



Study of Effect of Pneumoperitoneum on Liver Function Following Laparoscopic Cholecystectomy

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Abstract

This study was undertaken in 60 patients with the aim of assessing the presence and significance of disturbances in liver enzymes following laparoscopic cholecystectomy. The liver function parameters measured preoperatively and post operatively on day 1 and day 7 were - Total bilirubin, Aspartate aminotransferase, Alanine aminotransferase and Alkaline phosphatase . Duration of pneumoperitoneum was noted in all cases.

Observations and Results - *Serum bilirubin was elevated in the immediate post-operative period, which came back to near pre-op values within 1 week. Similarly, liver enzymes, Serum AST, ALT and Alkaline phosphatase levels were found to be significantly elevated in 48 hours postoperatively which returned to near pre-op values by 7 days postoperatively. This was more pronounced in those patients who had prolonged CO₂ insufflation time.*

Conclusion- *These transient changes might be attributed to hepatocellular dysfunction secondary to combination of CO₂ pneumoperitoneum, diathermy on liver and general anaesthesia. The transient elevation of enzymes showed no apparent clinical implication in the patients. These result indicate that if the pre-operative liver function was very poor, laparoscopic cholecystectomy might not be the optimal choice for treating cholelithiasis.*

Keywords – *Laparoscopic, Cholecystectomy, Pneumoperitoneum, Liver enzymes.*

INTRODUCTION

Minimally invasive surgery has changed the face of general surgery. The goal of laparoscopic surgery is to perform standard, classical surgical operations via laparoscope to make the procedure more patient friendly. The main advantages of laparoscopic cholecystectomy include the

reduction of tissue trauma due to small skin incisions, reduction in adhesion formations, reduction in patient morbidity, shortening in hospital stay, and early return to normalcy⁽¹⁾.

During the last decade many studies have disclosed 'unexplained' changes in postoperative liver function tests in patients undergoing

laparoscopic cholecystectomy⁽²⁾. One of the important hemodynamic changes is the transient reduction in hepatic blood flow caused by pneumoperitoneum⁽³⁾. Application of carbon dioxide pneumoperitoneum in critically ill patients with cardiovascular, respiratory or renal insufficiency may induce undesirable consequences due to either hypercapnia or increased intra-abdominal pressure⁽⁴⁾.

The pressure of pneumoperitoneum and its duration was shown to cause elevations in liver enzymes^(5,6) and might be attributed to secondary hepatocellular dysfunction. These results indicate that, if the patient's preoperative liver function was very poor, laparoscopic surgery might not be the optimal choice for treating cholelithiasis⁽⁷⁾. Tan et al have observed that although changes in liver enzymes do not seem to be clinically important, care should be taken before deciding to perform laparoscopic cholecystectomy, in patients with hepatic insufficiency⁽⁸⁾. However, Mehdad et al have observed that early elevation of LFTs soon after surgery should not cause major concern as they usually return to normal without intervention⁽⁹⁾.

This study is intended to assess the prevalence and clinical significance of unexplained disturbances in liver enzymes following laparoscopic cholecystectomy and its relevance in postoperative recovery phase.

AIMS AND OBJECTIVES

- 1) To study the significance of liver function alterations in patients and the safety of laparoscopic cholecystectomy as regards to CO₂ pneumoperitoneum.
- 2) To estimate the changes in serum Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline Phosphatase (ALP) and Total Bilirubin in patients undergoing laparoscopic cholecystectomy preoperatively and postoperatively on day 1 and day 7.

- 3) To correlate the duration of laparoscopic cholecystectomy with elevation of liver enzymes.

MATERIALS AND METHODS

A prospective study was done in a tertiary care hospital in 60 patients who underwent laparoscopic cholecystectomy, after obtaining proper consent. Any patient with pre-operative abnormality in liver enzymes, common bile duct pathology, conversion to open cholecystectomy, and intraoperative bile leakage were excluded from study.

