Liver Enzyme Alterations after Laparoscopic Cholecystectomy

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Abstract

Aims. We aimed to investigate the alterations in serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl-transferase (GGT), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) in patients who had undergone laparoscopic cholecystectomy (LC) and compare these changes with those occurring after open cholecystectomy (OC). **Methods**. Of 267 patients who underwent LC between January 2003 and December 2005, 86 patients without complications were eligible for study. Twenty-six patients who underwent OC during the same interval were also enrolled in the study as a control group. Blood samples were taken preoperatively and 24 hours after operation for biochemical tests. **Results**. Statistical analyses revealed significant increases in AST, ALT, GGT and LDH levels in the LC group postoperatively. Compared with the OC group, the differences between elevations of enzyme levels were also significant for LC group. **Conclusion**. We conclude that these enzyme elevations could mostly be attributed to the negative effects of the pneumoperitoneum on the hepatic blood flow. Although these changes do not seem to be clinically important, care should be taken before deciding to perform LC in patients with hepatic insufficiency.

Key words

Laparoscopic cholecystectomy – pneumoperitoneum - liver function tests

Introduction

For over 25 years, laparoscopic cholecystectomy (LC) has replaced open cholecystectomy (OC) in the management of benign gallbladder diseases and has become the gold standard for symptomatic cholelithiasis. As it gained worldwide popularity, it has become one of the most common operations performed in general surgical practice. Although LC offered many advantages over laparotomy, new concerns arose regarding the effects of a pneumoperitoneum on the cardiovascular and respiratory system (1).

One of the important hemodynamic changes is the transient reduction in hepatic blood flow caused by a pneumoperitoneum (2-5). The pressure of a created pneumoperitoneum and its duration was shown to influence the degree of hepatic ischemia by causing elevations in liver enzymes (3,6,7).

In this study we aimed to investigate the alterations in the serum levels of liver enzymes after LC performed under constant intraperitoneal pressure (14mmHg) and compare the differences in patients who had undergone OC.

Methods

Between January 2003 and December 2005, 267 patients with cholelithiasis underwent LC in Ankara Oncology Research and Training Hospital. Patients whose blood biochemistry for aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH) and gamma-glutamyltransferase (GGT) was obtained both preoperatively and 24 hours after the operation and all data charts were fully completed, were enrolled in the study. Patients with concomitant bile duct stones, high levels of enzymes before operation, in whom complications such as bile duct injury or bleeding from the liver bed were observed, were excluded from the study. Patients with co-morbidities such as diabetes mellitus and/ or positive serology for hepatitis B or C viruses were also excluded. Statistical analyses were done for 86 uncomplicated patients. Sixty-five (75.6%) of 86 patients were female and 21 (24.4%) were male. Mean age was 50.03 (range 20-76) years.

During the same time interval, 54 patients underwent OC in our hospital, mostly because of temporary technical

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failure of the laparoscopy unit. Twenty-six uncomplicated patients, whose enzyme levels both preoperatively and 24 hours after the operation were known and who were administered the same anaesthetic protocol as for patients in whom LC was performed were also enrolled in the study as the control group. Of them, 21 (80.7%) were female and five (19.3%) were male with a median age of 54.12 (range 26-71) years.

LC was performed under general anaesthesia with i.v. anaesthesia induction followed by continuous volatile anaesthesia under mechanical ventilation. Sodium thiopental, vecuronium bromide and fentanyl were used for induction and sevoflurane and nitrous oxide and oxygen mixture were used for maintenance of anesthesia. Although the same class of agents were used for all patients, the dosages of the anaesthetic agents were individually titrated.

Laparoscopic operations were performed using four trochars with the standard American technique. 14mmHg of pneumoperitoneum was created and maintained by intraperitoneal carbon dioxide (CO_2) insufflations with an automatic insufflator.

Mean operation time was 70.38±22.38 minutes for the LC group, calculated as the duration between intubation till extubation. Mean duration of the pneumoperitoneum was 60.9±18.86 minutes.

OC was performed by the same surgical team via right subcostal incision. Monopolar electrocautery was used to dissect gallbladders from their liver beds in both groups.

Intraoperative arterial blood pressure, oxygen saturation and pulse rates of the patients were closely monitored. No arterial blood pressure changes were noted in either group.

