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Original Research Article

Effect of laparoscopy on liver enzymes

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ABSTRACT

Background: Laparoscopic procedures have gained popularity in recent days because of advantages like small incision, less postoperative pain and discomfort, short hospital stay, early ambulation and early discharge. Very few studies are available to correlate Laparoscopic Surgeries and liver enzyme elevation. This effect may be due to either CO2 pneumoperitoneum, diathermy extruding liver, injury to branch of the hepatic artery or general anesthesia. This study was done to evaluate the changes in liver enzymes pre-operatively and post-operatively following laparoscopy.
Methods: This prospective study included 103 patients who underwent various laparoscopic surgeries over a period of 2 years in Bharati Hospital & Research Centre, Pune, India. Serum AST, ALT and bilirubin levels were measured preoperatively and on post-operative day 1 and post-operative day 3. Patients with coexisting liver disease, Patients on long term use of hepatotoxic drugs, patients who developed complications such as CBD injury, obstruction, infection, leakage and high grade fever during surgery and in the post-operative period were excluded.
Results: All laparoscopic procedures cause a transient elevation of serum bilirubin and liver enzymes. Elevation in the liver enzymes correlated directly with the duration of pneumoperitoneum. Elevation in the serum bilirubin but doesn't correlates with the duration of pneumoperitoneum. These elevations do not have clinical significance in patients with normal hepatic function preoperatively.
Conclusions: Duration of laparoscopic procedure should be kept to minimum and undue prolongation should be avoided. Decision to convert the operation to open surgery from a laparoscopic surgery should be prompt.

Keywords: Laparoscopy, Liver enzymes, Pneumoperitoneum

INTRODUCTION

The new era has seen several changes in the field of medicine. With newer technology and access to advanced services provided by different fields of medicine, the surgical skills have improved from older mind set of bigger incision, better surgeries to a less tissue damaging, cosmetically acceptable small incision or laparoscopic surgeries which have better patient acceptability. Laparoscopic surgeries have changed many general surgical procedures from performing standard open procedures to minimally invasive procedures which have better cosmesis, less tissue damage, thereby leading to better patient compliance.

Many diseases in the past were not managed surgically due to high chances of damaging surrounding structures but the present day scenario is different as these situations are managed easily with laparoscopic approach, like impalpable testes, gallbladder disease, Hirschsprung's disease and many more such procedures which have more complications if done via open surgical approach.[1] Any technique has its own pros and cons, which applies to laparoscopic surgeries also. The adverse effects of laparoscopic surgeries on patient's body are often neglected. The widely known adverse effect of laparoscopic surgeries is its effects on liver function. In the last few years, many studies have shown 'unexplained' changes in liver enzymes during postoperative period after laparoscopic procedures. The

serum liver enzymes increase significantly in many patients who had a normal liver enzyme before the procedure.[2-4] Very few studies are available to justify the correlation between Laparoscopic Surgeries and liver enzyme elevation. The cause for elevated liver enzymes has remained unknown so far. This effect may be due to either CO2 pneumoperitoneum, diathermy extruding liver, injury to branch of the hepatic artery or general anesthesia.[5] This study was done to evaluate the changes in serum liver enzymes pre-operatively and post-operatively following laparoscopic procedure.

METHODS

This prospective study was done to evaluate the effect of laparoscopic surgeries on hepatic function. The patient population included in the study were selected by purposive sampling method from those who underwent laparoscopic surgeries in Bharati Hospital and Research Centre, Pune. The study was conducted from October 2017 to August 2019.

All the patients studied were selected using Purposive sampling method for laparoscopic surgeries after routine history taking, physical examination and investigations to exclude pre-existing liver diseases. Various laparoscopic procedures were performed on 103 patients and they constituted the study population. Sample size was estimated by using the proportion of subjects with increased AST in laparoscopic subjects was 58.2% from the study by Singal R, Singal RP, Sandhu K, Singh B, Bhatia G, Khatri A studied on Evaluation and comparison of postoperative levels of serum bilirubin, serum transaminases and alkaline phosphatase in laparoscopic cholecystectomy versus open cholecystectomy.[4] All Patients undergoing laparoscopic procedures in the Department of General Surgery, Bharati Hospital and Research Centre, Pune were included in this study.

All patients with coexisting liver disease, Patient on long term use of hepatotoxic drugs, Patients that develop complications such as CBD injury, obstruction, infection, leakage and high grade fever during surgery.

