Alterations In Liver Function Tests Following Laparoscopic Cholecystectomy

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Citation

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Abstract

Background: The pneumoperitoneum and the resulting high intraabdominal pressure may have several systemic effects including splanchnic ischemia. Disturbances of liver function tests following laparoscopic cholecystectomy have been previously reported although their etiology still remains uncertain. This prospective study was planned to explore further the incidence and significance of this alteration.

Materials and Methods: Over a two-year period, laparoscopic cholecystectomy was performed in 262 consecutive patients with symptomatic cholelithiasis. Total and indirect bilirubin (TB and IB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and ã-glutamyl-transpeptidase (□-GT) were tested preoperatively as well as 24 hours following surgery. Strict exclusion criteria were adopted in order to eliminate any known cause of possible liver function disturbances.

Results: Totally 198 patients fulfilled the criteria and were included in the study. A statistically significant increase of TB, IB, ASP, ALT and a significant decrease of ALP were noted postoperatively, whereas □-GT showed slight not significant elevation. A 48.4% mean increase of TB value, duplication of IB in 16% of cases, and an up to 100% mean increase of both ASP and ALT values were seen.

Conclusion: Transient alterations of hepatic enzymes are frequently observed after uneventful laparoscopic cholecystectomy, presumably attributed to the elevated intraabdominal pressure of the pneumoperitoneum. Further studies could enlighten the exact pathogenetic mechanism.

INTRODUCTION

The introduction of laparoscopic surgery has changed dramatically the management of gallstone disease establishing the laparoscopic cholecystectomy as the method of choice for treating uncomplicated cholelithiasis. Furthermore, the feasibility and safety of fluoroscopic intraoperative cholangiography and the laparoscopic common bile duct exploration have extended the role of laparoscopic techniques in the management of choledocholithiasis as well ([1,2]). However, the application of carbon dioxide pneumoperitoneum in high-risk patients may induce undesirable consequences in critically ill patients with cardiovascular, respiratory or renal insufficiency due to either hypercapnia or increased intraabdominal pressure ([3,4,5,6]). Some recent trials have shown that the high intraabdominal pressure during laparoscopic cholecystectomy leads to reduced portal venous flow and compromised intraabdominal blood flow ([7,8,9,10]). On the other hand, there are controversial studies showing that intraabdominal pressures ranging between 11 and 13 mm Hg are not associated with compromised splanchnic circulation ([11]). Furthermore, an elevation of serum liver enzymes after uncomplicated laparoscopic cholecystectomy has been reported ([12,13,14,15,16]) and that seems to be attributed to splanchnic ischemia ([17,18]). Due to all these observations, gasless laparoscopy has been proposed by some surgeons ([19]). This study was planned explore further the incidence and clinical significance of serum liver test changes after uneventful laparoscopic cholecystectomy.

MATERIALS AND METHODS

A prospective study was carried out at this Academic

Surgical Department over a 2-year period (2003 and 2004), after a long time experience on laparoscopic cholecystectomies (up to one thousand cases were performed previously). Written consent from the patients as well as ethical approval by the scientific committee of our hospital were provided.

During this period laparoscopic cholecystectomy was attempted in 262 consecutive patients suffering from symptomatic cholelithiasis. However, 64 patients were excluded from the study. The exclusion criteria were set up in order to eliminate any other known cause of possible liver function disturbances, and involved: conversion to open cholecystectomy, acute inflammation or any other complication of gallstone disease, recent ERCP and endoscopic sphincterotomy, choledocholithiasis, hematological disorders, co-existent liver disease, any intra-/postoperative complication, and incomplete data.

Laparoscopic cholecystectomy was performed under general anesthesia with the patient in a slight reverse Trendelenburg position with the 4-trocar technique, according to the ‘‘American'‘ variable. All patients received similar anaesthetic drugs that are known not to affect the hepatic enzymes. The pneumoperitoneum was created by insufflation of warm carbon dioxide via an inserted Verres needle. Intraabdominal pressure was maintained stable at 12 mm Hg in all cases. Monopolar diathermy was used for hemostasis and gallbladder detachment from its liver bed. Six liver function parameters were measured preoperatively and 24 hours following surgery: total and indirect bilirubin (TB–IB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and γ-glutamyl-transpeptidase (γ-GT).

Results were expressed as mean value ± standard deviation. The data were compared with analysis of variances (ANOVA) and paired t-test. Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL, USA). P values <0.05 were considered statistically significant.

RESULTS

Totally 198 patients fulfilled the criteria and were included in the study. There were 143 women (72%) and 55 men (28%), with mean age of 55 years (range 20 to 82). The mean duration of the operation was 55 minutes (range 40 to 70). The mean duration of the pneumoperitoneum was 45 minutes (range 35 to 65). All patients recovered well and had an uneventful postoperative course.

The preoperative total bilirubin (0.64 ± 0.24 mg/ml) was increased up to 48.4% postoperatively (0.95 ± 0.58 mg/ml). This was statistically significant (p=0.001). An increase was found in 81.8% of the patients.

Likewise, the preoperative indirect bilirubin (0.53 ± 0.21 mg/ml) was increased up to 49.1% postoperatively (0.79 ± 0.49 mg/ml). This was statistically significant (p=0.001). An increase was found in 77.5% of the patients, while this increase was up to 2-fold in 16% of cases.

