

Effect of Pneumoperitoneum during Laparoscopic Cholecystectomy on Liver Function Tests

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ABSTRACT

Background: Laparoscopic Cholecystectomy has become one of the most commonly performed general surgical procedures, and entails creation of pneumoperitoneum with pressures of up to 12 mmHg. It is known that creation of pneumoperitoneum artificially increases the intra-abdominal compartment pressure. Increased intraperitoneal pressure exerts several undesirable effects on visceral perfusion. The present study was conducted to observe the effects of Laparoscopic cholecystectomy on liver function tests in Cholelithiasis patients who had normal liver functions preoperatively. **Aims and objectives:** To statistically compare pre-operative levels of Serum Bilirubin, SGOT, SGPT and Serum Alkaline phosphatase with post-operative levels of These parameters 24 and 72 hours after surgery. **Materials and methods:** The present study was conducted at the Department of Surgery, of a zonal hospital in Pune, India. A total of 50 patients diagnosed with Cholelithiasis who underwent Laparoscopic cholecystectomy were studied from Oct 2022 to Jul 2023. The studied population consisted of subjects from both genders aged between 19 and 75 years. All patients had normal LFT values pre operatively and underwent LC at CO₂ pneumoperitoneal pressure of 12 mmHg. LFT consisting of Serum Bilirubin, SGOT, SGPT and Serum Alkaline phosphatase was conducted on the day prior to LC and repeated 24 hours and 72 hours after Surgery. The results were statistically compared. Only those patients were included in the study that had normal base line LFT on the day prior to surgery and no evidence of obvious or suspected bile duct injury or bile spillage during the procedure. Patients with preoperative diagnosis of choledocholithiasis / biliary strictures, serologically proven hepatitis and pregnant patients were excluded from the study. **Results:** After 24 hours of the procedure elevation of the levels of all four tested parameters was observed to an extent of double their pre-operative values. All Four parameters showed a declining trend at 72 hours post-surgery **Conclusions:** Transient increase in Serum Bilirubin, SGOT, SGPT and Alkaline phosphatase is observed after uncomplicated laparoscopic cholecystectomy and may be attributed to CO₂ pneumoperitoneum, surgical manipulation and diathermy. Liver function tests revert back to normal limits or show a significant reducing trend to near normal levels within 3-4 days of Laparoscopic cholecystectomy. Routine post-operative testing of LFT parameter values is unnecessary in the absence

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of objectively proven deterioration in the patients' clinical condition.

Keywords: Pneumoperitoneum, Laparoscopic Cholecystectomy, Liver Function Tests, SGOT, SGPT

Abbreviations: LFT: Liver function test; S Bil: Serum Bilirubin; SGOT: Serum Glutamic Oxaloacetic Transaminase; SGPT: Serum Glutamic Pyruvic Transaminase; ALP: Serum Alkaline Phosphatase; mmHg: millimeters of mercury CO₂: Carbon Di Oxide LC: Laparoscopic Cholecystectomy; INR: International Normalized Ratio; Q: Quaque; NSAID: Non-Steroidal Anti-Inflammatory Drugs; Mm: Millimeter; ANOVA: Analysis of Variance; F: Female; M: Male; Pre op: Pre-Operative