No other medication was administered to the patients prior or after the operation except for i.v. antibiotics (cefazolin or ampicillin/sulbactam) and diclophenac sodium for postoperative pain control. All patients were given saline and dextrose solutions for the first 24 hours.

Blood samples were taken from a superficial vein in the antecubital region of each patient before the operation as a part of routine preoperative preparation and 24 hours after the operation for comparison of the enzyme level alterations.

Patients who underwent LC were discharged on first postoperative day after blood samples were taken and all patients were advised to come back for follow up.

Biochemical analyses for enzymes were done using the same analyzer. The accepted normal values for enzymes were; for AST 8-41 IU/L, for ALT 8-54 IU/L, for GGT 7-50 IU/L, for LDH 98-192 IU/L and for ALP 38-126 IU/L.

Patients were seen between an interval of one week and one month after the operation on an outpatient basis. Whole blood count and biochemical analyses for serum glucose, AST, ALT, LDH, ALP, GGT and electrolytes were re-checked.

Enzyme levels were calculated as a mean ± SD for both groups and for both preoperative and postoperative values. The Kolmogorov-Smirnov test was used to appraise the presence of normal distribution. The Student *t* test was used to assess the difference between laparoscopic and open cholecystectomy groups and the paired samples test was used to evaluate the significance of daily enzyme changes in the laparoscopic group. Two-tailed p value smaller than 0.05 was considered to be statistically significant.

Results

No postoperative morbidity or mortality occurred in any of the patients studied. All patients were hemodynamically stable during the operations and none of them needed other medication than the planned anaesthetic protocol.

In the LC group, AST, ALT, GGT and LDH increased significantly 24 hours after the operation (Fig.1). In addition, postoperative means of AST and ALT were almost three-fold elevated with respect to the initial means and AST, ALT and LDH levels reached a mean value over the upper normal limit 24 hours after operation. No significant change was observed in ALP levels before and after the operation (Table I).

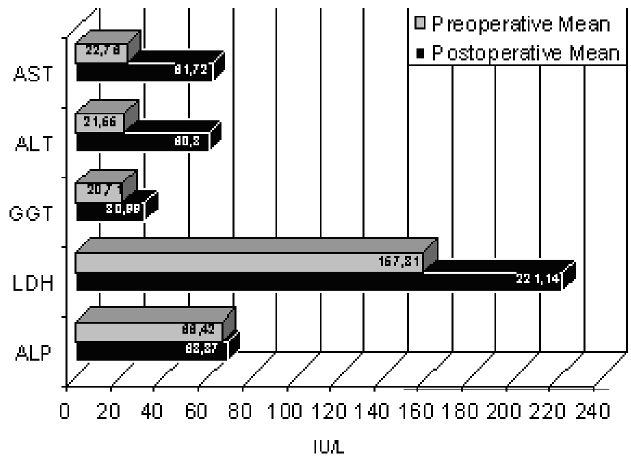

Fig.1 Mean values of enzymes before and 24 hours after LC.

Table I Mean values for postoperative enzyme changes after laparoscopic cholecystectomy*

Enzyme	Preoperative Mean ± SD	Postoperative Mean ± SD	p*	95% Confidence Interval
AST	22.76 ± 6.44	61.72 ± 28.13	0.0001	-44.6 – -33.2
ALT	21.55 ± 8.92	60.30 ± 32.17	0.0001	-45.4 – -32.0
GGT	20.71 ± 10.25	30.99 ± 20.63	0.0001	-14.5 – -6.0
LDH	157.81 ± 22.96	221.14 ± 55.92	0.0001	-73.8 – -52.8
ALP	66.42 ± 19.40	68.37 ± 18.28	0.131	-4.5 – 0.5

* Paired Samples Test

Mean AST, ALT, GGT, LDH and ALP levels before and 24 hours after the operation in the OC group occurred are shown in Table II. The increase of mean enzyme levels did not even reach two-fold. In addition, postoperative mean levels of studied enzymes remained within the normal limits.

When the enzyme alterations were compared with the OC group, increase in AST, ALT and LDH were significant for LC group (p=0.0001 for each enzyme). GGT increase was also significant on the edge (p=0.041). However, the change in ALP levels were insignificant (Table II).

