Original Article

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Effect of CO2 Pneumoperitoneum on Liver Function Following Laparoscopic Cholecystectomy

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Abstract

Background: Laparoscopic provides access to abdominal cavity for both diagnostic and therapeutic surgical interventions which were previously only possible through laparotomy. Recent studies have shown marked rise in serum liver enzymes after laparoscopic surgeries which is considered to be related to the impaired liver and splanchnic perfusion. The present study has been carried out with the aim to comprehend changes in liver enzymes after laparoscopic vs conventional cholecystectomy and the effects of these on outcomes of surgery. **Subjects and Methods:** Between January 2018 and June 2019, 100 patients with symptomatic gall stones which were eligible for cholecystectomy were enrolled in this prospective clinical observational trial. Randomisation to laparoscopic or open cholecystectomy was performed by using a sealed envelope technique just before surgery. All cases were operated by the same consultant surgeon with a standard anaesthetic protocol. Liver function tests were performed before surgery, at 24 hours and day seven postoperatively. **Results:** In the laparoscopic group, a statistically significant rise in liver enzymes both aspartate aminotransferase and alanine aminotransferase was observed after 24 hrs of surgery as compared to preoperative values ($p<.001$) and then again touching normal serum level on 7^{th} day postoperatively. Whereas in open cholecystectomy patients, only a slight variation in the liver enzymes was observed, which was not significant compared to preoperative level ($p>.05$). No statistically significant changes in serum level of GGT, ALP and bilirubin was seen in either group. No mortality or bile duct injury was observed in this study. **Conclusion:** Transient elevation in level of liver enzymes occurs after cholecystectomy in both open and laparoscopy group but more in laparoscopic arm attributed to CO2 pneumoperitoneum with possibly some other factors contributing to this. These changes return to normal in a week time after the procedure, and no major complication is generally seen in these patients with normal preoperative liver function, but these temporary derangements at times may be of concern to surgeons for its implication to the integrity of biliary tract.

Keywords: Cholecystectomy, laparoscopic, pneumoperitoneum, liver function tests

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Introduction

Minimally access surgery has changed the face of general surgery with a goal to perform standard, classical open surgical procedures via laparoscope to make the operative procedure more patient-friendly. Laparoscopic surgery allows a better access to coelomic cavity for both diagnostic and therapeutic surgical procedures which were previously possible through laparotomy alone. Since the introduction of minimally access cholecystectomy technique nearly 33 years back, the knowledge about difficulties associated with these procedures and the awareness of all potential complications has definitely risen. Acquisition of proper technical knowledge and skills to overcome all hurdles, early detection of complications and their timely management are the mainstay for the success of all laparoscopic related procedures. The major benefits of minimally access cholecystectomy technique include: minimal tissue trauma, subsequent decreased incidence of intra abdominal adhesions, less post operative pain, decreased duration of stay in hospital, early resumption to work, improved cosmesis and quality of life. Today majority of gall bladder removal (>90%) are being performed by laparoscopic technique. A temporary rise in intra-peritoneal pressure following CO2 insufflation during laparoscopic cholecystectomy is seen to be causing only the minimal detrimental effects. Numerous recent articles have shown that the level of serum liver enzymes rise significantly following laparoscopic procedures, which might be attributed to altered hepatic and splanchnic circulation, there-

fore explaining the intention of our study. The extent of rise in serum level of these liver enzymes has been demonstrated to be directly related to the pressure level created, thereby seen more in high-pressure pneumoperitoneum. [1] This temporary rise of liver enzymes during laparoscopic cholecystectomy is usually self-limiting and is generally not marker of any complication in patients having normal hepatic function. The clinical observation of significant change in serum level of certain hepatic enzymes in majority of patients with previous normal hepatic function raises several questions like if there is any clinical significance of these changes in liver function tests, mechanism responsible, is there any role of laparoscopic technical modifications to prevent these changes? Temporary rise of hepatic enzymes has shown no evident clinical implication in most patients however, in patients with preoperative poor liver functions, surgery via laparoscopic method might not be the optimal choice. Present prospective clinical study is being conducted to see role of CO2 pneumoperitoneum during laparoscopic cholecystectomy on serum hepatic enzymes and effects of alterations in liver enzymes on outcomes of procedure.