INTRODUCTION

Laparoscopic Cholecystectomy is one of the most widely practiced surgical procedures nowadays for treating Symptomatic patients of Gall Stone disease [1]. We observed deranged liver function test values after every Laparoscopic cholecystectomy for symptomatic Gallstone disease that we conducted at our institution during the year 2022. On searching the available literature, we found a number of studies, the earliest one was conducted by R Halevy, et al. in 1994 [2], which corroborated our observation. The adverse physical effects of intra-abdominal hypertension caused by CO₂ insufflation have since been reviewed in detail by a number of studies [3]. A 2013 study showed that hepatic microcirculation fell significantly during LC performed with a pneumoperitoneum of 12 mmHg, indicating splanchnic ischemia [4]. Studies conducted in 2001 & 2012 showed that intra-abdominal pressure of Carbon di oxide at 12 mmHg was higher than the normal portal blood pressure of 7-10 mmHg and was therefore capable of causing alteration in hepatic function [5,6]. Other studies have shown that Free radicals generated at the end of laparoscopic procedures by inflation and deflation of pneumoperitoneum can damage Kupffer cells and endothelial cells of the hepatic sinusoids [7, 8]. A 2015 study by Singhal et al. concluded that Surgical manipulations, diathermy, patient position, arterial injury and CO₂ pneumoperitoneum are the contributory factors for liver enzymes changes. These changes have no clinical consequences in patients with normal hepatic function. In light of the above-mentioned background, we decided to carry out an inferential study at our institution, using standard statistical tools to test if there was significant derangement in LFT values after Laparoscopic cholecystectomy.

MATERIALS AND METHODS

The present study was conducted at the Department of Surgery, of a Zonal Hospital in Pune, India. The studied sample was drawn randomly from a population consisting

of patients of Cholelithiasis, seen at the Surgical Outpatient Department of our institution.

SAMPLE SIZE: 50 patients

INTERVENTION: All patients underwent LC between 26 Oct 2022 & 31 Jul 2023.

GENDER: Male and female patients were enlisted.

AGE: Age of the subjects ranged between 18 and 75 years.

Detailed History and physical examination were conducted pre operatively. Complete blood count, Renal Function test, LFT & PT INR values and viral marker status were obtained for all patients. Ultra sound study of the abdomen was done prior to surgery. LFT consisting of Serum Bilirubin, SGOT, SGPT and Serum Alkaline phosphatase was conducted on the day prior to LC and repeated 24 hours and 72 hours after Surgery. The values were statistically compared.

INCLUSION CRITERIA

Normal base line liver function tests during Pre anesthesia checkup & on the day prior to surgery

Normal Gall bladder & Biliary anatomy on Abdominal ultrasonography

EXCLUSION CRITERIA

Pregnancy

Choledocholithiasis

Biliary Stricture

Serologically Proven Hepatitis

Evidence of obvious or suspected bile duct injury or bile spillage during the procedure.

Biochemical Analyzer used for all measurements taken during the study: Siemens Dimension EXL 200. Normal ranges of test result values for this analyzer are given below:

Serum Bilirubin (Total) = 0.1 – 1.2 mg / dl

Serum SGOT = 8 – 48 U / L

Serum SGPT = 7 – 55 U / L

Serum Alkaline Phosphatase: 40 – 129 U/L

STATISTICAL TESTS USED: Student t test, ANOVA

Follow-Up: -

All patients enrolled were planned for follow-up visit to our institution on 10th post operative day for suture removal, detailed history taking, physical & Bio chemical examination if indicated. Subsequent visits would be three monthly for a period of one year.

OBSERVATIONS AND ANALYSIS

The mean age of subjects in the study was 44.94 years. There

were 39 female and 11 male patients. The mean duration of surgery was 66.68 minutes. Mean pre op, POD1 & POD 3 - LFT values are summarized in Table 1. Changes in LFT values are graphically represented in Figures 1, 2, 3 & 4.

T TEST ANALYSIS RESULTS AT SIGNIFICANCE LEVEL 0.05

Rise in level of Serum Bilirubin (predominantly unconjugated) was statistically significant on POD 1 as compared by paired t test with Pre op Serum Bilirubin; t-value was -13.54 and p-value < 0.0001.

The difference between sample means was statistically insignificant for Pre op Serum Bilirubin levels and those on POD 3; t-value was -0.42 and p value was 0.68.

Serum SGOT levels on POD 1 as well as on POD 3 were statistically significantly raised when compared with pre-operative values; t-values were -13.73 & -2.46 respectively and p-values were < 0.0001 & 0.02 respectively.

