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Prospective Study of Effect of Carbon Dioxide (CO2) Pneumoperitoneum on Hepatic Function in Laparoscopic Cholecystectomy

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ABSTRACT
Gallstones constitute a significant health problem in developed societies. To investigate the incidence of alterations in liver function tests following laparoscopic cholecystectomy and their association with age, gender and duration of surgery. This prospective observational study was conducted from January 2023 to August 2024,conducted in the Department of Surgery with the help of Department of Biochemistry, JLN Medical College and Hospital, Ajmer. In our study there is significant postoperative rises were observed in mean SGOT, SGPT, total bilirubin and direct bilirubin levels at 24 hours, returning to near preoperative values within 72 hours, while ALP showed no significant changes. In laparoscopic cholecystectomy, transient liver function test alterations primarily due to CO2 pneumoperitoneum are clinically insignificant in healthy patients, suggesting routine post-operative assessments may not be needed except for those with hepatic compromise.

INTRODUCTION

Gallstones constitute a significant health problem in developed societies[1]. The prevalence of gallbladder stones varies widely in different communities in India. In north India gallbladder stones are 7 times more common as compared to southern region of India[2]. The evolution of gallbladder surgery began with Jean-Louis Petit in 1733, who advocated for gallstone removal and drainage. Over the years, surgical criteria were refined, notably with J.L.W. Thudichum's two-stage elective cholecystostomy in 1859 and Marion Sims's pioneering work on the first cholecystostomy. A significant advancement came in 1882 when Carl Johann August Langenbuch performed the first successful cholecystectomy, establishing it as the gold standard for treating symptomatic cholelithiasis for over a century[3]. The introduction of laparoscopic surgery transformed the approach to gallbladder removal. Utilizing a laparoscope, surgeons perform laparoscopic cholecystectomy through several small incisions, allowing for a magnified view of the surgical area. This minimally invasive technique relies on creating a pneumoperitoneum with CO2, significantly enhancing recovery and reducing complications compared to traditional methods[4]. While laparoscopic cholecystectomy offers many advantages, it also presents drawbacks such as increased bile duct injuries[5] and longer operation times. Challenges like limited three-dimensional depth perception can hinder visualization of internal structures[6]. Studies, including one by Halevy *et al.*, indicate that factors like increased intra-abdominal pressure, liver compression from gallbladder retraction and general anesthesia can elevate liver enzyme levels during the procedure[7]. Although the CO pneumoperitoneum is often cited as a key factor in these changes, they typically do not lead to adverse clinical outcomes. Liver function tests, particularly AST and ALT, remain highly sensitive in detecting bile flow obstructions[8]. Studies indicate that changes in liver function following laparoscopic cholecystectomy, often attributed to CO pneumoperitoneum, typically do not result in adverse clinical outcomes. Liver function tests (LFTs), particularly AST and ALT, show high sensitivity in detecting bile flow obstructions. Research by Neri V *et al.* found significant increases in AST and ALT levels within 24-48 hours post-surgery, while total and direct bilirubin changes were not statistically significant. Alkaline phosphates (ALP) and gamma-glutamyl transferase (GGT) levels decreased significantly. LFTs returned to normal within three days in patients with previously normal levels and changes were transient and clinically silent. However, higher BMI and pre-existing liver dysfunction are important factors to consider preoperatively[9]. In a study by Sakorafas G *et al.,* liver function was assessed in 72 patients undergoing laparoscopic cholecystectomy, with serum enzyme levels measured preoperatively and at intervals post-surgery[10]. Significant increases in ALT and AST were noted 24 and 72 hours after the procedure, but other liver function markers like ALP and bilirubin showed no significant changes.

Aims and Objectives: To investigate the incidence of alterations in liver function tests following laparoscopic cholecystectomy and their association with age, gender and duration of surgery.

MATERIALS AND METHODS

This prospective observational study was conducted from January 2023 to August 2024,conducted in the Department of Surgery with the help of Department of Biochemistry, JLN Medical College and Hospital, Ajmer. involving 100 patients undergoing elective laparoscopic cholecystectomy. Ethical approval was obtained from the Institutional Ethical Committee and all patients provided written consent after a comprehensive explanation of the research protocol. The study included patients over 18 years of age who were scheduled for elective surgery. Exclusion criteria encompassed individuals with pre-operative liver enzyme abnormalities, suspected chronic liver diseases, common bile duct pathology, those requiring conversion to open cholecystectomy and patients with hematological disorders. Additionally, patients who experienced intra operative complications such as common bile duct injury, jaundice, or cholangitis were excluded. Those who had undergone endoscopic retrograde cholangiopancreatography or standing within the week prior to the procedure, as well as patients on hepa to toxic medications and those with a BMI greater than 24.9, were also not included. This methodology ensured a homogenous study population to accurately assess the incidence of alterations in liver function tests following laparoscopic cholecystectomy.