RESULTS

In this study preoperative mean AST was 34.83±24.80 U/L which increased to 53.8±28.96 U/l on 1st post-operative day and again reduced near to pre- operative value of 37.06±22.08 U/l on 3rd post-operative day. There was significant increase in mean AST values between Pre-operative and 1st Post- operative day (p<0.001) (Table 1).

In this study preoperative mean ALT was 35.93±26.51 U/l which increased to 54.58±29.28 U/l on 1st post-operative day and again reduced near to pre- operative value of 37.06±22.08 U/l on 3rd post-operative day. There was significant increase in mean ALT values between Pre-operative and 1st post-operative day (p<0.001) (Table 2).

Table 1: Comparison of mean AST at different time interval.

	Mean	SD	P value
AST pre op in U/l	34.83	24.80	
AST postop1 in U/l	53.80	28.96	<0.001*

Table 2: Comparison of mean ALT at different time interval.

	Mean	SD	P value
ALT pre op in U/l	35.93	26.51	
ALT post op1 in U/l	54.58	29.28	<0.001*

Table 3: Comparison of mean serum ALP at different time interval.

	Mean	SD	P value
ALP pre op in U/l	98.42	51.64	
ALP post op 1 in U/l	122.96	46.67	<0.001*

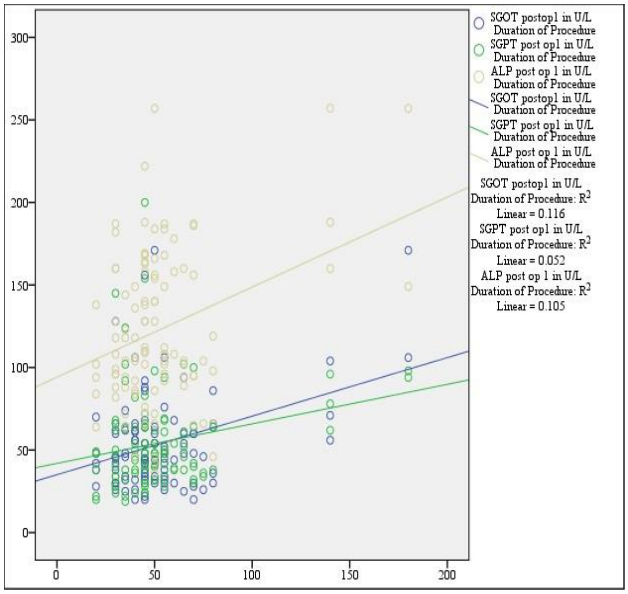

Figure 1: Correlation between duration of procedure and AST, ALT and ALP at 1 day post-operative period.

Table 4: Comparison of mean serum total bilirubin at different time interval.

	Mean	SD	P value
STB preop in mg/dl	0.62	0.31	
STB post op 1 in mg/dl	0.82	0.36	<0.001*

In this study preoperative mean ALP was 98.42±51.64 U/l which increased to 122.96±46.67 U/l on 1st post-operative day. There was significant increase in mean

ALP values between Pre-operative and 1st Post-Operative day (p<0.001) (Table 3).

Scatter plots were constructed by using duration of procedure in X axis and Liver enzymes in Y axis (Figure 1).

In this study the pre-operative mean serum total bilirubin (STB) was 0.62±0.31 mg/dl, which raised to 0.82±0.36 mg/dl on 1st post-operative day and again reduced to 0.63±0.27 mg/dl on 3rd post-operative day. There was significant increase in mean STB between pre-operative and 1st post-operative day (p value <0.001) (Table 4).

In the study there was significant positive correlation between Duration of procedure and Post- operative day 1 values of AST, ALT and ALP i.e. with increase in duration of procedure, there was more increase in Post-operative day 1 AST, ALT and ALP and vice versa. There was no significant correlation between Duration of procedure and mean STB on post-operative day 1 (Table 5). In the study there was no significant correlation between Inflation pressure and Post-operative values of STB, AST, ALT and ALP on day 1.

Table 5: Correlation between duration of procedure and liver enzymes at 1 day post-operative period.

Correlations						
		Duration of procedure	**STB post op 1 in mg/dl**	**AST postop1 in U/l**	**ALT post op1 in U/l**	**ALP post op 1 in U/l**
Duration of procedure	Pearson correlation	1	0.008	0.340**	0.227*	0.325**
	P value		0.939	<0.001*	0.021*	0.001*
	N	103	103	103	103	103
**. Correlation is significant at the 0.01 level (2-tailed).						