Table II Mean values for postoperative enzyme changes after laparoscopic and open cholecystectomy*

Enzyme	Laparoscopic cholecystectomy group (n=86)		Open cholecystectomy group (n=26)		p value of difference**	95% confidence interval
	Preoperative	Postoperative (after 24h)	Preoperative (after 24h)	Postoperative		
AST	22.76 ± 6.44	61.72 ± 28.13	26.54 ± 6.38	40.69 ± 15.96	0.0001	13.9 – 35.7
ALT	21.55 ± 8.92	60.30 ± 32.17	23.42 ± 8.09	32.73 ± 11.60	0.0001	17.0 – 41.8
GGT	20.71 ± 10.25	30.99 ± 20.63	22.15 ± 8.89	24.27 ± 8.39	0.041	0.3 – 15.9
LDH	157.81 ± 22.96	221.14 ± 55.92	149.50 ± 19.44	172.35 ± 27.27	0.0001	20.9 – 59.9
ALP	66.42 ± 19.40	68.37 ± 18.28	76.04 ± 19.96	79.54 ± 19.81	0.524	-6.3 – 3.2

*Values are mean ± standard deviation
**Student *t* test

All elevated enzyme levels were found to return to their normal levels after the operation in the LC group according to the biochemical tests performed on their follow up visits. When questioned, none of the patients complained about anything warranting future evaluation.

Discussion

Once considered as incidental, elevation of liver enzymes such as AST and ALT after non-complicated laparoscopic cholecystectomy has become a well known finding. Although the clinical importance of these enzyme elevations has not been clarified, transient hepatic malfunction was suspected in previous studies (2,3,6,7).

Halevy et al suggested increased intraperitoneal pressure, squeezing the liver by cranial retraction of gallbladder during LC, cauterization of the liver bed for hemostasis, manipulation of external bile ducts and effects of general anaesthesia as possible causes of elevation of certain liver enzymes (8). However, liver retraction for better exposure, manipulation of biliary tract for detecting possible common duct stones, electrocauterization of the liver bed were routinely performed in OC as well. We compared the enzyme alterations in LC patients with those in the OC group who were given the same anesthetic agents and same antibiotics to equalize the possible effects of these drugs on hepatic function. The only suggested factor that might cause these alterations in our study was the elevated intraperitoneal pressure created during LC.

Knowing the fact that normal portal venous pressure is between 7-10mmHg and about half of the hepatic blood flow comes from the portal venous system, 14mmHg of pneumoperitoneum created with CO_2 is stated to be the major cause of transient hepatic ischemia during LC (2,6,9-11). Jakimowicz et al showed that 14mmHg of intraperitoneal pressure reduced the portal blood flow by 53% using the Doppler technique (10). Richter et al, in an experimental rat model, demonstrated that pneumoperitoneum under 12-15mmHg of pressure reduces normal hepatic blood flow and causes different degrees of ischemia in liver tissue (11). Hasukic et al, in their randomized study comparing the effects of low and high pressure pneumoperitoneum on liver functions, stated that AST and ALT elevations were significantly higher in patients operated under high pressure (14mmHg) pneumoperitoneum than those under low pressure (7mmHg) (6). In a study comparing hepatic enzyme alterations in LC, gasless LC and LC under low pressure (below 10mmHg) pneumo-peritoneum, Giraudo et al found significant enzyme level rises after LC that are not seen after gasless or low pressure LC, underlining the absolute effect of intraperitoneal pres-sure on hepatic perfusion by means of enzyme level changes (7). Morino et al investigated the duration of pneumo-peritoneum at constant pressure and found that when the duration of operation exceeds 60 minutes, elevations in AST and ALT levels become more significant (3).

Studies comparing the enzyme changes between LC and non-cholecystectomy laparoscopic operations were also conducted to examine effects of a pneumoperitoneum on these changes more accurately, excluding the other possible factors such as liver tissue damage and biliary tract manipulations that might interfere with results. The same significant enzyme level elevations were also observed in laparoscopic colectomy patients suggesting that a pneumoperitoneum plays the key role in transient hepatic ischemia causing enzyme elevations (3,9).

Preoperative and postoperative levels of AST, ALT, GGT, ALP, LDH, prothrombin time and bilirubin have been investigated in various studies to determine the physiological basis of hepatic malfunction (2-7,12). However significant elevations after LC compared with OC have been defined for only AST and ALT levels. Time controlled studies have shown that these enzyme elevations last for about 3 days postoperatively and the significance between LC and OC values fade away after 2 days (3,6,9).

