

Evaluation of the Effects of Laparoscopic Surgeries on Hepatic Enzymes

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Abstract

Aim And Objective: This study was designed to investigate the effect of laparoscopic surgeries on liver function tests and the possible mechanisms behind such effect, in our Hospital by statistical analysis.

Material And Methods: A prospective study was conducted in 60 patients who were undergoing various types of laparoscopic procedure in our Hospital. Blood sampling were collected both preoperatively and post operatively on day 1 and day 7 for liver function tests by comparing the level of serum bilirubin, serum alanine amino transferase (ALT), serum aspartate amino transferase (AST) and serum alkaline phosphatase (ALP). The time duration of CO₂ insufflation was also measured.

Result: The level of serum bilirubin, serum aspartate amino transferase, serum alanine amino transferase and alkaline phosphatase increased significantly during the first 24 hours post operatively. Doubling of pre-op values of AST was seen in 46%, ALT in 32% and S. Bilirubin in 35% patients. These values returned to near pre-operative value by the 7th day post operation.

Interpretation And Conclusion: In this study we conclude that there was transient elevation of hepatic enzymes after laparoscopic surgery. The major causative factor would be the carbon-dioxide pneumoperitoneum. In majority of the laparoscopic surgery patients, the transient elevation of serum liver enzymes showed no apparent clinical manifestations. However, if preoperative liver function was very poor, laparoscopic surgery may not be the best choice for the treatment of abdominal diseases. Care should be taken before deciding to perform laparoscopic surgery in patients with hepatic dysfunction.

Keywords: Laparoscopic surgery, Laparoscopy, Liver enzyme, Pneumoperitoneum.

I. Introduction

During the past several decades, numerous individuals cultivated and promoted the access for laparoscopy. The big development in the field of laparoscopy was made by invention of computer chip television camera. This scientific modernization implement the means to program a magnified picture of the operation field on to the monitor, facilitating performance of complex laparoscopic procedures, better results with least damage. The future is today however the emerging of any advanced machinery built upon how well our practice is. Some of diseases which were not dealt due to fear of damage to surrounding structures during access are presently been treated easily with laparoscopic surgery. Laparoscopy has had a profound influence on treatment of patients with impalpable testes, gallbladder disease, endometriosis, colorectal diseases and Hirschsprung's disease'. Everything comes with having both the advantages and disadvantages. Main advantages of laparoscopic surgery include; reduction of tissue trauma due to small skin incisions, reduction in adhesion formation, reduction in patient morbidity, shortening of duration of hospital stay and early return to normal activity. Furthermore, when the laparoscopic procedures are performed in a minimally invasive pattern there will be less chance of internal scarring correlated to standard open surgery. With the interest to achieve maximum outcome with the best cosmesis, advances like laparoscopy, Natural orifice transluminal endoscopic surgery all are becoming popular and being widely accepted and practiced all over the world. But unfortunately very little importance is being given on the adverse effects of laparoscopy on the patient's body. Liver function abnormalities are one of the known effects of laparoscopic surgery. The level of serum liver enzymes

increased noticeably in those patients who had a pre-operative liver function tests were within normal range. No causes for this elevation are documented till now, so we decided to perform a study to correlate the changes in serum liver enzymes pre-operative and post operation.

II. Aims And Objectives

1. To study the effects of laparoscopic surgery on liver enzymes Aspartate Aminotransferase (SGPT), Alanine Aminotransferase (SGOT), Alkaline Phosphatase (ALP) and Serum Bilirubin.
2. To correlate the duration of laparoscopic procedure with elevation of liver enzymes.
3. To evaluate the cause and clinical implication of unexplained disturbances in liver enzymes consecutive to laparoscopic procedure.

III. Material And Methods

A prospective study was conducted to evaluate the outcome of laparoscopic surgeries on liver function in 60 patients who were undergoing various laparoscopic surgeries in our Government Rajaji Hospital, Madurai. Blood sampling for liver function tests were collected both preoperatively and post operatively on day 1 and day 7 by comparing the level of serum bilirubin, serum alanine amino transferase (ALT), serum aspartate amino transferase (AST) and serum alkaline phosphatase (ALP). The time duration of carbon-dioxide insufflation was also measured.