Subjects and Methods

From January 2018 to June 2019, 100 patients presenting with symptomatic gall stones willing for cholecystectomy were included in this prospective clinical observational trial conducted in our tertiary care post graduate teaching institute. Randomisation to laparoscopic (LC) or open cholecystectomy (OC) was performed by using sealed envelope technique just before surgery. All cases were performed by same consultant surgeon with more than twenty years of experience in open and laparoscopic surgeries. Patients who underwent cholecystectomy were solicited to take part in trial and a written well explained consent in patient language was duly signed. Institutional ethical committee approval was sought before start of study to see incidence of change in liver functions subsequent to laparoscopic gallbladder removal and the relevance of these related to the safety of procedure. All patients underwent the following clinical and laboratory evaluation i.e ultrasonography, complete hemogram, hepatic function tests: AST (aspartate aminotransferase), ALT (alanine aminotransferase), ALP (alkaline phosphatase) and bilirubin. The normal range for liver enzymes were AST (10-40U/L; UV Kinetic), ALT (10-40 U/L; UV Kinetic), ALP (39–117U/L; PNP-AMP Kinetic) and total bilirubin (0.2.8 mg/dL;Evelyn-Malloy). Inclusion criteria were: ASA grade I &II patients, patients with preop normal liver function, age 18-60 years, normal BMI. Patients with previous biliary tract surgery, post ERCP, those who required per op cholangiography, chronic liver disease, hematological disorders, conversion to open cholecystectomy, HBsAg/HCV positive, per/post-operative bile duct injury, gall stone related complications i.e cholangitis, pancreatitis, Mirrizis syndrome were excluded from the study. Laparoscopic cholecystectomy was carried out using the standard four port technique and insufflating abdomen with CO2 to a maximum pressure of 12 mmHg. Open cholecystectomy was performed with a right subcostal incision. A standardised institutional anaesthetic drug protocol was used for all patients in either group. Liver function tests were performed before surgery, at 24 hours and at day 7 postoperatively. Single dose of inj cefuroxime 1gm was given in all patients just before surgery. The data was expressed as mean + standard deviation and differences among both groups were determined using chi square test for categorical variables while for continuous scale variables student unpaired t-test was used. P value of <0.05 was considered statistically significant.

Outcomes

Both the groups were having similar and comparable demographics(age, sex, BMI, ASA grade), duration of surgery (time of Veress needle insertion to applying last skin stitch in laparoscopic group and skin incision to suturing in open group)[Table1]. There was no bile duct injury or mortality in either group.

At 24 hrs in laparoscopic cholecystectomt group there was statistically significant rise in ALT and AST level rather than preoperatively (p <0.001) [Table II]. The mean before surgery ALT, AST values were 18.3+ 10.4U/L and 20.6 +12.8 U/L in laparoscopic cholecystectomy group vs 19.6 + 10.9 and 18.6 +11.3U/L in open cholecystectomy group respectively. Post operatively at 24 hours, ALT and AST increased to 92.6 +20.2 U/L and 89.6 +24.2 in LC group (p<.001). In open surgery group serum value of ALT and AST increased at 24 hrs post operatively but not to significant level compared to preoperative level (ALT 41.4 + 11.3 U/L and AST 43.1+ 7.3U/L, p>0.05). On 7^{th} postoperative day, value of ALT and AST returned to almost normal level in both groups. The serum values of bilirubin, GGT and alkaline phosphatase did not show any significant rise in postoperative period compared to preoperative value (p >.05).

Discussion

Presently laparoscopic cholecystectomy (LC) is considered as the gold standard procedure for removal of diseased gallbladder and one of the commonest surgeries performed globally; it is performed by insufflating abdominal cavity with CO2 to get good lookout of the surgical field. Generally an IAP of 10-15mmHg is maintained for laparoscopic cholecystectomy. This increased intra-abdominal pressure is considered to be the main factor leading to the impairment of pulmonary, cardiovascular, metabolic, neurologic, renal and hepatic functions depending on intraperitoneal pressure grade and ischemia. This resulting hepatic ischemia leads to

Table 1: Patient demographics in both groups

Parameters	LC Group (50)	OC Group (50)	P- value
Age (mean+SD)	48.23+12.98	46.71+ 10.34	0.34
Sex M/F	34/16	35/14	0.89
Body Mass Index	24.56±3.47	24.68±3.18	0.9
ASA Grade 1/II	38/12	37/13	0.76
Duration of Surgery (minutes)	62.82 + 16.402	66.70 + 16.816	0.79

