Comparison of Alteration in Liver Function Tests in Patients undergoing High Pressure Laparoscopic Cholecystectomy Versus Low Pressure Cholecystectomy

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ABSTRACT

Introduction: Cholelithiasis is one of the most common surgical diseases. Laparoscopic cholecystectomy has been universally accepted as gold standard for treatment of cholelithiasis. Although many studies have shown post-operative changes in liver function tests after high pressure pneumoperitoneum during laparoscopic cholecystectomy, but very few studies have investigated the effects of low pressure pneumoperitoneum on hepatic functions.The present study was designed to compare post-operative changes in liver function tests among patients randomized to either low pressure laparoscopic cholecystectomy(LPLC) (i.e.8 mmHg) or high pressure laparoscopic cholecystectomy(HPLC) (i.e.14 mmHg).

Material and methods: After taking a well informed written consent,150 cases undergoing laparoscopic cholecystectomy were enrolled in the study and randomised preoperatively into two groups (LPLC and HPLC). Liver function tests (LFTs) including Total Bilirubin, Conjugated Bilirubin, Aspartate Transaminase (AST), Alkaline Phosphatase(ALP), Alanine Transaminase (ALT), Gamma-glutamyl Transferase (GGT), Total Serum Protein, Total Serum Albumin) were done on post-operative day (POD) 1 and day 7 and compared with preoperative LFTs in both groups.

Results: The study demonstrated significant increase in Conjugated bilirubin on POD 1($p < .001$), AST on POD 1 (p: .005), ALT on POD 1 ($p < .001$), ALP on POD 1 ($p < .001$) in HPLC as compared to LPLC patients. LFTs in both groups were found to be normal on POD 7 without significant difference between the two groups.

Conclusion: Low pressure laparoscopic cholecystectomy has less adverse effects on liver functions as compared to the high pressure laparoscopic cholecystectomy

Keywords: Laparoscopic cholecystectomy (LC), Low Pressure Laparoscopic Cholecystectomy (LPLC), High Pressure Laparoscopic Cholecystectomy(HPLC)

INTRODUCTION

Cholelithiasis is one of the most common surgical diseases encountered worldwide leading to morbidity and mortality in wide range of population.[1] The prevalence of cholelitiasis appears to be lower in Asia and Africa as compared to western countries.[2] Laparoscopic cholecystectomy(LC) has become the gold standard in treatment of benign gallbladder diseases such as cholelithiasis and cholecystitis.[1,3]

Laparoscopic cholecystectomy requires sufficient working space and adequate surgical exposure in the abdomen which is produced by creating pneumoperitoneum by insufflating carbon dioxide upto pressures of 12-14 mm Hg.[4,5]

High pressure pneumoperitoneum reduces portal venous flow, compromises intra-abdominal blood flow and causes physiologic alterations in liver function. Although these changes do not have any clinical relevance in healthy patients, the decrease in organ blood flow may result in deterioration in patients with underlying organ dysfunction.[6]

To minimize the adverse effects of pneumoperitoneum, a new technique of low pressure pneumoperitoneum and gasless pneumoperitoneum using a laparotensor for abdominal wall lifting has been developed. Gasless technique is similar to low pressure technique in terms of post-operative pain and recovery, but this technique provides an inferior level of exposure and the operation takes a longer time to perform.[1] It is well established in many previous studies that low pressure is superior to high pressure pneumoperitoneum in terms of lower incidence of postoperative pain, shoulder tip pain.[7]

The present study was designed to specifically compare the post-operative changes in liver function tests amongst patients randomized to either low pressure laparoscopic cholecystectomy (8 mmHg) or HPLC(14 mmHg).

MATERIAL AND METHODS

The present study was conducted over a period of 2 years and 150 cases who underwent laparoscopic cholecystectomy were enrolled in the study as per the below mentioned criteria.

Inclusion Criteria

- Age group: 18 to 70 years.
- Gender: Both male and female.
- Patients with uncomplicated gall stone disease.
- Normal pre-operative liver function tests.

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How to cite this article: Manav Goyal, Rajesh Bansiwal, Deeksha Mehta. Comparison of alteration in liver function tests in patients undergoing high pressure laparoscopic cholecystectomy versus low pressure cholecystectomy. International Journal of Contemporary Medical Research 2020;7(6):F1-F5.

DOI: http://dx.doi.org/10.21276/ijcmr.2020.7.6.3

- Patients categorised as American Society of Anesthesiologists (ASA) grade 1.

