 days.^{5,6}

In this study of 100 subjects with mean age of 47 years, It was observed that there was significant increase in bilirubin (total), AST, ALT, ALP and decrease of serum albumin and total proteins after doing laparoscopic cholecystectomy when compared to normal values. Our results were similar with the previous studies. However, these results were clinically insignificant.

It was also observed that there was more increase in liver function tests when the surgeries were prolonged for more than 80 minutes. However the rise in LFTs was not found to be significant.

Most of the patients were discharged around post-operative day 4. No patient developed any complication. This signifies that the alterations in liver enzymes were temporary and without complications.

CONCLUSION

Laparoscopic cholecystectomy has replaced open cholecystectomy in the management of benign gallbladder diseases and has become the gold standard for symptomatic cholelithiasis.

There is transient decrease in liver blood flow, as a result of pneumoperitoneum and can be because of high pressure of pneumoperitoneum. These result in elevation in liver enzymes bilirubin (total), AST, ALT, ALP and decrease in levels of total proteins and serum albumin. But clinically there is no significant effect. However, surgeons should be cautious before doing LC in patients with known liver diseases.

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