Serum SGPT levels on POD 1 as well as on POD 3 were statistically significantly raised when compared with pre-operative values; t-values were -14.68 & -5.71 respectively and p-values were < 0.0001.

Rise in level of Serum ALP was statistically significant on POD 1 as compared by paired t test with Pre Serum-ALP; t-value was -10.89 and p-value < 0.0001, however the difference between sample means was statistically insignificant for Pre op Serum ALP levels and those on POD 3; t-value was -1.19 and p-value was 0.24.

Comparison of Serum Bilirubin levels on POD 1 and POD 3 showed statistically significant reduction in levels on POD 3; t-value was 11.1 and p-value < 0.0001. Serum SGOT levels on POD 1 showed statistically significant reduction in levels on POD 3; t-value was 12.73 and p-value < 0.0001. Serum SGPT levels on POD 1 showed statistically significant reduction in levels on POD 3; t-value was 11.71 and p-value < 0.0001. Serum ALP levels on POD 1 showed statistically significant reduction in levels on POD 3; t-value was 10.48 and p-value < 0.0001.

ANOVA ANALYSIS AT 0.05 SIGNIFICANCE LEVEL

There was statistically significant variance among Serum Bilirubin values on Pre op Day, POD 1 and POD 3. The f-ratio value was 121.50841. The p value was < 0.00001.

There was statistically significant variance among Serum SGOT values on Pre op Day, POD 1 and POD 3. The f-ratio value was 151.33643. The p value was < 0.00001.

There was statistically significant variance among Serum SGPT values on Pre op Day, POD 1 and POD 3. The f-ratio value was 159.45843. The p value was < 0.00001.

There was statistically significant variance among Serum

Alkaline phosphatase values on Pre op Day, POD 1 and POD 3. The f-ratio value was 79.60143. The p value was < 0.00001.

SUMMARY OF OBSERVATIONS ON POD3

We found that on the 3rd post-operative day Serum Bilirubin levels of all 50 patients had settled down to levels below the upper limit of normal range (0.1 – 1.2 mg / dl). In all patients the increased serum Bilirubin levels observed on the first and third post-operative days consisted of an increased indirect Bilirubin fraction. Serum SGOT levels of 7 out of 50 patients still remained elevated beyond the upper limit of normal range (8 – 48 U/L), ranging between 50 – 58 U/L but significantly reduced as compared with levels on post-operative day 1. 14 out of 50 patients enrolled in the study still had SGPT levels elevated above the upper limit of normal range (7 – 55 U/L), ranging between 56 – 67 U/L, but significantly reduced as compared with Post-operative day 1. Serum Alkaline phosphatase levels of all but 1 out of 50 patients enrolled in the study remained elevated beyond the upper limit of normal range (40 – 129 U/L) on POD 3. This patient's Serum Alkaline phosphatase level on POD 3 was 138 U/L. All Liver function test parameter levels showed a reducing trend by Postoperative day 3. All patients enrolled in the study had an uneventful post-operative recovery period, with adequate pain relief and were discharged on post-operative day 3. All patients were afebrile, accepting normal diet and had normal bowel and bladder functions at discharge. The patient whose ALP value had stayed elevated beyond upper limit of normal range, showed no evidence of clinical deterioration

DISCUSSION

We found in our study that liver function test parameters showed significant elevation from baseline pre-operative levels after Laparoscopic Cholecystectomy. However, these increased levels were always consistently below the population mean levels (Normal level ranges as measured by Siemens Dimension EXL 200 Biochemical analyzer). These results compare well with other Indian and International Studies. We found that Serum Bilirubin levels returned to normal in all patients by 72 hours after surgery. All but one patient showed near complete resolution of Serum Alkaline phosphatase levels at 72 hours post-surgery. We also found that all measured variables showed a significant reducing trend 72 hours after surgery. Serum SGPT was the only parameter that stayed elevated beyond the upper limit of normal range at 72 hours after surgery in approximately one third of our patients. This elevation was consistently below two-fold rise in levels. Less than one sixth of the patients enrolled in the study showed SGOT levels elevated beyond the upper limit of normal after 72 hours of surgery. This discrepancy can be attributed to the fact that the half-life in

the circulation is about 47 hours for SGPT & 17 hours for total SGOT, on average [9].