Exclusion Criteria

- Patients with common bile duct stone.
- Patients with associated jaundice.
- Patients with deranged preoperative liver function tests.
- Patients unfit for laparoscopic surgery.
- Patients with conversion to open cholecystectomy.
- Patients having previous intervention in the biliary tract

All enrolled patients who underwent laparoscopic cholecystectomy were randomised preoperatively into two groups by the sealed envelope method.

Group-1: Laparoscopic cholecystectomy with high pressure pneumoperitoneum (14 mm of Hg). (HPLC)

Group-2: Laparoscopic cholecystectomy with low pressure pneumoperitoneum (8 mm of Hg).(LPLC)

A standardized anaesthetic technique was used for all the patients and they were operated upon, by means of standard 4 port laparoscopic cholecystectomy. Pneumoperitoneum was created by insufflation with Carbon dioxide (CO2) and all patients were kept in the reverse Trendelenberg's position. The group of patients with high pressure pneumoperitoneum were operated at a pressure of 14 mm Hg and the group with low pressure pneumoperitoneum was operated at a pressure of 8 mm Hg.

Liver Function Tests were done on post-operative days 1 and 7 and compared with the patient's pre-operative LFTs. All these investigations were carried out at the clinical biochemistry laboratory of our tertiary care hospital.

STATISTICAL ANALYSIS

NPAR test and Mann Whitney tests are used. The statistical analysis was carried out using Stastical Package for Social Sciences (SPSS Inc., Chicago, IL, Version 18.0 for windows)

RESULTS

Out of all the patients admitted to the study institute for Laparoscopic cholecystectomy over a set period of 2 years, 150 patients gave their consent for enrollment into the present study and qualified as per our inclusion and exclusion criteria. Upon evaluation, the following results were obtained from our study

Liver Function Tests

Total Bilirubin: The preoperative total bilirubin levels expressed as (Mean ± SD) in the HPLC were (.535± .2536) and in the LPLC were (.617 ± .2760). Comparison of these two groups using Mann Whitney test yielded p value .066 (> .005) which was statistically not significant.

The total bilirubin on postoperative day 1 expressed as (Mean ± SD) in the HPLC and LPLC groups were (0.958 ± 0.6609) and (0.648 ± 0.2753) respectively. Comparison of these groups using Mann Whitney test yielded p value of 0.060 which was statistically not significant.

The total bilirubin on postoperative day 7 in the HPLC and LPLC was (0.614 ± 0.3103) and (0.509 ± 0.2231) respectively. Comparison yielded a p value of 0.069 which

	NPAR Tests					
Group		**HPLC**		**LPLC**		**p-value**
		Mean	**S.D.**	**Mean**	**S.D.**	
Pre Op	**T bil**	0.54	0.25	0.62	0.28	0.066
	C.Bil	0.21	0.14	0.25	0.12	0.108
	AST	26.77	9.63	27.38	8.11	0.358
	ALT	27.85	12.01	29.12	13.18	0.690
	ALP	78.55	23.83	78.31	17.36	0.340
	GGT	22.91	8.37	23.78	9.94	0.819
	T.Protein	7.58	0.57	7.64	0.71	0.449
	S.Albumin	4.26	0.46	4.30	0.47	0.702
Post Op1	**T bil**	0.96	0.66	0.65	0.28	0.060
	C.Bil	0.49	0.36	0.19	0.12	<.001**
	AST	49.07	22.52	39.01	15.62	.005**
	ALT	53.35	31.13	37.09	20.65	<.001**
	ALP	89.83	33.35	71.56	19.81	<.001**
	GGT	33.89	21.20	27.45	15.89	0.059
	T.Protein	6.86	0.61	6.76	0.72	0.395
	S.Albumin	4.02	0.48	4.03	0.42	0.777
Post Op7	**T bil**	0.61	0.31	0.51	0.22	0.069
	C.Bil	0.28	0.24	0.26	0.19	0.976
	AST	40.80	16.33	40.31	18.95	0.677
	ALT	45.75	25.58	38.79	17.93	0.182
	ALP	77.25	24.16	75.63	42.12	0.156
	GGT	30.88	20.66	28.55	25.62	0.190
	T.Protein	7.05	0.49	7.21	0.54	.012*
	S.Albumin	4.02	0.55	4.17	0.51	0.063

Table-1: Mean values of liver function tests in HPLC and LPLC groups. NPar test used.

was statistically not significant.

Conjugated Bilirubin: Preoperative Conjugated Bilirubin levels expressed as (Mean± SD) in HPLC and LPLC groups were (0.211± 0.1394) and (0.247± 0.1172) respectively and comparison of these groups yielded a p value of 0.108 which was statistically not signif niicant.

