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Original Article

Liver Function Following Carbon-Di-Oxide Pneumoperitoneum in Laparoscopic Cholecystectomy

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Abstract

Background: Laparoscopic surgery is performed by the insufflation of gas like carbon di oxide (CO_2) into the peritoneal cavity by artificial port which is called creating pneumoperitoneum. The CO_2 pneumoperitoneum causes changes in the splanchnic microcirculation and can affect liver physiology. Although laparoscopic cholecystectomy offered many advantages over laparotomy, new concerns arose regarding the effects of CO_2 pneumoperitoneum on liver function. Knowledge of the effects of CO_2 pneumoperitoneum on liver function can help minimize complications while profiting from the benefits of LC without concerns about its safety. It was noticed in many studies that following laparoscopic cholecystectomy (LC), liver function parameters were disturbed.

Aims: To observe any alteration in liver function by carbon dioxide pneumoperitoneum in laparoscopic cholecystectomy.

Methods: Ninety-four patients with cholelithiasis having normal liver function enrolled in this study. Test obtained preoperatively including serum bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) then 24 &72 hour post operatively to compare and proceed. Statistical analyses of the results were obtained by using window-based computer software devised with Statistical Packages for Social Sciences (SPSS22).

Results: The findings showed that mean duration of pneumoperitoneum was 43.8±9.1minutes. The mean serum bilirubin pre-operatively was 0.75±0.21 (mg/dL), post-operative 24 hours value was 0.77±0.23 (mg/dL) and post-operative 72 hours value was 0.73±0.18 (mg/dL). No significant difference was observed in pre-operative and postoperative values. The mean serum ALT preoperatively was 33.81±7.83 (IU/L), post-operative 24 hours value was 52.51±25.9 (IU/L) and postoperative 72 hours value was 46.3±21.33 (IU/L). The mean serum AST pre-operatively was 33.84±6.83 (IU/L), post-operative 24 hours value was 48.94±19.23 (IU/L) and post-operative 72 hours value was 44.36±15.7 (IU/L). The mean serum alkaline phosphatase pre-operatively was 72.57±25.95 (IU/L), post-operative 24 hours value was 88.26±41.69 (IU/L) and post-operative 72 hours value was 85.32±38.85 (IU/L). There were significant increase of post-operative 24 hours and 72 hours value of liver enzymes when compared to preoperatively.

Conclusion: There was significant increase in, AST, ALT, ALP post-operative 24 hours and 72 hours after doing laparoscopic cholecystectomy when compared to preoperatively. There may be a transient elevation of hepatic enzymes after LC and the major causative factor seemed to be CO2 pneumoperitoneum.

Keywords: laparoscopic cholecystectomy, pneumoperitoneum, liver function test, carbon di oxide pneumoperitoneum.

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Introduction:

Laparoscopic cholecystectomy, is now firmly established as the gold standard therapy for symptomatic gallstone disease[1].

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It is a minimal-access approach surgery. Its advantages are well recognized and include reduced post-operative pain, shorter length of hospital stay, superior cosmetic results and cost effective. From several studies it has also been

observed that, more than 4000 patients undergoing laparoscopic cholecystectomy, have less complication rate about 4%. Conversion to open laparotomy that occurs in 5% of patients; the death rate is remarkably low (i.e., 0.1%); bile duct injuries are unusual (i.e., 0.20.5%), 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[2]. Laparoscopic surgery is performed by the insufflation of gas into the peritoneal cavity; so that anterior abdominal wall is lifted away from organs creating a potential space in which surgeon can maneuver his instrument and perform the surgery. Although laparoscopic cholecystectomy offered many advantages over laparotomy, new concerns arose regarding the effects of pneumoperitoneum on liver function. Various gases have been used to create pneumoperitoneum like nitrous oxide, air, helium, carbon dioxide[3].

During the most cases of the surgery, a pneumoperitoneum of 12-14 mm Hg CO2 is established[4, 5]. Carbon dioxide has 20 times more solubility in serum than room air or oxygen and has been shown to be absorbed 32 times more quickly than room air when used for double contrast barium enemas[6]. This use of carbon dioxide to create pneumoperitoneum; resulting in increased partial pressure of carbon dioxide (CO2) and intraperitoneal pressure which leads to the changes in pulmonary function and hemodynamic measurements. Increased level of Carbon dioxide in blood stream leads to visceral organ ischemia including liver and venous stasis/thromboembolism or both due to impaired flow[7].