1. Laparoscopic cholecystectomy was performed under general anesthesia with the patient in slight reverse Trendelenburg position with the 4-trocar technique.
2. Pneumoperitoneum was created by insufflation of carbon dioxide via an inserted verres needle and Intraabdominal pressure was maintained at 13 mm Hg.
3. Postoperatively, all patients were given the same intravenous fluids and electrolytes plus antibiotics for 3 days (IV ceftriaxone and metronidazole).
4. Four liver function parameters were measured preoperatively (24hrs prior) and post operatively on day 1 and day 7 i.e. Total bilirubin (TB), Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Alkaline phosphatase (ALP).
5. Duration of pneumoperitoneum was noted in all cases.

OBSERVATIONS & RESULTS

1. **Sex distribution:** 45 patients were females and 15 were males.
2. **Age distribution:** All patients were between 24 and 60 years, majority being between 31 – 40 years.
3. **Serum Bilirubin:** Mean S. Bilirubin was 0.70 mg/dl preoperatively, 1.10 mg/dl on postoperative day 1 and 0.75 mg/dl on postoperative day 7. When compared to pre-op levels, Serum bilirubin values

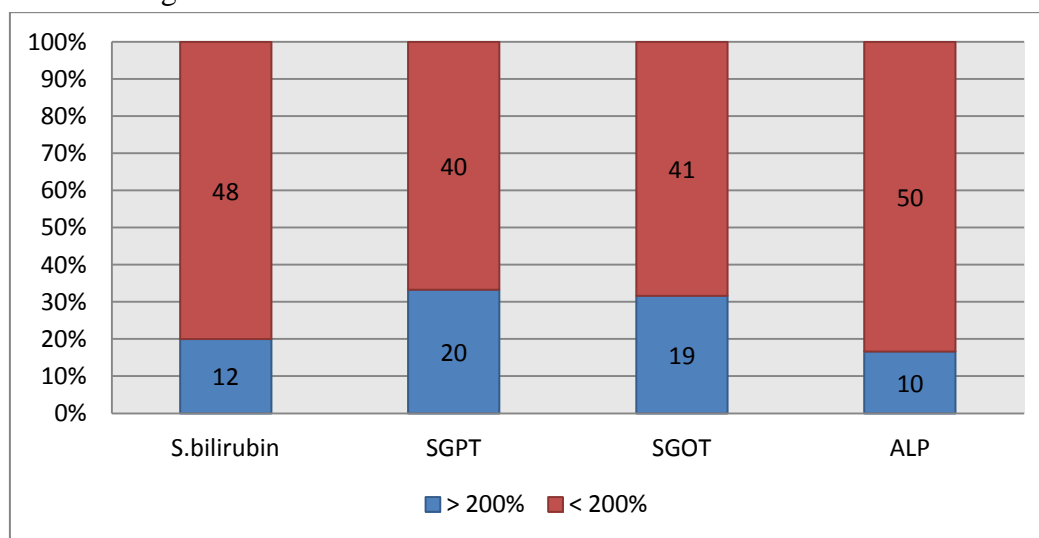
increased significantly on post-op day 1 with a mean increase of 0.4050. It came down to near pre-op levels by post-op day 7 with a mean increase of 0.0483.

4. **SGPT/AST Levels:** The Mean SGPT levels were 19.52 U/L preoperatively, 30.13 U/L on postoperative day 1 and 19.97 U/L on postoperative day 7. They increased significantly on post-op day 1 with a mean increase of 10.61 and came down to near pre-op levels by post-op day 7 with a mean increase of 0.4500.
5. **SGOT/ALT Levels:** The Mean SGOT levels were 22.56 U/L preoperatively, 38.63 U/L on postoperative day 1 and 25.45 U/L on postoperative day 7. They increased significantly on post-op day 1

with a mean increase of 16.06 and came down to near pre-op levels by post-op day 7 with a mean increase of 2.8.

6. **Alkaline phosphatase levels:** The Mean AP levels were 103.81 U/L preoperatively, 147.71 U/L on postoperative day 1 and 108.01 U/L on postoperative day 7. They increased significantly on post-op day 1 with a mean increase of 43.90 and came down to near pre-op levels by post-op day 7 with a mean increase of 4.20.
7. **Double change:** Almost double the pre-op values were found in post-op day 1 in 20% cases in S. bilirubin, 33.3% cases in SGPT, 31.7% cases in SGOT and 16.7% cases in Alkaline Phosphatase values.