Table 6: Correlation between inflation pressure and liver enzymes on post-operative day 1 period.

Correlations						
		Inflation pressure	**STB post op 1 in mg/dl**	**AST postop1 in U/l**	**ALT post op1 in U/l**	**ALP post op 1 in U/l**
Inflation pressure	Pearson correlation	1	-0.078	0.124	0.118	0.051
	P value		0.436	0.210	0.235	0.607
	N	103	103	103	103	103
**. Correlation is significant at the 0.01 level (2-tailed).						

DISCUSSION

Laparoscopic procedures have gained popularity in recent days because of newer technologies like endoscopic optics, video cameras and endoscopic instrumentation, to add on to this many other advantages are incision is small, less postoperative pain, less postoperative discomfort, hospital stay is shortened, patients are ambulated early and can return to their routine activities early.[6]

Laparoscopic surgeries are also accompanied by unexplained significant physiological changes which are specifically unique to these procedures. There are unexplained changes in postoperative liver function reflected in serum liver enzymes in patients who have undergone laparoscopic procedures which is hypothetically attributed to CO_2 pneumoperitoneum. This study was undertaken to assess the change in liver enzymes and serum bilirubin after laparoscopic surgeries and if it has any clinical significance.

In laparoscopy insufflation of gases through Veress needle at the rate of 1-2 L/min, pneumoperitoneum is initiated. Overall pressure of the diaphragm at this point is about 50 kg in the Trendelenburg position at an IAP of 15mm Hg once pneumoperitoneum is achieved.

Increased IAP, temperature variations (hypothermia), CO_2 absorption, and neuro-hormonal stress response is produced as a result of pneumoperitoneum.

The introduction of several liters of gas into the abdominal cavity results in an increased intra-abdominal pressure. Cardiovascular changes associated with pneumoperitoneum depends on the interaction of factors including position of the patient, rate and amount of insufflation of CO_2.

IAP (>20 mm Hg) can lead to prograde flow with increased vascular resistance thereby adversely affecting the abdominal vasculature. Marked decrease blood supply is seen mostly in portal system of about 60 per

cent causing liver dysfunction with increase of IAP of >20 mmHg and this might persist postoperatively.[7]

Serum total bilirubin

This result correlated with study done by Marakis et al.[3] On alterations in liver function tests following Laparoscopic cholecystectomy in which the mean STB was 0.64±0.24 mg/ml preoperatively and was 0.95±0.58 mg/ml 24 hours post- operatively there was increase of up to 48.4% which was statistically significant.

Nahvi et al measured liver enzymes preoperatively, 24 hours post-operatively and on 7th postoperative day. Their study population was divided into 2 groups. Group A patients underwent low pressure laparoscopic cholecystectomy (LPLC) that is pneumoperitoneum maintained at 8mm of Hg and group B patients were subjected to high pressure laparoscopic cholecystectomy (HPLC) in which pneumoperitoneum was maintained at 14 mm of Hg. In HPLC group mean value of pre-operative STB was 0.75±0.10 mg/dl, which increased to 0.79±0.09 mg/dl on post-operative day one and returned to near pre-operative values of 0.73±0.08 mg/dl on post-operative day 7. Whereas no significant change was noted in LPLC group.

Serum AST/ SGOT

Our result correlating this with study done by Hameed et al on impact of pneumoperitoneum on hepatic functions after laparoscopic cholecystectomy (LC) showed that mean AST pre operatively was 31.23±5.51 U/l which increased to 53.79±12.92 U/l on 2nd postoperative day and returned to 31.20±5.75 U/l on 10th post-operative day.[2] There was statistically significant increase in the levels of mean serum AST on 2nd post-operative day and by 10th post-operative day the values returned pre-operative levels. Changes in serum liver enzymes after laparoscopic procedures was the study done by Tan et al, showed that mean AST increased after laparoscopic cholecystectomy from 28.4±20.2 to 41.5±24.7 U/L on post op day 1 ($p<0.05$) and in laparoscopic colorectal cancer resection surgeries from pre-operative mean value of 27.3±16.1 to 40.7±27.3 U/l on postop day 1 ($p<0.05$), Both of which were statistically significant.[5] No statistical difference was noted in open cholecystectomy and open colorectal cancer resection surgeries patients.

