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A Prospective study on the effect of Carbon dioxide Pneumoperitoneum on liver function in laparoscopic cholecystectomy(lc) in Tertiary health centre

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Abstract
BACKGROUND
The laparoscopic cholecystectomy has replaced open cholecystectomy as a gold standard for treatment of gall stones. Laparoscopic cholecystectomy is considered to be a safe procedure as compared to open cholecystectomy in regards of metabolic, hormonal and immunological changes. The pneumoperitoneum which is used to create space in laparoscopic cholecystectomy is kept at pressure of 10-15mm of Hg. This high pneumoperitoneum pressure is likely to cause impedance in splanchnic perfusion and decrease the hepatic perfusion. This can cause disturbances in liver functions.
MATERIALS AND METHODS
This is a prospective and observational study conducted in the department of General Surgery, SVRRGGH Tirupati, from July 2019 to June 2020. The study was done on 50 cases with comparative control group of 40 cases with symptomatic or asymptomatic cholelithiasis or choledocholithiasis, aged 20 to 80 yrs.
RESULTS
Effect of Co_2 pneumoperitoneum was studied and preop and post op direct bilirubin didn't show significant rise [P is 0.2939].
The following observations were made, (i)usage of co2 as pneumoperitoneum laparoscopic cholecystectomy has no significant changes on post-operative liver enzymes, (ii)variation in insufflation pressure has no effect on enzyme rise significantly, (iii)duration of surgery with co2 pneumoperitoneum has no effect on postoperative LFT level.
CONCLUSION
From this study, it can be concluded that usage of co2 as pneumoperitoneum in laparoscopic cholecystectomy has no significant changes on post-operative liver enzymes.
The variation in insufflation pressure has no effect on enzyme rise significantly. It can be observed that duration of surgery with co2 pneumoperitoneum has no effect on postoperative LFT level.
Thus, co2 in safe pneumoperitoneum can be safely used in laparoscopic surgeries.
Keywords: *Pneumoperitoneum, liver function tests, laparoscopic cholecystectomy*

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I. Introduction

The laparoscopic cholecystectomy has replaced open cholecystectomy as a gold standard for treatment of gall stones. Laparoscopic cholecystectomy is considered to be a safe procedure as compared to open cholecystectomy in regards of metabolic, hormonal and immunological changes(1).The aim of laparoscopic surgery is to perform operations via laparoscope to make the procedure more patient friendly and to decrease the morbidity. The main advantages of laparoscopic cholecystectomy include the decrease in tissue trauma due to small skin incisions, reduction in adhesion formations, reduction in patient morbidity, shortened hospital stay, and early discharge.

In laparoscopic cholecystectomy, carbon dioxide gas is used for insufflation into peritoneum. The pneumoperitoneum which is used to create space in laparoscopic cholecystectomy is kept at pressure of 10-15mm of Hg. The normal portal pressure is 7-10 mm of Hg(1). This high pneumoperitoneum pressure is likely to cause impedance in splanchnic perfusion and decrease the hepatic perfusion. This can cause disturbances in liver functions. The liver function tests provide quantitative assessment of the liver function but cannot be used to differentiate between causes of liver diseases. However liver function tests are used to determine the presence of liver disease, diagnosis of liver diseases and monitoring of liver diseases. Several tests are used to detect the derangement of liver functions(2).

The commonly used tests are Serum Bilirubin, Alanine Aminotransferase, Aspartate Aminotransferase, Alkaline Phosphatase. These enzymes normally concentrated in liver are also present in low concentration in plasma normally. The plasma concentration of these enzymes is determined by rate of release from hepatocytes and its plasma clearance. High concentration of these enzymes in plasma is present when there is hepatocellular damage. The AST, ALT and AST: ALT ratio signifies hepatocellular damage, ALP signifies cholestasis and organic anion metabolism(3). Pre-operative and Post-operative analysis of these tests can detect any alteration in liver functions following laparoscopic cholecystectomy. These studies have attributed changes in liver function tests to hepatocellular damage due to pneumoperitoneum. During the last decade many studies have disclosed 'unexplained' changes in postoperative liver function tests in patients undergoing laparoscopic cholecystectomy. One of the important hemodynamic changes is the transient reduction in hepatic blood flow caused by pneumoperitoneum(4).

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. The pressure of pneumoperitoneum and its duration was shown to cause elevations in liver enzymes and might be attributed to secondary hepatocellular dysfunction. if the patient's preoperative liver function was very poor, laparoscopic surgery might not be the optimal choice for treating cholelithiasis. 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. To study the incidence of changes in liver function following laparoscopic cholecystectomy, the significance of changes in patients and the safety of the procedure.

II. Aims And Objectives

1. To study the incidence of changes in liver function following laparoscopic cholecystectomy in the Indian population.
2. To study the significance of these changes in patients and the safety of the procedure.

III. Materials And Methods

This is a prospective and observational study conducted in the department of General Surgery, SVRRGGH Tirupati, from July 2019 to June 2020. The study was done on 50 cases with comparative control group of 40 cases.