We investigated the alterations in AST, ALT, GGT, LDH and ALP levels before and 24 hours after the operations in LC patients and compared this change with the OC patients who were anesthetized with the same protocol. AST, ALT, GGT and LDH levels were elevated significantly 24 hours after LC. In LC patients, postoperative mean values of AST, ALT and LDH exceeded the upper limits of normal ranges. However, postoperative enzyme levels were within the normal ranges in patients who underwent OC. When compared with the OC patients the rise in AST, ALT, GGT and LDH levels were still significant for the LC group. In addition to AST and ALT, we found that GGT and LDH were also influenced after LC. LDH elevations might be due to high intraperitoneal pressure making similar effects on intestines by reducing the mesenteric venous flow causing passive venous congestion. However, elevation in LDH levels needs further investigation using objective screening tests before assuming such a conclusion.

Nevertheless, in otherwise healthy patients, these hepatic enzyme alterations observed after LC have not been shown to be clinically important (2-4,9). We also did not experience any problems or complications at control visits to warrant further investigation in LC performed patients having enzyme elevations postoperatively. Although laparoscopic cholecystectomy is considered as a high risk procedure in patients with decompensated cirrhosis (Child-Pugh class C), it is not clear whether the increased morbidity in these patients is a result of a pneumoperitoneum (13).

To conclude, our present study demonstrated that AST, ALT, GGT and LDH elevations could occur after LC. Even three-fold increases could be noted in AST and ALT levels. When analyzed together with the data collected from previous studies, these changes may be attributed to the reduction of portal venous flow under high pressures of a pneumoperitoneum. There has been no proof to state that these enzyme changes are reflecting a true hepatic or other organ ischemia in otherwise healthy patients, but surgeons should be cautious before planning to perform LC in patients with known hepatic insufficiency. LC performed under a low pressure pneumoperitoneum or gasless LC using abdominal wall retractors might be feasible in these patient populations.

References

1. Odeberg-Wernerman S. Laparoscopic surgery - effects on circulatory and respiratory physiology: an overview. Eur J Surg Suppl 2000;585:4-11.
2. Saber AA, Laraja RD, Nalbandian HI, Pablos-Mendez A, Hanna K. Changes in liver function tests after laparoscopic cholecystectomy: not so rare, not always ominous. Am Surg 2000;66:699-702.
3. Morino M, Giraudo G, Festa V. Alterations in hepatic function during laparoscopic surgery. An experimental clinical study. Surg Endosc 1998;12:968-972.
4. Sakorafas G, Anagnostopoulos G, Stafyla V, et al. Elevation of serum liver enzymes after laparoscopic cholecystectomy. N Z Med J 2005;118:U1317.
5. Hasukic S, Kosuta D, Muminhodzic K. Comparison of postoperative hepatic function between laparoscopic and open cholecystectomy. Med Princ Pract 2005;14:147-150.
6. Hasukic S. Postoperative changes in liver function tests: randomized comparison of low and high-pressure laparoscopic cholecystectomy. Surg Endosc 2005;19:1451-1455.
7. Giraudo G, Brachet Contul R, Caccetta M, Morino M. Gasless laparoscopy could avoid alterations in hepatic function. Surg Endosc 2001;15:741-746.
8. Halevy A, Gold-Deutch R, Negri M, et al. Are elevated liver enzymes and bilirubin levels significant after laparoscopic cholecystectomy in the absence of bile duct injury? Ann Surg 1994;219:362-364.
9. Tan M, Xu FF, Peng JS, et al. Changes in the level of serum liver enzymes after laparoscopic surgery. World J Gastroenterol 2003;9:364-367.
10. Jakimowicz J, Stultiens G, Smulders F. Laparoscopic insufflation of the abdomen reduces portal venous flow. Surg Endosc 1998;12:129-132.
11. Neudecker J, Sauerland S, Neugebauer E, et al. The European Association for Endoscopic Surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery. Surg Endosc 2002;16:1121-1243.
12. Andrei VE, Schein M, Margolis M, Rucinski JC, Wise L. Liver enzymes are commonly elevated following laparoscopic cholecystectomy: is elevated intra-abdominal pressure the cause? Dig Surg 1998;15:256-259.
13. Curro G, Iapichino G, Melita G, Lorenzini C, Cucinotta E. Laparoscopic cholecystectomy in Child-Pugh class C cirrhotic patients. J Soc Laparoendosc Surg 2005;9:311-315.