IV. Study Method

Aim And Objectives:-

1. To study the effects of laparoscopic procedure on liver enzymes serum bilirubin, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT) and Alkaline Phosphatase (ALP).
2. To correlate the duration of laparoscopic procedure with elevation of liver enzymes.
3. To evaluate the cause and clinical significance of unexplained disturbances in liver enzymes following laparoscopic procedure.

Inclusion Criteria:-

1. Patients of any age group undergoing laparoscopic surgeries in our Government Rajaji hospital, Madurai with preoperative liver function test within normal limits.

Exclusion Criteria:-

1. Patients with coexisting liver disease/preoperative deranged liver function tests/long term use of hepatotoxic drugs/generalized debility.
2. Patients who develop complications such as bile duct injury, obstruction, infection, leakage.
3. Patients who had undergone endoscopic retrograde cholangio pancreatography and endoscopic sphincterotomy before surgery.

History:-

1. Patients characteristics age, sex, duration of symptoms was noted.
2. All details regarding presenting complaints were noted.
3. Past history of any disease or any drug history was noted.
4. Personal history like smoking, alcohol consumption, diet was enquired.

All the patients were selected after routine history taking, physical examination and investigations serum bilirubin, serum alanine amino transferase (ALT), serum aspartate amino transferase (AST) and serum alkaline phosphatase (ALP) to exclude pre-existing liver disease.

Protocol:-

Those patients selected for the study, the levels of Serum bilirubin (normal range < 1 mg/dL), Aspartate Aminotransferase (AST or SGPT, normal range < 35 U/L), Alanine Aminotransferase (ALT or SGOT, normal range < 40 U/L) and Serum Alkaline Phosphatase (normal range 60-170 U/L) were measured pre-operatively and then post-operatively on Day 1 and Day 7. Serum bilirubin was measured by Identikit by using calorimetry. Aspartate Aminotransferase, Alanine Aminotransferase were measured by Raichem spectrophotometer capable of accurate measurement at 3440nm. Serum alkaline phosphatase was measured by Raichem spectrophotometer or calorimeter capable of accurately measuring absorbance changes at 405 nm.

During the procedure, the intra-abdominal pressure was continued at a range of 12-14 mmHg. The carbon-dioxide insufflation time was recorded in each operation. All patients were bladder catheterized before the surgery. Routine Preoperative antibiotics were administered in all patients.

Statistical Analysis:-

All data were expressed in mean \pm standard deviation. Paired t test was analyzed for finding the significance of the effect of laparoscopy on hepatic function. The P value less than 0.05 was considered to be statistically significant.

V. Observation And Analysis Of Results

The study group comprised of 60 patients undergoing various laparoscopic surgeries. Out of the 60 patients in study group 34 were males and 26 females.

Table 1 Age Wise Distribution Of Patients In Study Group

AGE (YEARS)	NO.OF PATIENTS
<20	8
21-30	16
31-40	20
41-50	11
>51	5
TOTAL	60

Out of the 60 patients in study group more number of patients was below age 50 years. Mean age is 35 Years

TABLE 2

SEX WISE DISTRIBUTION OF PATIENTS IN STUDY GROUP

SEX	NO OF PATIENTS
MALES	34
FEMALES	26
TOTAL	60

Out of 60 patients in the study group, majority of them are males (34) than females (26).

Table 3 Type Of Laparoscopic Surgery In Study Group

TYPE OF LAPAROSCOPIC SURGERY	NO. OF PATIENTS
Appendectomy	18
Cholecystectomy	28
Diagnostic	6
Hemioplasty	8
Total	60

Out of the 60 patients in the study population, 28 patients underwent cholecystectomy, 18 patients appendectomy, 8 patients had undergone hemioplasty and 6 diagnostic.