Graph – 1: Double Change



8. **Corelation of CO₂ insufflation time with liver enzymes** - Duration of carbon dioxide pneumoperitoneum lasted for 55 to 75 minutes. There was a significant change in liver enzymes where duration lasted more than 70 minutes.

Table - 1: Corelation of Co2 Insufflation Time with Liver Enzymes

Mean bilirubin change	Duration of co2 pneumoperitoneum	
	More than 70 minutes	Less than 70 minutes
Mean bilirubin change [preop and post op day1]	0.52	0.23
Mean SGPT change [preop and post op day1]	19.13	9.67
Mean SGOT change [preop and post op day1]	22.34	14.75
Mean ALP change in [preop and postop day1]	56.34	48.54

Cases which took more than 70 minutes had mean increase of serum bilirubin of 0.52 as compared to

0.23 in cases which took less than 70 minutes. Similar changes were noted in SGPT, SGOT and ALP values.

DISCUSSION

Laparoscopic cholecystectomy, first performed by Boblengen in Germany in 1985, is now one of the most commonly undertaken procedures in general surgery, with more than 500,000 performed annually⁽¹⁰⁾. The growing interest in laparoscopy is attributable to cumulative evidence suggesting reduction in patient morbidity, shortening of hospital stay and early return to normal activity. Carbon dioxide gas insufflation is preferred because it has high diffusion coefficient, is rapidly cleared from body and has lowest risk of gas embolism. Many studies have disclosed unexplained changes in postoperative liver function in patients undergoing laparoscopic cholecystectomy and CO₂ pneumoperitoneum might be one of the main reasons for this. This study is therefore intended to assess the presence of clinical significance of unexplained disturbances in liver enzymes following laparoscopic cholecystectomy.

The primary mechanism for elevation of liver enzymes after laparoscopic abdominal surgery is likely due to the increased intra-abdominal pressure and its effects on portal venous flow. The 11–15 mm Hg of CO₂ that is used is higher than the normal portal pressure of 7–10 mm Hg, resulting in reduced portal blood flow^(11,12). Free radicals are generated at the end of a laparoscopic procedure, possibly as a result of an ischemia-reperfusion phenomenon induced by the inflation and deflation of the pneumoperitoneum⁽¹³⁾, which can damage the Kupffer and endothelial cells of the hepatic sinusoids resulting in increase in liver enzymes postoperatively.

In our study in the 60 patients who constituted the study population, 45 were females and 15 were males. All the patients were between 24 and 75 years of age, with majority of cases [33.3%] in age group of 30 – 40 years. Pradhan et al also

have found that most commonly involved age group for cholelithiasis [32.5%] is 30–39 years⁽¹⁴⁾. The mean level of S. bilirubin preoperatively was 0.70 ± 0.14 mg/dL. Postoperatively on day 1 and day 7 the levels were 1.10 ± 0.32 mg/dL and 0.75 ± 0.18 mg/dL respectively. Similarly, the mean level of serum AST pre-operatively was 19.52 ± 15.99 U/L. Postoperatively day 1 and day 7 the levels were 30.13 ± 9.80 U/L and 19.97 ± 5.2 U/L respectively. The mean level of serum ALT preoperatively was 22.56 ± 5.09 U/L. Postoperatively day 1 and day 7 the levels were 38.63 ± 12.17 U/L and 25.45 ± 5.94 U/L respectively. Thus, there was a significant rise ($P = 0.001$) in Bilirubin, AST and ALT levels in the immediate post-op period when compared to the pre-op values which came down to near pre-op values by post-op day 7. Alterations in AST, ALT, bilirubin and ALP were noted by Nasir zaheer et al on the first post operative day in his study and LFTs performed after 3 weeks on follow up were found to be within normal limits⁽¹³⁾.

The mean level of serum Alkaline phosphatase pre-operatively was 103.81 ± 23.30 U/L. Post operatively on day 1 and day 7 the mean levels were 147.71 ± 36.50 U/L and 108.01 ± 21.92 U/L respectively. A significant rise ($P = .001$) in value was seen on the postop day 1 which came down to near pre-op values within a week. Sakorfas et al in their study found that 24 hrs after procedure in Laparoscopic cholecystectomy group values of AST and ALT significantly increased on 1st and 3rd day and returned to normal by 10 days, whereas in open cholecystectomy patients there was no significant change⁽⁶⁾.