The conjugated bilirubin values on postoperative day 1 expressed as (Mean ± SD) in the HPLC and LPLC groups were (0.485± 0.3563) and (0.191± 0.1239). Comparison of these groups using Mann Whitney test yielded p value < 0.001 which was statistically significant.

The conjugated bilirubin values on postoperative day 7 expressed as (Mean ± SD) in the HPLC and LPLC groups were (0.277± 0.2407) and (0.263± 0.1923). Comparison of these groups using Mann Whitney test yielded p value 0.976 which was statistically not significant.

Aspartate Transaminases (AST): The preoperative AST levels expressed as (Mean ± SD) in the HPLC were (26.77± 9.628) and in the LPLC were (27.38± 8.111). Comparison of these two groups using Mann Whitney test yielded p value of 0.358 (> 0.005) which was statistically not significant.

The AST on postoperative day 1 expressed as (Mean ± SD) in the HPLC and LPLC groups were (49.07± 22.520) and (39.01± 15.618) respectively. Comparison of these groups using Mann Whitney test yielded p value 0.005 which was found to be statistically significant.

The AST levels on postoperative day 7 expressed as (Mean ± SD) in the HPLC and LPLC groups were (40.80± 16.331) and (40.31± 18.954) respectively. Comparison of these groups using Mann Whitney test yielded p value of 0.677 which was statistically not significant.

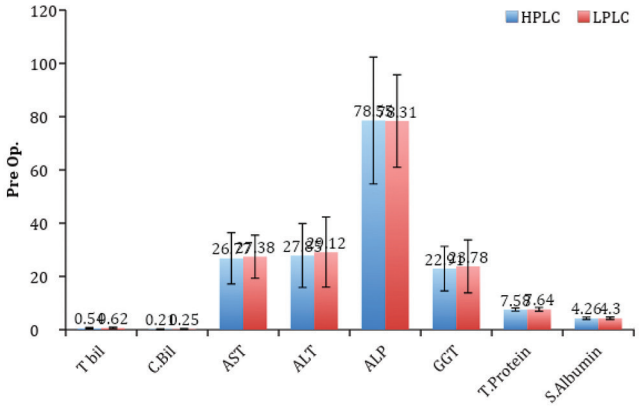
Alanine Transaminases (ALT): The preoperative ALT levels expressed as (Mean ± SD) in the HPLC were (27.85± 12.006) and in the LPLC were (29.12± 13.178). Comparison of these two groups using Mann Whitney test yielded p value 0.690 (> 0.005) which was statistically not significant.

The ALT on postoperative day 1 expressed as (Mean ± SD) in the HPLC and LPLC groups were (53.35± 31.132) and (37.09± 20.672) respectively. Comparison of these groups using Mann Whitney test yielded p value < 0.001 which was statistically significant.

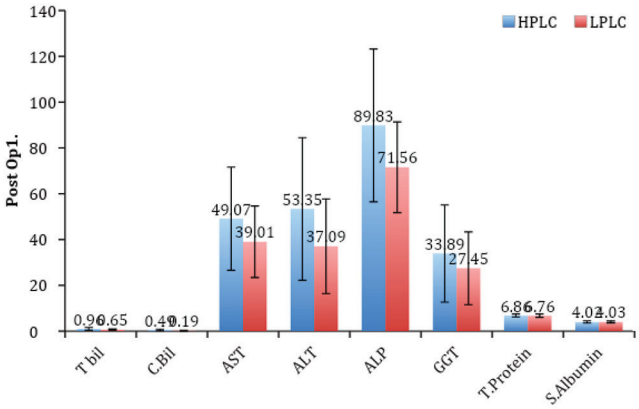
The ALT on postoperative day 7 expressed as (Mean ± SD) in the HPLC and LPLC groups were (45.75± 25.584) and (37.09± 20.652) respectively. Comparison of these groups using Mann Whitney test yielded p value 0.182 which was statistically not significant.

Alkaline Phosphatase (ALP): The preoperative ALP levels expressed as (Mean ± SD) in the HPLC were (78.55± 23.828) and in the LPLC were (78.31± 17.359). Comparison of these two groups using Mann Whitney test yielded p value 0.340(> 0.005) which was statistically not significant.