Serum ALT/SGPT

In this study correlates this with the study done by Hameed et al on impact of pneumoperitoneum on Hepatic Functions after LC showed that ALT pre operatively was 28.19±5.29 U/l, 2nd day postoperatively was 51.11±13.06 U/l and on 10th post op day 29.16±5.40 U/l there was statistically significant increase in the levels of serum ALT was noted in samples of 2nd post-operative day and on 10th post op day the values returned preoperative levels.[2]

Changes in serum LFT's after laparoscopic surgery was the study done by Tan et al showed that mean value of ALT increased after laparoscopic cholecystectomy from pre-operative value of 23.3±11.6 U/l to 38.8±15.2 U/l on post op day 1 ($p<0.05$) and it was 25.1±14.3 U/l on postoperative day 7.[5] In open cholecystectomy the ALT values were 21.8±16.7 U/l on preoperative day, 28.2±13.7 U/l on post op day 1, 27.3±18.3 U/l on post op day 2 and 24.2±11.1U/l on day 7. There was statistically significant increase in ALT levels postoperatively in patients underwent laparoscopic surgeries but no significant changes preoperative and postoperative ALT values in open cholecystectomy group.

Serum ALP

Our results are Correlated with the study done by Rao et al on Alterations in liver function tests following laparoscopic surgery and showed that mean value of ALP in preoperative period was 101.03±21.279 U/l, its value was 135.517±31.472 U/L on post-operative day 1 and on postoperative day 3 it was 107.583±22.865 U/l, showing that mean values of ALT increased significantly ($p<0.001$) by post-operative day 1.[9]

A study was done by Hameed et al on Impact of Pneumoperitoneum on Hepatic Functions after Laparoscopic Cholecystectomy showed that mean ALP pre-operatively was 204.46±43.67 U/l, on 2nd day postoperatively was 84.51±41.80 U/l and on 10th post-operative day it was 203.42±43.04 U/l which was not significant.

Duration of pneumoperitoneum

In our study a positive correlation was noted between the duration of pneumoperitoneum and increased in serum bilirubin and liver enzymes which is similar to other study conducted by Hameed et al, effect of pneumoperitoneum on hepatic functions after LC.[2]

Pneumoperitoneum pressure

Intra-abdominal pressure in all the patients of our study was maintained between 12-14mmHg which was higher than normal portal venous pressure of 7-10mmHg. Thus, the elevation in Serum bilirubin and liver enzymes can be attributed to relative ischemia of liver, as major blood to liver is supplied by portal vein. Pneumoperitoneum at 15 mmHg causes decrease blood flow to all abdominal organs, by 40-54% to stomach, by 44% to colon, by 39% to liver, by 32% to jejunum and by 60% to peritoneum.[10] Study conducted by Nahvi et al has evaluated the changes in the liver function tests and their clinical significance after uneventful laparoscopic cholecystectomy at different intra-abdominal pressures.[8] They have observed that laparoscopy cholecystectomy done at low pressure of 8 mm Hg does not produce elevation in liver enzymes. Study conducted by Giraudo et al concluded that

laparoscopic surgery without creating pneumoperitoneum does not produce much alterations in hepatic function.[11]

Authors have found that serum total bilirubin and the serum liver enzymes (serum AST, ALT and Alkaline phosphatase levels) were found to be significantly elevated on 1st post-operative day irrespective of type of laparoscopic procedure. Patients with prolonged duration of pneumoperitoneum showed more elevation in the liver enzymes. Elevation of serum bilirubin does not correlate with prolonged duration of pneumoperitoneum. On post-operative day 1 maximum raise was found in mean values of AST and ALT i.e., 34.91% and 34.65% respectively followed by serum total bilirubin which increased by 21.87% and least increase was noted in the mean values of ALP that increased by 19.85%

No clinical significance was found to be associated with such elevation.

CONCLUSION

From this study authors hereby conclude that, all laparoscopic procedures cause a transient elevation of serum bilirubin and liver enzymes, elevation in the liver enzymes correlated directly with the duration of pneumoperitoneum, elevation in the serum bilirubin but doesn't correlates with the duration of pneumoperitoneum, these elevation does not have clinical significance in patients with normal hepatic function.

Thus, duration of laparoscopic procedure should be kept to minimum and undue prolongation should be avoided. Decision to convert the operation to open surgery from a laparoscopic surgery should be prompt.

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