RESULTS AND DISCUSSIONS

The study evaluated 100 subjects, with a mean age of 48.33±14.43 years, including 36 under 40 years, 64 over 40 years, 15 males and 85 females. The mean duration of surgery in our study came out to be 71.46+12.68mins. Thus the patients were divided into two groups of >70mins and <to 70mins to study the alteration in liver function test with mean duration of surgery. Preoperative mean values for SGOT, SGPT, total bilirubin, direct bilirubin, alkaline phosphates, GGT and INR were 33.15IU/L, 40.46IU/L, 0.74mg/dl, 0.22mg/dl, 72.89IU/L, 30.08IU/L and 1.11, with subsequent values of 65.11IU/L, 71.21IU/L, 1.45mg/dl, 0.51mg/dl, 84.49IU/L, 42.67IU/L and 1.22 and other variations of 26.65IU/L, 31.58IU/L, 0.77mg/dl, 0.33 mg/dl, 77.01IU/L, 33.10IU/L, 1.15 and 28.02IU/L, 30.09 IU/L, 0.78mg/dl, 0.25mg/dl, 77.00IU/L, 19.55IU/L and 1.12. Significant rises in mean SGOT and SGPT values

Table 1 : Age Distribution and Gender Distribution

Age(in years)	Number of Patients	Percent
Less than 40	36	36
More than 40	64	64
Total	100	100
Gender		
Male	15	15
Female	85	85
Total	100	100

Table 2:Duration of Surgery (min)

Duration of Surgery (min)	Number of Patients	Percent
<70 min	51	51
>70 min	49	49
Total	100	100

Table 3 : liver Function Test (Pre-Operatively) Postoperatively After 24 Hours)Postoperatively After 72 Hours) Post Operative 10th Day

Liver Function Test	Pre operatively		After 24 hours (Postoperatively)		After 72 hours (Postoperatively)		On Post Operative 10th day	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
S. bilirubin (Total) (mg/dl)	0.7	0.1	1.4	0.4	0.8	0.08	0.8	0.1
S. bilirubin (Direct) (mg/dl)	0.2	0.1	0.5	0.1	0.33	0.07	0.3	0.1
SGOT	33.2	22.2	65.1	23.7	26.65	8.64	28.0	8.9
SGPT	40.5	24.2	71.2	23.4	31.58	8.46	30.1	9.0
ALP (units)	72.9	25.0	84.5	26.8	77.01	14.19	77.0	13.2
GGT (units)	30.1	13.7	42.7	8.2	33.10	7.19	19.6	5.5
INR	1.1	0.2	1.2	0.2	1.15	0.19	1.1	0.2

Table 4:Comparison of Mean SGOT, Mean SGPT Values at Various Time Intervals

Comparison of	SGOT Mean T-value	SGOT Mean P-value	SGPT T-value	SGPT P-value
Pre operative vs Post Operative at 24 hrs.	9.586	P<0.0001	8.812	P<0.0001
Pre operative vs Post Operative at 72 hrs.	2.733	0.0068	3.458	0.0007
Pre Operative vs Post Operative at 10^{th} Day	2.158	0.0321	4.032	0.0001
Post Operative at 24 hours vs Post operative 72 hours	14.52	P<0.0001	14.67	P<0.0001
Post operative at 24 hours vs post operative 10^{th} day	14.015	P<0.0001	15.21	P<0.0001

Table 5:Comparison of Mean Total Bilirubin Values ,Mean Direct Bilirubin Values at Various Time INTERVALS

Comparison of	TB T-value	TB P-value	DB T-value	DB P-value
Pre operative vs Post Operative at 24 hrs.	16.76	P<0.0001	24.44	P<0.0001
Pre operative vs Post Operative at 72 hrs.	2.288	0.0232	11.94	P<0.0001
Pre Operative vs Post Operative at 10^{th} Day	2.879	0.0044	4.366	P<0.0001
Post Operative at 24 hours vs Post operative 72 hours	16.47	P<0.0001	14.33	P<0.0001
Post operative at 24 hours vs post operative 10^{th} day	16.37	P<0.0001	22.45	P<0.0001

Table 6:Comparison of Mean Alkaline Phosphates Values ,Mean GGT Values, Mean INR Values at Various Time Intervals