A prospective study done in 2009 to investigate the effect of pneumoperitoneum on LFTs after Laparoscopic Cholecystectomy with intra-abdominal pressure of 12 mmHg. 37.5% studied subjects showed more than 100% increase in at least one parameter of liver function. The authors stated that subclinical hepatic dysfunction after LC could mostly be attributed to the negative effects of pneumoperitoneum on hepatic blood flow [10].

The “squeeze” effect of pneumoperitoneum on liver parenchyma along with damage of liver cells by prolonged use of diathermy on the liver surface has been postulated to cause transient spillage of liver enzymes into the circulation [2]. Kinking and tenting of the Common bile duct occurs during surgery, leading to transiently raised liver enzyme levels [2]. Since pneumoperitoneal pressure of 12 mm Hg exceeds mean portal pressure (7-10 mm Hg), this may adversely affect hepatic perfusion leading to derangement of LFT [11]. Several studies have demonstrated that in 1.2% to 12.4% of cholecystectomies there occurs silent passage of small stones through the cystic duct down into the Common Bile Duct [12, 13]. A 2010 study conducted by Bhoorasingh et al. observed that CO₂ pneumoperitoneum activates the sympathetic nervous system [14].

A 2009 study by El Leathy MM, et al. found elevated levels of serum ALT and AST within 24-48 hours following Laparoscopic maneuver for undescended testicle in pediatric patients compared with those who underwent Open maneuver for undescended testis. The degree of change in ALT following LMUDT was greater than OMUDT and this difference was statistically significant (P<0.05). On the seventh day following the operations, both enzymes returned to normal value in LMUDT, and OMUDT patients [15].

A 2003 study by Tan, et al. investigated the effects of Laparoscopic procedures on liver enzymes and found that Serum bilirubin levels were transiently increased after such procedures. They concluded that such transient changes in LFTs do not have any clinical implications [16]. We found similar results in our study. Tan, et al. reported elevated levels of liver enzymes till as late as day 7 after surgery. However, these levels were significantly less than those on Day 2 following surgery [16]. The findings of our own study were similar although we found a significant reducing trend in all Liver enzyme levels by day 3 after surgery.

A 2011 study by Ahmed, et al. reported that the rise in Serum alkaline phosphatase is minimal following LC and that mild

to moderate elevation in levels of liver enzymes do not have any deleterious effects [17]. In our study too we found that Serum alkaline phosphatase was the parameter which showed insignificant change as compared with base line levels (in all our patients except one) on day 3 after surgery.

We place on record the following inferences drawn from the findings of our study

Laparoscopic cholecystectomy causes transient rise in levels of liver enzymes and Serum bilirubin, in patients without pre-existing liver disease / biliary injury / biliary strictures.

Liver enzyme levels return to base line by 72 hours after Laparoscopic Cholecystectomy

The transient changes seen in LFTs do not have any deleterious effects on the clinical condition of patients and do not affect their recovery.

CONCLUSION

From the present study we conclude that levels of Serum Bilirubin, Serum SGOT, Serum SGPT and Serum Alkaline phosphatase are elevated transiently following Laparoscopic Cholecystectomy as compared to base line level of these liver function test parameters. Liver enzyme levels rise significantly within 24 hours of surgery and settle down to levels within normal range by the third day following surgery. We conclude that the derangement seen in Liver function test parameters does not affect the patient's clinical condition or recovery when observed in the absence of pre-existing liver disease, Hepatitis, Bile duct injury / strictures. The changes may be caused by CO₂ Pneumoperitoneum, Surgical manipulation and the use of diathermy. We propose that routine pre-operative and post-operative testing of Liver enzyme levels in absence of documented deterioration in clinical condition of patients is unnecessary.

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