Inclusion criteria-

- Patients with symptomatic or asymptomatic cholelithiasis or choledocholithiasis, age 20 to 80 yrs.

Exclusion criteria

- Any patient with pre-operative abnormality in liver enzymes.
- Suspected chronic liver diseases
- Common bile duct pathology
- Conversion to open cholecystectomy
- Hematological Disorders
- Intra – Operative Complication – CBD injury
- Incomplete data

Method of sampling was non-random, purposive. After admission short history was taken and physical examination was conducted on each patient admitted in surgery department with features suggestive of extrahepatic biliary lithiasis. Baseline investigations, as routinely required, were done, followed by imaging studies like ultrasound. Patients were then explained about their disease and the possible line of our management. All the necessary information regarding study was explained to the patients or their valid guardian. Informed written consent was taken from the patients and/or their guardian who is willing to participate in the study. Detailed history was taken from all the patients in the study group to establish proper diagnosis. Thorough physical examination was done in every patient. Data collection sheets were filled in by the investigator himself. All of the preoperative factors related to the patient were noted down in the data sheet. After proper evaluation and preparation, patients who required surgical management were taken up for surgery. Strict aseptic precautions were followed during the operation. Meticulous techniques were practiced as far as possible. The operation procedure and related preoperative factors were observed directly and recorded in the data collection sheet instantly.

STATISTICAL ANALYSIS: The study is based on additive ANOVA model. The effect of Co2 on individual liver enzymes were studied. The surgery is classified based on emergency or elective. Based on duration of study classified as group 1<30 min, group 2, 30-90 min, group 3,90-135 min, group 4, >135 min. Then the pre-op and post-op values were compared.

IV. Results

The mean age of patients was 44.75 with more than half of the patients (38%) belonging to the 26-35 age group. The male to female ratio was 1:4.

Co_2 pneumoperitoneum was used as variable, group 1 as 12mm Hg pressure, group 2 as 13mm Hg pressure and group 3 as 15 mm Hg pressure. group 2 is used as standards. preoperative T.B did not show significant rise {P>0.5}.

Effect of Co_2 pneumoperitoneum was studied and preop and post op direct bilirubin didn't show significant rise [P is 0.2939].

Co2 pneumoperitoneum pressure also didn't have any effect over the rise in serum direct bilirubin levels {P is 0.2}.

COMPARISION FOR TOTAL BILIRUBIN PREOP AND POSTOP

Descriptive Statistics

	CO2 Pressure used	**Mean**	**Std. Deviation**	**N**
	GROUP 1	1.150	.4590	16
	GROUP 2	1.171	.5977	17
PRE_TB				
	GROUP 3	1.153	.4598	17
	Total	1.158	.5002	50
	GROUP 1	1.006	.3678	16
	GROUP 2	1.106	.4175	17
POST_TB				
	GROUP 3	1.082	.3909	17
	Total	1.066	.3874	50

Effect of Co_2 pneumoperitoneum was studied and preop and post op direct bilirubin doesn't show significant rise[P is 0.2939].

COMPARISION BETWEEN CO2 PRESSURE AND DIRECT BILIRUBIN

Descriptive Statistics

	CO2Pressure used	**Mean**	**Std. Deviation**	**N**
	GROUP 1	.325	.1693	16
	GROUP 2	.347	.2939	17
PRE_DB				
	GROUP 3	.418	.2186	17
	Total	.364	.2328	50
	GROUP 1	.244	.1590	16
	GROUP 2	.213	.1100	17
POST_DB				
	GROUP 3	.312	.1900	17
	Total	.256	.1589	50

variable co2 pneumoperitoneum pressure doesn't have any effect over the rise in serum direct bilirubin levels {P is 0.267}.

COMPARISION BETWEEN PREOP AND POST OP SGOT

Descriptive Statistics

	CO2 Pressure used	**Mean**	**Std. Deviation**	**N**
	GROUP 1	30.56	16.749	16
	GROUP 2	31.94	13.530	17
PRE_SGOT				

	GROUP 3	34.12	17.744	17
	Total	32.24	15.831	50
	GROUP 1	34.56	15.327	16
	GROUP 2	32.88	15.419	17
POST_SGOT				
	GROUP 3	32.06	16.338	17
	Total	33.14	15.421	50

Descriptive Statistics for SGPT

	CO2 Pressure used	**Mean**	**Std. Deviation**	**N**
	GROUP 1	30.31	8.670	16
	GROUP 2	27.47	10.235	17
PRE_SGPT				
	GROUP 3	33.59	16.447	17
	Total	30.46	12.331	50
	GROUP 1	34.81	7.756	16
	GROUP 2	31.53	11.336	17
POST_SGPT				
	GROUP 3	32.24	15.393	17
	Total	32.82	11.821	50

Descriptive Statistics for ALP

	CO2Pressure used	**Mean**	**Std. De- viation**	**N**
	GROUP 1	48.81	32.421	16
	GROUP 2	66.24	83.140	17
PRE_ALP				
	GROUP 3	48.71	34.657	17
	Total	54.70	55.145	50
	GROUP 1	56.63	40.512	16
	GROUP 2	53.82	43.411	17
POST_ALP				
	GROUP 3	50.24	23.618	17
	Total	53.50	36.150	50

V. Discussion

Laparoscopic cholecystectomy has now become the gold standard procedure for symptomatic gallbladder benign diseases, such as gallstones and cholecystitis. An open cholecystectomy is currently left for special indications only. Despite the many clinical advantages of laparoscopic surgery with the pneumoperitoneum, it might lead to a complex of adverse effects on cardiovascular, respiratory, and renal systems, in addition to the known effects on the liver. Although these changes are of no clinical relevance in healthy patients, they may compound the problem in patients with underlying organ dysfunction.