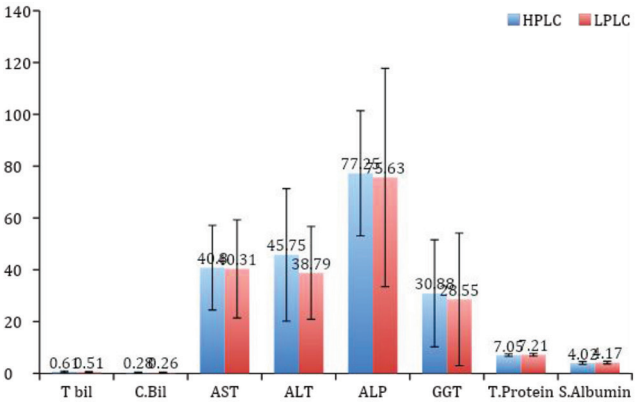
The ALP levels on postoperative day 1 expressed as (Mean ± SD) in the HPLC and LPLC groups were (89.83±33.350) and (71.56±19.806). Comparison of these groups using Mann Whitney test yield p value < .001 which was statistically



Graph-1: Preoperative LFTs in patients of HPLC and LPLC



Graph-2: Post Operative Day (POD) 1 LFTs in patient undergone HPLC and LPLC



Graph-3: POD 7 LFTs in patient undergone LPLC and HPLC.

significant.

The ALP levels on postoperative day 7 expressed as (Mean ± SD) in the HPLC and LPLC groups were (77.25±24.162) and (75.63± 42.117) respectively. Comparison of these groups using Mann Whitney test yielded p value 0.156 which was statistically not significant.

Gamma Glutamyl Transpeptidase (GGT): The preoperative GGT levels expressed as (Mean ± SD) in the HPLC were (22.91± 8.373) and in the LPLC were (23.78±9.944). Comparison of these two groups using Mann Whitney test yielded p value 0.819 (> 0.005) which was statistically not significant.

The GGT levels on postoperative day 1 expressed as (Mean

± SD) in the HPLC and LPLC groups were (33.89±21.199) and (27.45±15.889) respectively. Comparison of these groups using Mann Whitney test yielded p value 0.059 which was statistically not significant.

The GGT levels on postoperative day 7 expressed as (Mean ± SD) in the HPLC and LPLC groups were (30.88±20.655) and (28.55±25.617) respectively. Comparison of these groups using Mann Whitney test yielded p value 0.190 which was statistically not significant.

DISCUSSION

With the advent of minimal access surgery, there has been a constant effort to reduce postoperative complications, improve cosmesis, decrease hospital stay and enable an earlier return to routine activity after any surgical procedure. Laparoscopic cholecystectomy was first reported in Germany in 1985 and in France in 1987 and since then it has become the procedure of choice in the management of biliary tract disease.[8]

For laparoscopic surgeries, a pneumoperitoneum is required to create a workspace between the abdominal wall and intraabdominal organs. However, increased intraabdominal pressure may have negative implications on pulmonary, cardiovascular, and even intraabdominal organ functioning.[9] While creating pneumoperitoneum, the diaphragm gets elevated causing a decrease in the functional capacity of lungs, resulting in increased ventilation pressure and decreased compliance of lungs.[10] It also leads to an impaired venous return to the heart, thus decreasing stroke volume and cardiac output. There is an overall decrease in the renal, hepatoportal and splanchnic blood flow.[10] This decrease in organ blood flow may result in deterioration of function in patients with any underlying organ dysfunction. Venous return from lower limbs is also reduced which gets further aggravated by the reverse Trendelenburg position used during laparoscopic cholecystectomy.[10]

In order to minimize the adverse effect of pneumoperitoneum, there has been a modification to this conventional laparoscopic approach i.e. the use of low pressure pneumoperitoneum instead of normal or high pressure pneumoperitoneum. These modifications help to minimize the systemic derangements caused by high pressure laparoscopic cholecystectomy (HPLC).[11]

Low pressure laparoscopic cholecystectomy (LPLC) can be done by either low pressure or by gasless technique to decrease the deleterious effects of HPLC. LPLC has shown to cause fewer abnormalities in liver function tests (LFTs) compared with HPLC.[11]

Safety of LPLC has been established by many clinical studies in terms of feasibility of procedure and fewer hemodynamic effects on peritoneal insufflation. It has an additional benefit of lesser post-operative shoulder tip pain, and a shorter hospital stay post surgery.[7,12]

Abnormalities of LFTs during laparoscopic cholecystectomy (LC) can also be caused by cranial retraction of the gallbladder, cauterization of the liver bed, and manipulation of external bile ducts or effects of general anesthesia in addition to the known adverse effects of pneumoperitoneum.[15] These effects become more important in patients with chronic liver disease and hence it is advisable to try LPLC in them.[4,13]