Serum bilirubin levels:

**Table 4: Paired Sample Statistics
Parameter: S.BILIRUBIN (mg/dl)**

Day	N	Mean	Standard Deviation	ANOVA F Statistic	PVALUE
Pre-op	60	0.712	0.151	115.66	.000
Day 1	60	1.097	0.297		HS
Day7	60	0.758	0.182		

Table 5: Pair wise comparison

I	J	Difference in mean	Std Error	P value	Inference
FACTOR Pre op	FACTOR Day 1	-0.385	0.031	0.0001	HS
Pre op	Day7	-0.047	0.018	0.0114	HS
Day 1	Day7	0.338	0.032	0.0001	HS

When correlated to pre-op levels, serum bilirubin values increased by 54% in post op day 1 (p =0.0001). This value returned to near pre-op levels by day 7. Highly significant.

Sgpt i ast levels:

Table 6: paired sample statistics parameter: sgpt (u/l)

Day	N	Mean	Standard Deviation	ANOVA F Statistics	PVALUE
Pre-op	60	18.9	4.55	122.19	.000
Day 1	60	31.83	9.8259		HS
Day7	60	21.6	5.484		

Table 7: Pair wise comparison

I	J	Difference in Mean	Std Error	P value	Inference
FACTOR Pre-op	FACTOR Day 1	-12.93	0.995	.000	HS
Pre-op	Day7	-2.70	0.451	.000	HS
Day 1	Day7	10.23	1.045	.000	HS

When correlated to pre-op values, SGPT levels increased on post-op day 1 (p= 0.0001). This value reverted back to near pre-op level by day 7 post-op. Statistically significant.

Sgot/alt levels:

Table 8: Paired Sample Statistics Parameter: SGOT (U/L)

Day	N	Mean	Standard Deviation	ANOVA F Statistic	PVALUE
Pre-Op	60	24.533	4.8344	143.79	.000
Day 1	60	40.8833	12.3248		HS
Day7	60	27.1	5.9765		

Table 9: Pairwise comparison

I	J	DIFFERENCE IN MEAN	Std Error	p VALUE	INFERENCE
FACTOR Pre-op	FACTOR Day 1	-16.35	1.215	.000	HS
Pre-op	Day7	-2.57	0.45	.000	HS
Day 1	Day7	13.78	1.244	.000	HS

When correlated to pre-op levels, SGOT/ALT values increased on post-op day 1 (P = .000). The value came down to near pre-op by day 7 post-op.

Alkaline phosphatase levels:

Table 10: Paired Sample Statistics Parameter: S.ALP (U/L)

Day	N	Mean	Standard	ANOVA F	P VALUE
Pre-op	60	107.65	Deviation 22.3355	Statistic 124.55	.000
Day 1	60	151.466	35.2615		HS
Day 7	60	111.183	22.0343		

Table 11: Pairwise comparisons

I FACTOR	J FACTOR	DIFFERENCE IN MEAN	Std Error	p value	INFERENCE
Pre-op	Day 1	-43.82	3.659	.000	HS
Pre-op	Day 7	-3.53	1.242	.0061	HS
Day 1	Day 7	40.28	3.689	.000	HS

When correlated to pre-op levels, Alkaline phosphatase values increased on post-op day 1 (p=.0001). They dropped to near pre-op levels by post-op day 7. All these are statistically significant.

table 12: Comparison of CO₂ insufflation time with level of serum enzymes

	Serum Bilirubin	SGPT	SGOT	ALP
Pearson coefficient @	0.4031	0.4427	0.4502	0.5181
P value	0.0014 HS	0.0003 HS	0.0003 HS	0.000
N	60	60	60	60

In this study, statistically significant correlation was found between the CO₂ insufflation time and with elevated liver enzyme levels.

VI. Discussion

The evolution in laparoscopic procedures has greatly been due to the scientific approach in endoscopic optics, video cameras and endoscopic instrumentation. The concept of surgery has changed from bigger incision - better surgeon to exactly the opposite in the field of laparoscopic surgery, better results with least damage in terms of life, tissue and cosmesis. Despite they are visibly 'minimally invasive' to the patient, the intraoperative condition of laparoscopic procedure produce important physiological alterations, a few of which are exclusive to these procedures. Several studies have concluded unexplained changes in post-operative liver function in patients undergoing laparoscopic surgery. CO₂ pneumoperitoneum efficacy be single most reasoning for this altered serum liver enzymes, as this is one of the main difference in laparoscopic surgeries had when compared with open surgeries. Our study performed to assess the presence of clinical significance of unexplained alterations in liver enzymes subsequent to laparoscopic surgeries.