Presently, the association between the duration of CDP in laparoscopic abdominal surgery and hepatic injury is not fully understood. One of the important hemodynamic changes to have been understood is the transient reduction in hepatic blood flow caused by the pneumoperitoneum(5). The pressure of a created pneumoperitoneum and its duration was shown to influence the degree of hepatic ischemia. This results in elevations in liver enzymes ALT, AST, alkaline phosphatase, GGT, bilirubin, and INR. Although laparoscopic cholecystectomy is associated with transient elevation of liver enzymes, the disturbances after laparoscopic cholecystectomy are self-limited and not associated with any morbidity in patients with a normal liver function(6). Previously the elevation of liver enzymes such as AST and ALT after non-complicated laparoscopic cholecystectomy was considered to be incidental but now it has become a well-known finding.

This prospective, observational and comparative study was con- ducted among 50 purposively selected patients with evidence of chole- lithiasis in department of General Surgery, SVRRGGH, Tirupathi. The study was carried out with a view to determine the effect of co2 as pneumoperitoneum on liver functions during laparoscopic cholecystectomy in view of determining its importance as it have no such role in raising the liver enzymes. Age of 50 patients ranged from 28-77 years. Most of the patients (19,38%) were in between 25-36 years; with mean age 44.75 years and standard deviation 1.83 years. 20% of the patients were males while 80% of the patients were females. The male to female ratio was ~ 1 : 4.females are predominating the study. In a similar study conducted by Srikantaiah *et al.*, the mean age of the study population was 47.18 years with a standard deviation of 7.02. This was slightly higher when compared to this study. In the same study, out of 50 subjects, 6 where male, and the rest were females(7).

The study is based on additive ANOVA model. The effect of Co2 on individual liver enzymes were studied. The surgery is classified based on emergency or elective. Based on duration of study classified as group 1<30 min, group 2, 30-90 min, group 3,90-135 min, group 4, >135 min. Preoperative T.B. shows mean value of 1.171 and standard deviation of 0.5977 and post op T.B. mean value of 1.106 and SD of 0.4175. Preop mean D. Bilirubin was 0.347 mg/dl with SD 0.29. Post op mean D.B. was 0.213 mg/dl and SD of 0.11 with p value of 0.77. Pre-operative SGOT with mean 31.94 IU/L and SD 13.53 and post-operative SGOT with mean 32.88 IU/L and SD 15.4 with p value 0.197. Preoperative ALP was mean with SD is 66.24 and 83.14 and post-operative value 53.82 and SD 43.411 and p value was 0.125. The liver enzymes where not elevated significantly in this study.

However, in the study conducted by Srikantaiah *et al*, significant elevation in the liver function was observed except for ALP(7). Pre op total bilirubin pre operatively was found to be 0.510 mg/dl whereas the post op value was found to be 0.684mg/dl. Pre op direct bilirubin was 0.221 mg/dl whereas post op value was found to be 0.221 mg/dl. The pre op SGOT and ALP value was found to be 22.68 U/L and 72.62 U/L respectively whereas post op values was found to be 32.74 U/L and 56.14 U/L respectively.

In the current study, the following observations were made,

- usage of co2 as pneumoperitoneum laparoscopic cholecystectomy has no significant changes on post-operative liver enzymes.
- variation in insufflation pressure has no effect on enzyme rise significantly.
- duration of surgery with co2 pneumoperitoneum has no effect on postoperative LFT level.

However, the results were not consistent with the findings of other studies. This could be due to the difference in the population characteristics of the sample subjects, and the lesser sample size.

LIMITATIONS OF THE STUDY

As this study has been carried out over a limited period of time with a limited number of patients and there was lack of financial and infrastructural support, it could not have been large enough to be of reasonable precision. All the facts and figures mentioned here may considerably vary from those of large series covering wide range of time, but still then, as the cases of this study were collected from a tertiary level hospital in our country.

VI. Conclusion

This prospective observational study was conducted in department of General Surgery, SVRRGGH Tirupathi, from July 2019 to June 2020. It can be concluded from the findings of this study that usage of co2 as pneumoperitoneum in laparoscopic cholecystectomy has no significant changes on post-operative liver enzymes.

It can be concluded that variation in insufflation pressure has no effect on enzyme rise significantly.

It can be observed that duration of surgery with co2 pneumoperitoneum has no effect on postoperative LFT level.

Thus, co2 in safe pneumoperitoneum can be safely used in laparoscopic surgeries.

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