On reviewing literature, results similar to this study were found by Neogi, Probal et al. They have reported that levels of mean serum AST, serum ALT, and LDH increased significantly (P<0.05) in immediate postoperative period and a further increase was observed after 24 hours (P<0.05) in the HPLC group only.[13]

Similarly, Saber et al, compared changes in LFTs in patients of LC to open cholecystectomy (OC) and observed that, within 48 hours of surgery, ALT doubles in 58.2% of LC patients versus 6.8% in OC patients. AST doubled in 38.2% in LC patients versus only 6.3% in OC group.[14] Correlation of intra-abdominal pressure during LC with blood flow to the liver has also been shown in many studies. Studies have also demonstrated pneumoperitoneum induced hepatic hypoperfusion, and intra-abdominal hypertension induced ischemic injury to hepatocytes. Significant reduction (p<0.001) in the portal venous flow during LC at high pressure(14 mm Hg) than low pressure (7 mm Hg) is also reported. Elevated intra-abdominal pressure itself probably plays a significant part in the elevation of liver enzymes. Since normal portal venous pressure is between 7 and 10 mmHg, increase in intra-abdominal pressure above this level reduces portal blood flow and may cause a certain degree of hepatic ischemia.[9]

Tan M et al, concluded in their study that levels of AST and ALT increase significantly during the first 48 hours post operatively in both LC and laparoscopic colorectal cancer resection as compared to OC and open colorectal cancer resection patients.[10] They attributed these changes to hepatocellular dysfunction either due to CO_2 pneumoperitoneum or use of diathermy on liver bed or injury to the liver bed or branch of hepatic artery or due to drugs used for general anaesthesia. Based on their findings, it may be presumed that carbon dioxide pneumoperitoneum might be one of the main reasons for the change of serum liver enzymes.

Marakis G et al, concluded in their study that statistically significant increase of serum total bilirubin, indirect bilirubin, AST, ALT, and decrease of ALP were noted post-operatively whereas GGT showed slight but not significant elevation. A 48.4% mean increase of total bilirubin value, duplication of indirect bilirubin in 16% of cases and upto 100% mean increase of both AST and ALT values were seen post operatively.[16] The present study however, showed statistically significant increase in all the parameters i.e. serum conjugated bilirubin, AST, ALT, ALP levels in post-operative period in patients of HPLC.

Giraudo et al and Gupta et al, concluded in their individual studies that duration and pressure level of pneumoperitoneum are the main factor of post-operative alteration of liver functions tests.[8,4] They found that the serologic changes in AST and ALT in the gasless group were significantly lower than in the LC group with pneumoperitoneum of 14 mm Hg, but there was statistically no significant difference between

gasless group and LC group with pneumoperitoneum of 10 mm Hg. Slow and progressive return to normal parameters was observed 48 to 72 hrs after surgery. In the present study also, LFTs returned to normal by POD 7 with no statistically significant difference in these values in both HPLC and LPLC group on POD 7.

Another study by Joshipura et al, comparing LPLC and HPLC, used an initial relatively higher pressure at the time of insertion of ports i.e. 12mm hg to avoid trocar related injuries.[17] In the present study during LPLC, pressure was kept low i.e 8mm throughout the procedure while in HPLC group, it was kept at 14mm Hg throughout the procedure. There was no incidence of any trocar related injury in any of the patients.

LFTs in both group were found to be normal on POD 7 without significant difference. Denise et al in their large systemic review also found that in none of the trials they studied, persistent elevation of liver enzymes or liver failure was ever observed.[9]

Further, we did not experience any complications at follow up in patients with elevated liver enzymes level and did not warrant further investigation.

CONCLUSION

Thus, we can safely conclude, that LPLC has less adverse effects on liver functions as compared to the HPLC. The major causative factor seems to be high pressure pneumoperitoneum which may compromise the hepatic blood flow causing alterations in the microcirculation. Despite the fact that high pressure pneumoperitoneum does not have any adverse effects in otherwise healthy patients, it can deteriorate the liver functions in the patients with compromised liver functions. So, low pressure pneumoperitoneum should surely be considered in patients with compromised liver function who are being considered for laparoscopic intervention. We further conclude that LC is feasible at low pressure pneumoperitoneum with desired safety and comfort levels in the hands of an experienced surgeon and does not pose any increase in intra-operative complications.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 28-04-2020; **Accepted:** 16-05-2020; **Published:** 14-06-2020