Out of 60 patients in our study population, 34 were male patients and 26 were females. Most of the patient age range from 31-40 years. Mean age 35 years. Our study included patients who underwent various types of laparoscopic surgeries. IS patients underwent laparoscopic appendectomy. Laparoscopic cholecystectomy was done in 28 patients, mostly for cholelithiasis. In all patients, blood samples for serum bilirubin, serum AST, serum ALT and serum alkaline phosphatase were done preoperatively and post-operatively on day I and day 7. The mean value of S.bilirubin preoperatively was 0.712mg/dL. Postoperatively on day I and day 7 the levels were 1.097mg/dL and 0.758mg/dL respectively. Thus it was found that there was a significant rise (P=0.000) in the serum bilirubin levels post-op day I which came back to near pre-op values on day 7 post-operatively.

The mean value of serum AST pre-operatively was 18.9U/L. Post-operatively day I and day 7 the levels were 31.83 U/L and 21.6U/L respectively. There was a symbolic increase (P=0.000) in serum AST levels post-operative day I when compared to the pre-op values, which came down to near pre-op value within a week time. The mean value of serum ALT preoperatively was 24.53 U/L. Post-operatively day I and day 7 the levels were 40.88 U/L and 27.1 U/L respectively. Here again there was a symbolic rise (P =0.000) in the serum ALT levels in the immediate post-op period when correlated to the pre-op values. The levels came down to near pre-op values by post-op day 7.

The mean value of serum alkaline phosphatase pre-operatively was 107.65 U/L. Post-operatively on day 1 and day 7 the mean levels were 151.46 U/L and 111.18 U/L respectively. A significant rise (P=.000) was seen in the post-op day 1 level of serum Alkaline phosphatase values when compared

to the pre-op level. This came down almost pre-op values within a week in the postoperative period. Irrespective of the type of laparoscopic surgery they underwent, transient post-operative increases in serum bilirubin and liver enzyme levels were seen in the study population. The values returned to near pre-operative concentrations within 7 days after surgery.

Also, the post-op day I level doubled the pre-op values in 35% patients in case of serum bilirubin. 46% patients had doubling of serum AST levels and 42% had doubling of serum ALT levels. Serum Alkaline phosphatase levels doubled only in 30% of the patients. All the patients in our study were subjected to CO₂ pneumoperitoneum during the surgery and they showed symbolic alteration during post-operative serum liver enzyme level (P = 0.001 HS).

Previous studies:

Study 1: Min Tan¹, Feng Feng Xu, Peng JS et.al. This study compared the preoperative and postoperative changes in AST between open and laparoscopic cholecystectomy (LC) as well as open and laparoscopic colorectal cancer resection (LCR) in 286 patients. The levels of serum SGOT and SGPT raised symbolically within 24-48 hours following LC and LCR whereas both open surgeries had normal levels and this was attributed to CO₂ pneumoperitoneum.

Study 2: In 2005 a study by George Sakorafas², concluded that 24 hours after the procedure SGOT and SGPT raised statistically significant. Levels returned to normality occurred 7-10 days after the procedure. ALT (24, 87.1 +/- 24.2 U/L, P < .001) AST (24, 82.8 +/- 19.1, P < .001).

Study 3: In 2005, a study by Guven HE³ performed in 86 patients who underwent LC to investigate the alterations in serum enzymes levels. He concluded that the differences between elevations of enzymes levels were significant for LC.