Comparison of	ALP T-value	ALP P-value	GGT T-value	GGT P-value	INR T value	INR P-value
Pre operative vs Post Operative at 24 hrs.	3.082	0.0023	0.052	0.0095	3.93	0.0001
Pre operative vs Post Operative at 72 hrs.	1.43	0.154	1.953	0.0522	1.412	0.0015
Pre Operative vs Post Operative at 10th Day	1.452	0.1482	7.134	P<0.0001	2.466	0.0145
Post Operative at 24 hours vs Post operative 72 hours	2.469	0.0144	8.745	P<0.0001	2.682	0.0079
Post operative at 24 hours vs post operative 10^{th} day	2.51	0.0129	23.29	P<0.0001	1.312	0.0019

were observed at 24 hours postoperatively compared to preoperative values (P<0.05), followed by significant decreases within 10 days postoperatively, returning to preoperative ranges (P<0.05). Significant rises in mean total and direct bilirubin levels were observed at 24 hours postoperatively compared to preoperative values (P<0.05), followed by significant decreases within 10 days postoperatively, returning to preoperative ranges (P<0.05). Significant results (P<0.05) were observed in the mean ALP values between preoperative 24 hours and postoperative 24 hours, between postoperative 24 hours and 72 hours, and between postoperative 24 hours and 10th day, as well as in mean GGT and INR values across all time intervals. In the present study, we evaluated a total of 100 patients undergoing LC. The mean age of the subjects was 48.33 years. Out of 100, 85 were females and 15 were males. The usual CO2 pressure during the surgery was 12mm Hg. The mean age of subjects observed in our study was in concordance with the mean age of subjects in the study conducted by Anand[10] and Hiremath[11] (45.2 years). We observed significant rise in the mean SGOT levels of the patients after 24 hours of the LC, which subsequently returned to near pre-operative values (P- value <0.05). The mean SGPT levels in our study at preoperative time, post-operative 24 hour, 72 hour and 10^{th} day of surgery were found to be 40.46IU/L, 71.21IU/L, 31.58 IU/L and 30.09IU/L respectively. In our study, Mean AST levels showed alterations similar to those shown by mean ALT levels. Ahmad[12] also reported similar alterations in the serum AST and ALT levels on the first postoperative day, in patients undergoing LC. Similar results have also been reported by Neri[9], who observed similar rise and fall in mean serum AST and AST values post-operatively in patients undergoing LC The mean total and direct bilirubin values pre-operatively were found to be 0.74 and 0.22mg/dl. We observed a significant rise in the total and direct bilirubin values after 24 hours of surgery which

returned near to its pre-operative levels within 72 hours of surgery, the results of which were found to be statistically significant (P-value <0.05). Our results were also in correlation with the results obtained by Bendre[13], who reported a rise in 39. the levels of serum bilirubin after 24 hours of surgery from the preoperative value and fall (near to normal value) after 72 hours of surgery. The mean ALP levels pre-operatively were found to be 72.89 IU/L. However, we didn't observe any significant alteration in the mean ALP levels in post-operative period, in comparison to the pre-operative values (P-value >0.05). Our results were in concordance with the results obtained by Godara[14] who also didn't report any significant alterations in the mean ALP levels post-operatively in patients undergoing LC[5]. In the present study, we observed that SGOT and SGPT levels were raised in 96% and 94% of patients in our study. Our results were in correlation with Be results obtained by Morino[15] and Mohindra[16] who reported a rise in post-operative serum AST and ALT in more than 90 percent of the patients undergoing LC. ALP levels were found to increase in 12% of patients undergoing LC in the present study. Hagras MMAE[17] and Mohindra M16 also showed an increase in ALP values in 6% and 18% of patients undergoing LC. TB and DB were raised in 85% and 80% of the patients in our study respectively, which is in concordance with the results obtained by Mohindra[16] who reported a rise in TB and DB in 73% and 70% of the patients undergoing LC. In the study, we observed that GGT levels were raised, preoperatively, mean GG T value was 30.08 which increased to mean 24 hour postoperative value of 42.67 and return to its previous levels after 72 hour postoperatively our finding was in correlation with study conducted by Hiremaths[11] and Khandelwal[18] who also reported similar trends. Mean duration of surgery in our study was 71.64+12.68min. with patients showing more derangement in LFT profiles with prolonged duration of pneumoperitoneum which is in correlation with the study conducted by Sunil[19] and Anand[10].

CONCLUSION

In patients undergoing laparoscopic cholecystectomy, our study demonstrates that liver function tests (LFTs) exhibit significant alterations primarily due to hepatocellular disturbance induced by CO2 pneumoperitoneum rather than biliary obstruction. Specifically, we observed marked increases in SGOT, SGPT, total bilirubin and direct bilirubin levels at 24 hours post-operation compared to pre-operative values, with levels returning to baseline within 10 days. Given that these changes typically lack clinical implications in otherwise healthy patients, routine post-operative LFT assessments may be unnecessary. However, caution is warranted for patients with existing hepatic compromise. This insight underscores the need for tailored monitoring strategies in the post-operative management of patients undergoing laparoscopic surgery.

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