Table 2: I: Preoperative and postoperative values of serum enzymes

Enzymes	LC Group (50)			OC Group (50)		
	Preop level	At 24 hrs	At day 7	Preop level	At 24 hrs	At day 7
ALT (U/L)	18.3+ 10.4	92.6 +20.2	31.3 +9.4	19.6 + 10.9	41.4 + 11.3	32.4 +10.7
AST (U/L)	20.6 +12.8	89.6 +24.2	29.5+ 11.2	18.6 +11.3	43.1+ 7.3	39.8 +11.4

elevation of liver enzymes level: alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and gamma glutamyl transferase. The raised intra peritoneal pressure leads to the compression of intra abdominal organs, potentially affecting the hepatic microcirculation leading to hepatocellular dysfunction. One study concluded that an increase of IAP from 10mm Hg to 15 mm Hg resulted in fall of hepatic blood flow by 39%, 60% to peritoneum, 40% to stomach, 32% to jejunum and by 44% to colon.[2] Further it was also demonstrated that, splanchnic circulation was also decreased with increase in operating time at a constant IAP. The other potential mechanism leading to change in serum level of hepatic enzymes after laparoscopic cholecystectomy is squeeze pressure effect on liver during gallbladder retraction which release the hepatic enzymes in blood stream.[3] Additionally the use of diathermy and general anaesthesia might be reason for the transient variation occurring.[4] These variations are seen to be occurring in approximately 80% cases of cholecystectomies; in some studies the changes are significantly higher by laparoscopic technique than by open cholecystectomy.[5–7] To ensure accurate conclusions a strict exclusion criteria was followed in our study and patients having hepatic function abnormality that could affect level of liver enzymes postoperatively i.e. conversion to open or other postoperative complications, were not included in our study. In the last decade many studies have demonstrated unexplained changes in level of post operative liver enzymes in patients undergoing laparoscopic procedures. CO2 pneumoperitoneum can be considered as one of the dominant factor leading to change in serum hepatic enzymes level, as this is the only main difference laparoscopic surgeries had when compared with open surgeries. It has been observed that most of laparoscopic operations can lead to transient elevation of liver enzymes and bilirubin level for which C02 pneumoperitoneum is the leading causal factor. In our study aspartate aminotransferase and alanine aminotransferase levels raised at 24 hours postoperatively in both LC and OC group but only in LC group this rise was statistically significant. Subsequently enzymes level in both groups returned to normal preoperative level on 7^{th} day. These results are comparable with recently published literature in the subject.[5,6,8,9] Syed Ibrahim et al in their study on 60 patients observed that increase in level of serum bilirubin, AST, ALT and ALP was statistically significant during first 24 hours after surgery. These changes in the liver enzymes are transient as the values of LFTs revert back to near preoperative value by post-operative day 5 as shown in our series also.[10] We have not observed significant changes in GGT, ALP and bilirubin. Similar results have been shown by various other authors.[8,10–15] In our study both groups are well matched and CO2 pneumoperitoneum is the only variable not present in patients undergoing open cholecystectomy hence might be one of the major causative factors. CO2 because of its high blood solubility leads to hypercapnia and respiratory acidosis. Further high intra-abdominal pressure (12-14 mmHg) of CO2 which is much higher than portal blood pressure (7-10 mmHg) can lead to decreased portal blood flow, altering hepatic function. Few modifications during laparoscopic surgeries i.e gasless techniques, minimal diathermy use, use of harmonic scalpel, ligasure might be having less alteration in hepatic enzymes. Hence the transient rise in level of liver enzymes tests after uncomplicated laparoscopic cholecystectomy might be a normal phenomenon without any obvious clinical implication since all values generally touches to normal within a week. A series of important studies in our literature have shown transient alterations in liver enzymes in immediate post operative period after laparoscopic cholecystectomy with hardly anyone showing effect on outcome. Clinician must be aware of these physiological changes and sound interpretation of investigations can avoid missing any bile duct injury and simultaneously not to worry for these minor changes. However multicenter, randomised, high volume, well controlled further

studies are required in this regard.

Conclusion

A temporary rise in hepatic enzyme levels after laparoscopic cholecystectomy is frequently seen and most probably occurs due to fall in hepatoportal blood flow caused by raised intraperitoneal pressure by C02 insufflation. No apparent clinical changes are seen in patients as a result of this alteration. As benefits of the procedure overcome its limitations, laparoscopic surgery is now emerging to be the gold standard for various other surgical procedures as for cholecystectomy. Clinicians need to be conscious in presence of serious liver disorder and decide the operative modality accordingly.

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