There was a mean increase of serum bilirubin of 0.52 in our cases which had > 60 minutes of pneumoperitoneum as compared to 0.23 in cases which took < 60 minutes with a statistically significant rise in the latter group. Similar readings were noted in levels of SGPT (19.13 in > 60 mins; 9.67 in < 60 mins), SGOT (22.34 in > 60 mins; 14.75 in < 60 mins), ALP (56.34 in > 60 mins; 48.84 in < 60mins) which were statistically significant. In a similar study done by Khalaf et al

on 100 patients they have noticed similar relationship of liver enzyme change with duration of CO₂ pneumoperitoneum⁽¹⁵⁾. In all the patients where there was a transient rise in the enzyme levels, the values returned to near-pre-operative concentrations within one week after surgery and none of the patients presented with clinical hepatic dysfunction after the surgery.

Because the intraabdominal pressure of 12-14mm Hg created by pneumoperitoneum is higher than the normal portal blood pressure of 7-10mm Hg, the portal blood flow is reduced and causes alteration in liver function⁽¹⁶⁾. The elevation and depression of intraabdominal pressure in a short time causing undulation of portal blood flow during the surgery might be causative as well. This undulation and “re-irrigation of organs” and blood flow may give rise to “ischaemia and re-irrigation” damage of tissues and organs, especially the Kupferr and endothelial cells of hepatic sinusoids causing free radical generation⁽¹⁷⁾. All the patients in our study were subjected to CO₂ pneumoperitoneum during the surgery and showed significant changes in post-operative serum liver enzyme level, as reported in other studies^(17,18).

In our study, as the time of CO₂ pneumoperitoneum increased, the elevations in liver enzymes are increased. This is probably due to reduced splanchnic blood flow caused by pneumoperitoneum, as also found out by Kotake et al in their study⁽¹⁸⁾. Also increased intraabdominal pressure triggers neurohumoral response of the vasopressin – renin-angiotensin- aldosterone system. Vasopressin and norepinephrine plays a significant role in causing damage to the hepatic function.

Another possible mechanism for alterations of liver enzymes after laparoscopic cholecystectomy is the “squeeze pressure” effect on the liver⁽⁸⁾. The traction of the gall bladder may free the liver enzymes into the blood stream. But it is not significant as similar traction is given also in open cholecystectomy. The elevation in enzymes may also be due to local effect of prolonged use of diathermy to the liver surface in laparoscopic

cholecystectomy and the spread of heat to liver parenchyma as shown by Capelluto et al⁽¹⁹⁾. However similar use of diathermy is done in open cholecystectomy also. Transient liver dysfunction was also found to occur in patients after some general anaesthesia associated with anesthesia induced changes in splanchnic blood flow and oxygen consumption. But anesthesia could not have acted exclusively as many studies have shown that there is no such change in open surgeries with general anaesthesia⁽⁴⁾.

According to our study we conclude that if the patients’ preoperative liver function is very poor, laparoscopic surgery might not be the optimal choice. Recent studies by Giraud et al suggest that recent advances in laparoscopic surgery like gasless laparoscopy can avoid causing alterations in hepatic function⁽²⁰⁾ and could be tried in patients with poor liver function.

CONCLUSION

The growth of laparoscopic surgery has developed exponentially, the main advantage of which is less tissue trauma, decrease in patient morbidity and decrease in patient hospital stay. Laparoscopic cholecystectomy has emerged as gold standard in treatment of cholelithiasis. However many studies have disclosed transient elevation in post-operative liver enzymes in this procedure. Concerns have been raised regarding the effects of carbon dioxide pneumoperitoneum causing decrease in the hepatic blood flow, responsible for the alteration in liver enzymes. This study was undertaken for the authentication of the same and was performed on 60 patients in a tertiary care hospital.

We conclude that in majority of patients there is a transient elevation of serum bilirubin and hepatic enzymes – SGOT, SGPT and ALP for which the major causative factor seems to be the CO₂ pneumoperitoneum. Though this change caused no apparent clinical implications in patients with normal liver function, we suggest that laparoscopic surgery may not be the best choice for patients with poor liver function.

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