One of the important hemodynamic changes is the transient reduction in hepatic blood flow caused by a pneumoperitoneum[8, 9]. The pressure of the created pneumoperitoneum and its duration was shown to influence the degree of hepatic ischemia[2]. Studies have shown rise in parameters of liver function test (LFT) following LC and have implicating hepatic hypo perfusion and ischemia. It has been noticed that following LC (laparoscopic cholecystectomy), preoperatively normal serum level of certain liver enzymes rises markedly[10].

Another study correlated that the patients undergoing laparoscopic cholecystectomy (LC), their intra-abdominal pressure with blood flow to the liver was measured using a Laser-Doppler technique, and tonometrically assessed gastric perforation. Both hepatic and gastric microcirculation fell significantly during LC performed with a pneumoperitoneum of 12 mmHg that's indicate ischemia of splanchnic circulation[11]. Other study assessed that there is splanchnic circulatory change during insufflation ofhigh-pressure carbon dioxide pneumoperitoneum. An increase of intra-abdominal (IAP) pressure 5 mm from 10 to 15 mm Hg resulted in a blood flow decrease by 60% to peritoneum & by 39% to liver, by 40-54% to stomach, by 32% to jejunum and by 44% to colon[12].On the other hand it was also found that, blood flow in splanchnic circulation decreases along with increase in operative time, despite a constant IAP. The increased IAP also triggers neurohumoral responses of the vasopressin renin-angiotensin-aldosterone system. Vasopressin and noradrenaline play animportant role in causing damage to hepatic function[12].

Other studies show that during LC, prolonged use of diathermy may produce local effect on liver surface and the heat can spread to liver parenchyma may be another possibility[13]. The compression pressure effect on the liver may be another possible mechanism for alterations of serum liver enzymes after laparoscopic cholecystectomy[13]. But it is not significant because studies show that when liver is not handled at all, similar changes are also seen in laparoscopic appendicectomies and laparoscopy assisted vaginal hysterectomies.[14]. And also studies show that these changes did not occur in patients undergoing open surgeries, where patients were divided into two groups, one group underwent laparoscopic cholecystectomy and the other open cholecystectomy. The changes were not significant in the levels of serum liver enzymes of patients undergoing open surgery[7].
The disturbances after the procedure are self-limited and not associated with any morbidity in

patients with normal liver function tests[2]. Although the exact mechanism for changes in the liver enzyme is not known. The initial factor of consideration here is carbon di oxide pneumoperitoneum[13]. Hence a study on effect of carbon di oxide pneumoperitoneum is necessary.

Methods:

This is a Prospective observational study carried out in the Department of General Surgery,

Sylhet M A G Osmani Medical College Hospital over a period of 1 year; from September 2018 to August 2019.

Ninety-four patients with cholelithiasis having normal liver function enrolled in this study. Test obtained preoperatively including serum bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) then 24 & 72-hour post operatively to compare and proceed. Any complication during or after procedure for example, conversion to open cholecystectomy, intraoperative common bile duct injury, post-operative wound infection, bile leakage excluded from the study.

Results

Table I: Comparison of preoperative & postoperative 24 & 72hours LFT in LC patients with minimum (25min=Group A) & maximum (60min=Group B) duration of CO_2 Pneumoperitoneum.

Parameter	Preoperative		Post-operative 24 hours		Post-operative 72 hours	
	A	B	A	B	A	B
Serum bilirubin (mg/dL)	0.8	0.6	0.8	0.9	0.7	0.8
ALT(IU/L)	45	34.7	52	102	40	81.7
AST(IU/L)	41	35.5	29	78.7	37	59
ALP(IU/L)	78	99.7	76	153.5	76	138.7

Data were presented as **mean**

Table II: Distribution of patients according to serum bilirubin (n=94)

Serum bilirubin[#]	Mean±SD	95% CI
Pre-operative	0.75±0.21	0.71-0.80
Post-operative 24 hours	0.77±0.23	0.72-0.82
Post-operative 72 hours	0.73±0.18	0.69-0.76

Data were presented as **mean ± SD&95% CI.**

Table III: Statistical analysis (level of significance) of Pre-operative, Post-operative data of 24 hours and 72 hours variation in serum bilirubin level.