Study 4: Tauro LF, Sheethal CM et.al⁴. Evaluation of effects of laparoscopic surgery on hepatic function in the year 2008, concluded that all types of laparoscopic procedures can cause transient elevation of hepatic enzymes and serum bilirubin for which CO₂ pneumoperitoneum is the causative factor. Halevy et.al⁵ first studied alterations in liver enzymes after laparoscopic surgeries. The possible mechanism included increased intra-abdominal pressure, squeeze pressure effect on the liver, pulling on the gall bladder, excessive use of diathermy". Vast investigation was done to evaluate the causes of this elevation and concluded that low pressure pneumoperitoneum was combined with lesser side effects on liver function.

The pneumoperitoneum pressure was above than the pressure in portal venous system which is used for laparoscopic procedure. This pressure disrupts portal circulation and decreases portal flow up to 50%, which causes abasement of the hepatic reticular endothelial system⁶. In our study also, the time of CO₂ pneumoperitoneum increased, there is elevation of intra-abdominal pressure resulting in increased levels of serum liver enzymes and is the causative factor. In a study, an increase of IAP 5mmHg from 10mmHg to 15 mm Hg resulted in a blood flow decrease by 39% to liver and by 60% to peritoneum. It was also found that, in spite of a constant intra-arterial pressure splanchnic blood flow decreased along with operative time. The elevation and depression of intra-abdominal pressure in a small period during the laparoscopic surgery efficacy also be innovative as the sudden alteration of intra-abdominal pressure would affect the portal blood flow. This re-creation of blood flow and organs would lead to ischemia and re-creation damage of organs and tissues, mainly the kupffer and endothelial cells of hepatic sinusoids". This can cause free-radical generation". The reperfusion relevant system after laparoscopy and the generation of free radicals are however smaller than open surgery. Another possible mechanism would be the local effect of extended need of diathermy to the liver surface in laparoscopic cholecystectomy and the increase of heat to liver parenchyma". This hypothesis is supported by some studies^{7,8}

However it is unexplained why there is hepatic enzyme elevation in surgeries away from the liver. After general anesthesia there was transient liver dysfunction in some patients. This reaction would be due to anesthesia induced changes in splanchnic blood flow and oxygen consumption". A probable structure for the disturbances of serum liver enzymes after laparoscopic surgery is the squeeze pressure effect on liver enzymes in to the blood". But this is not significant here since in our study similar changes are seen in other surgeries like laparoscopic appendectomies and laparoscopic hernia repair too, where liver was not handled at all.

Summary

- This study was carried out in 60 patients for evaluating the effects of laparoscopic surgery on hepatic enzymes.
- Out of the 60 patients in study group more number of patients was below age 50 years. Mean age is 35 years.
- In 60 patients, majority were males compared to females.
- Majority of patients in our study with diagnosis of cholelithiasis and appendicitis underwent for laparoscopic procedure.
- Serum bilirubin and the liver enzymes (serum AST, ALT and Alkaline phosphatase levels) were found to be significantly elevated post operatively in 24 hours duration. But it was found to be transient as the levels of these enzymes returned to near pre-op values by 7 days postoperatively.
- Doubling of pre-op values of AST was seen in 46%, ALT in 32% and Bilirubin in 35% patients.
- Patients with prolonged CO₂ insufflation time during surgery show more increase in the levels of serum liver enzymes.
- Other attributing factors to hepatocellular dysfunction could be a combination of CO₂ pneumoperitoneum, diathermy on liver and general anesthesia.
- No patients developed any complications or disability or adverse event. These signify that the changes in the liver enzymes are transient and recovered without any sequelae.

VII. Conclusion

In our study, we conclude that all types of laparoscopic procedures can cause transient elevation of hepatic enzymes for the hemodynamic changes occur that includes short-term reduction in hepatic blood flow, caused by CO₂ pneumoperitoneum. No apparent clinical changes were seen in the patients undergoing laparoscopic surgery due to these transient changes. Hence, as its benefits overcome its limitations, Laparoscopic surgery is soon emerging to be a gold standard for various surgical conditions. However, surgeons should take precautions before planning to perform in hepatic dysfunction patients. Laparoscopy performed under low pressure pneumoperitoneum might be feasible and liver functions should be monitored postoperatively.

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