Group comparison of the study subjects	Level of significance *p-value
Pre-operative Vs Post-operative 24 hours	0.534
Pre-operative Vs Post-operative 72 hours	0.484

*p- value reached from **Paired t-test**

The mean pre-operative serum bilirubin was 0.75±0.21 (mg/dL) with 95% CI 0.71-0.80. The mean post-operative serum bilirubin in 24 hours was 0.77±0.23 (mg/dL) with 95% CI 0.72-0.82. The mean post-operative serum bilirubin in 72 hours was 0.73±0.18 (mg/dL) hours with 95% CI 0.69-0.76 (Table II). Preoperative and post-operative values were compared and the result is not significant (Table III)

Table IV: Distribution of patients according to serum ALT (n=94)

Serum ALT[#]	Mean±SD	95% CI
Pre-operative	33.81±7.83	32.20-35.41
Post-operative 24 hours	52.51±25.9	47.21-57.82
Post-operative 72 hours	46.3±21.33	41.93-50.67

[#]Data were presented as **mean ± SD&95% CI.**

Table V: Statistical analysis (level of significance) of Pre-operative, Post-operative data of 24 hours and 72 hours variation in serum ALT level.

Group comparison of the study subjects	Level of significance *p-value
Pre-operative Vs Post-operative 24 hours	0.001
Pre-operative Vs Post-operative 72 hours	0.001

*p-value reached from **Paired t-test**

The mean pre-operative serum ALT was 33.81±7.83 (IU/L) with 95% CI 32.20-35.41. The mean post-operative serum ALT in 24 hours was 52.51±25.9 (IU/L) hours with 95% CI 47.2157.82. The mean post-operative serum ALT in 72 hours was 46.3±21.33 (IU/L) with 95% CI 41.93-50.67 (Table IV). Preoperative and post-operative values were compared and the result is significant (Table V).

Table VI: Distribution of patients according to serum AST (n=94)

Serum AST	Mean±SD	95% CI
Pre-operative[#]	33.84±6.83	32.44-35.24
Post-operative 24 hours[#]	48.94±19.23	45-52.88
Post-operative 72 hours[#]	44.36±15.7	41.15-47.58

[#]Data were presented as **mean ± SD&95% CI**

Table VII: Statistical analysis (level of significance) of Pre-operative, Post-operative data of 24 hours and 72 hours variation in serum AST level.

Group comparison of the study subjects	Level of significance *p-value
Pre-operative Vs Post-operative 24 hours	0.001
Pre-operative Vs Post-operative 72 hours	0.001

*p-value reached from **Paired t-test**

The mean pre-operative was 33.84±6.83 (IU/L) with 95% CI 32.44-35.24. The mean postoperative 24 hours was 48.94±19.23 (IU/L) with 95% CI 45-52.88. The mean post-operative 72 hours was 44.36±15.7 (IU/L) with 95% CI 41.15-47.58 (Table VI). Preoperative and postoperative values were compared and the result is significant (Table VII).

Table VIII: Distribution of patients according to Serum Alkaline Phosphatase (n=94)

Serum Alkaline phosphatase[#]	Mean±SD	95% CI
Pre-operative	72.57±25.95	67.26-77.89
Post-operative 24 hours	88.26±41.69	79.72-96.79
Post-operative 72 hours	85.32±38.85	77.36-93.28

[#]Data were presented as **mean ± SD&95% CI.**

Table IX: Statistical analysis (level of significance) of Pre-operative, Post-operative data of 24 hours and 72 hours' variation in serum Alkaline Phosphatase level.

Group comparison of the study subjects	Level of significance *p-value
Pre-operative Vs Post-operative 24 hours	0.002
Pre-operative Vs Post-operative 72 hours	0.008

*p-value reached from **Paired t-test**

The mean pre-operative was 72.57±25.95 (IU/L) with 95% CI 67.26-77.89. The mean postoperative 24 hours was 88.26±41.69 (IU/L) with 95% CI 79.72-96.79. The mean post-operative 72 hours was 85.32±38.85 (IU/L) with 95% CI 77.36-93.28 (Table VIII). Preoperative and postoperative values were compared and the result is significant (Table IX).

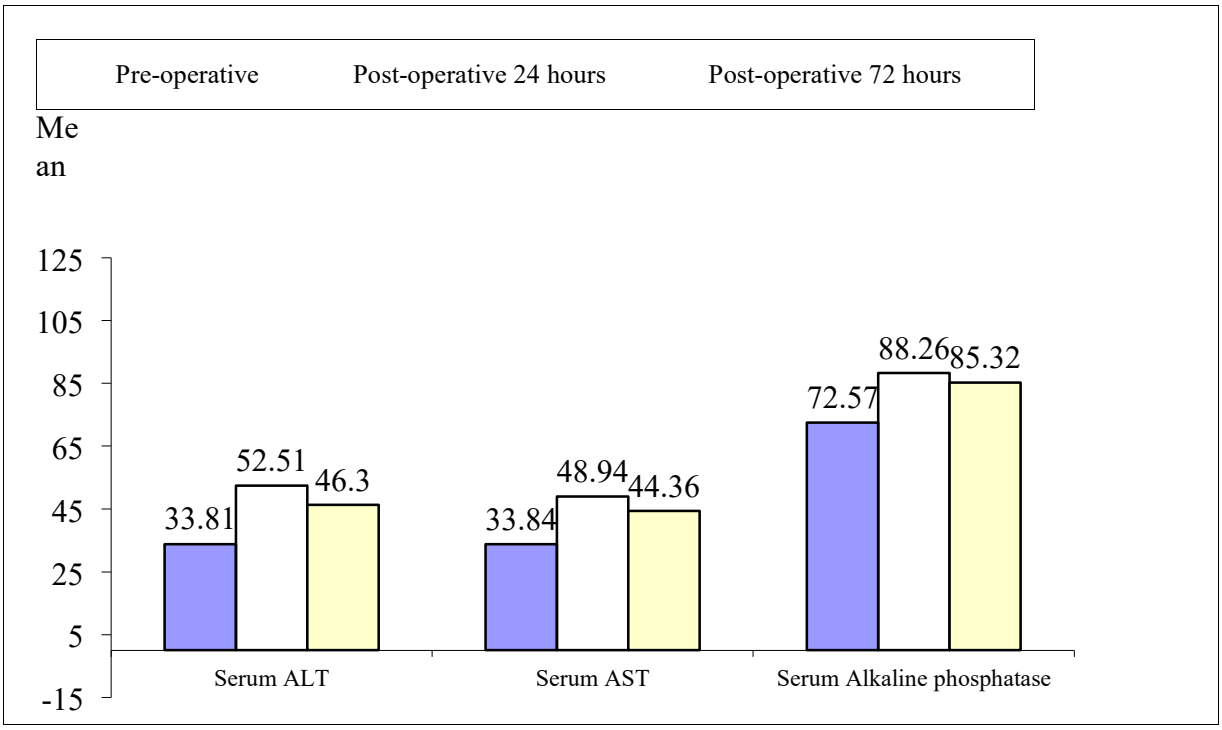

Figure 1: Bar diagram showing mean values of serum ALT, AST and Alkaline phosphatase increased significantly ($p < 0.05$) by 24 hours of operation and they came down to near pre-operative values within 72 hours of operation.

Discussion

Among the 94 patient it was observed that the mean duration of pneumoperitoneum was 43.8±9.1 with 95% CI 41.97-45.69. Also found that the patient with minimum duration of surgery (25 min) had less elevation in liver enzymes as compared to the patient with maximum duration (60 min) of CO_2 pneumoperitoneum which coincides with a study[14].

In this present study, it was observed that the mean serum bilirubin pre-operatively was 0.75±0.21 mg/dL with 95% CI 0.71-0.80. The mean serum bilirubin 24 hours post operatively was 0.77±0.23 mg/dL with 95% CI 0.72-0.82. The mean serum bilirubin 72 hours post-operatively was 0.73±0.18 mg/dL with 95% CI 0.69-0.76. No significant ($p>0.05$) change was found in serum bilirubin at post-operative period of 24 hours and 72 hours with pre-operative mean serum bilirubin level. A study[15] showed that there was no significant rise of bilirubin post operatively, which coincides with this study. But another study shows that comparing Pre-op and post-op values of serum bilirubin levels there was a mean difference in the p-value that was significant (<0.0001)[16,17]. The post-operative increase seen in the levels of serum bilirubin and liver enzymes was transient and occurred irrespective of the type of laparoscopic surgery they underwent. The values returned to near pre-operative levels within 3 days of surgery. None of the patients presented with post-operative clinical hepatic dysfunction in the follow up period[3,18].

In this current study, it was observed that the mean serum ALT pre-operatively was 33.81±7.83 (IU/L) with 95% CI 32.20-35.41. The mean serum ALT significantly raised to 52.51±25.9 (IU/L) with 95% CI 47.21-57.82 after 24 hours of surgery. A significant increase in the level of serum ALT was also seen 72 hours postoperatively when compared to pre-operative levels, but declined from 24 hour postoperatively. Where the mean serum ALT,72 hours post-operatively was 46.3±21.33 (IU/L) with 95% CI 41.93-50.67.Various studies found the mean serum ALT was normal pre-operatively, increased on post-operative day 1 and declined or near normal on postoperative

day 3[8,14,17] . Which is consistent with the current study.

In this study, it was observed that the preoperative mean serum AST was 33.84±6.83 (IU/L) with 95% CI 32.44-35.24. The mean serum AST significantly, rose to 48.94±19.23 (IU/L) with 95% CI 45-52.88 24 hours post operatively, also 72 hours post-operatively it was 44.36±15.7 (IU/L) with 95% CI 41.15-47.58. Similarly, the results of other studies are in agreement with this study, all of which show a significant rise in the values of AST in 24 hours postoperatively when compared to preoperative values. It was seen that these changes are transient and that the liver enzyme levels fell within 72 hours postoperatively[14,17,19].
In this study, it was observed that the mean preoperative serum Alkaline Phosphatase was 72.57±25.95 (IU/L) with 95% CI 67.26-77.89.The mean serum Alkaline phosphatase significantly ($p<0.05$) rose to 88.26±41.69 (IU/L) with 95% CI 79.72-96.79, 24 hours post operatively and a significant ($p<0.05$) increase in the level of serum Alkaline Phosphatase was also found postoperatively at 72 hour when compared to pre-operative levels but declined from 24 hour post-operative value which was 85.32±38.85 (IU/L) with 95% CI 77.36-93.28.Other studies also coincides where there was a significant rise in the level of serum alkaline phosphatase postoperatively compared to the preoperative value. These changes were transient and they returned to near normal values within a few days postoperatively[14, 17]. But some studies also show an insignificant rise of Alkaline Phosphatase[3, 17, 18, 20].
The main concern during LC was increased pneumoperitoneal pressure leading to hepatic dysfunction. This increased pressure, decreases cardiac output and stroke volume. The intraperitoneal pressure created during LC was higher than the pressure in the portal venous system which in turn blocks portal circulation and reduces portal flow up to 50.0%, therefore resulting in depression of the hepatic reticular endothelial system[21]. Thus, variations in liver function tests are directly proportional to the duration and pressure used for pneumoperitoneum. Hence, LC is not the choice of treatment in patients with severe liver diseases or liver cirrhosis because it can deteriorate the liver function further[22, 23]. Many studies were conducted to compare the alterations in liver enzyme levels in commonly practiced laparoscopic surgery to study the effects of pneumoperitoneum, which also shows transient elevation of liver enzymes for which Carbon di oxide pneumoperitoneum remains the major causative factor[17, 23, 24].

Conclusion

Serum bilirubin was almost consistent post-operatively at 24 hours and 72 hours in compare with preoperative value. However, there were significant increase in AST, ALT, ALP post-operatively at 24 hours and 72 hours after doing laparoscopic cholecystectomy when compared with preoperative value. Surgeons should be cautious before doing laparoscopic cholecystectomy in patients with known liver diseases. If the pre-operative liver function is very poor, laparoscopic surgery might not be the optimal choice for treating certain abdominal diseases and low-pressure pneumoperitoneum or gasless laparoscopy by abdominal wall lifting could be a reasonable alternative or surgeon can wait up to optimization of liver function if it is not an emergency.

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