The change in the values of aminotransferases was more remarkable. The preoperative AST (24.36 ± 24.01 U/ml) was increased up to 126% postoperatively (55.07 ± 40.39 U/ml). This was statistically significant (p=0.001). The preoperative ALT (31.88 ± 74.77 U/ml) was increased up to 93.28% postoperatively (61.62 ± 54.87 U/ml). This was also statistically significant (p=0.001).

The preoperative γ-GT (45.48 ± 86.58 U/ml) showed slight elevation postoperatively (46.72 ± 79.76 U/ml). This negligible increase was not statistically significant (p=0.783).

The preoperative alkaline phosphatase (70.16 ± 28.84 U/l) was decreased up to 9% postoperatively (63.69 ± 29.47 U/l). This was statistically significant (p=0.001).

All the above-mentioned values are summarized in Table 1.

Figure 1

Table 1: Changes in liver function tests after laparoscopic cholecystectomy

Value	TB	IB	AST	ALT	γ-GT	ALP
Preoperative mean	0.64	0.53	24.36	31.88	45.48	70.16
SD ±	0.24	0.21	24.01	74.77	86.58	28.84
Postoperative mean	0.95	0.79	55.07	61.62	46.72	63.29
SD ±	0.58	0.49	40.39	54.87	79.76	29.47
p	0.001	0.001	0.001	0.001	0.783	0.001

TB=total bilirubin, IB=indirect bilirubin, AST= aspartate aminotransferase ALT= alanine aminotransferase, γ-GT=γ-glutamyl-transpeptidase, ALP=alkaline phosphatase, SD=standard deviation, p<0.05 statistical significant

DISCUSSION

Disturbances in liver function tests in patients undergoing laparoscopic cholecystectomy have been already reported reaching up to 80% of cases in some studies ([15]). These rates are significantly higher than those seen after open cholecystectomy ([16,20]). Obviously, this fact leads to the conclusion that the laparoscopic procedure should be considered responsible for them.

To ensure accurate conclusions however, it is necessary to rule out all other possible reasons of hepatic enzymes abnormality such as those related to gallstone disease itself and its complications, or pre-existing chronic liver disease. Therefore, strict exclusion criteria have been set in this study in order to exclude patients with known liver function test abnormality, or any other condition, which could affect hepatic enzymes postoperatively, i.e. conversion to open cholecystectomy or other postoperative complications. Finally, 64 patients (24%) could not fulfill our criteria and were excluded from the study.

Additionally, the laparoscopic skills and previous experience are important factors for safe and reliable conclusions. Our teaching hospital has long time experience on biliary and laparoscopic surgery. The large number (up to one thousand) of laparoscopic cholecystectomies performed previously, ensure further reliability in the present prospective study.

Our results showed a statistically significant increase of total bilirubin from 0.64 mg/ml to 0.95 mg/ml and of indirect bilirubin from 0.53 mg/ml to 0.79 mg/ml. Transferases were significantly duplicated (AST: from 24.36 U/ml to 50.07 U/ml; ALT from 31.88 to 61.62 U/ml). A significant decrease of alkaline posphatase from 70.16 U/l to 63.29 U/l was noted. The increase of γ-GT was not statistically significant (p=0.783). These results are in accordance with most previously published literature in the subject (12,13,15,16,20).

The use of diathermy which may induce thermal damage to hepatic parenchyma, or the use of anaesthetic medications some of which might influence visceral blood flow have been addressed for these enzymatic changes. However, their effect is debatable, since both factors are used in the same manner in laparoscopic as well as in open cholecystectomy (16).

Thus, it is reasonable to speculate that reported differences in liver function tests could be caused by carbon dioxide pneumoperitoneum. The occurring pathophysiological changes may be due to both carbon dioxide insufflation and increased intraabdominal pressure. Carbon dioxide, has high solubility in the blood and may cause hypercapnia with respiratory acidosis resulting in increased heart rate, arterial pressure and systemic peripheral resistances (6). The increased intraabdominal pressure on the other hand, affects the cardiovascular system by compressing inferior vena cava and pericardium, and thus decreasing directly the venous blood return to the right atrium and the cardiac output (21). The usual level of intraabdominal pressure (12-14 mm Hg) is higher than that of portal vein system (7-10 mm Hg); consequently, it may lead to reduction of portal blood flow and abnormalities in liver perfusion. Experimental data showed that hepatic perfusion decreases when intraabdominal pressure increases over 6 mm Hg (4); portal blood flow decreases as much as 53% when intraabdominal pressure reaches 14 mm Hg (8); pressure of 12 mm Hg has been proved to decrease significantly the hepatic microcirculation (7). Finally, potential causes of splanchnic ischemia during pneumoperitoneum are direct vessel compression, release of vasoactive substances such as angiotensin, and hypercapnia. The deflation of the pneumoperitoneum restores the reduced splanchnic blood flow; thus, laparoscopy is considered a reperfusion phenomenon model and the disturbances of liver function tests could be attributed to free radical-induced lipid peroxidation seen at the end of the procedure (22). Furthermore, carbon dioxide pneumoperitoneum may cause alterations in acid-base balance as well (23,24).

The increase in liver function tests after uncomplicated laparoscopic cholecystectomy appears to be a phenomenon without clinical significance since all values generally return to normal within 48-72 hours (12,13,15,16,20). Persisting high values may be seen however, and if no findings of choledocholithiasis exist, this has been attributed to late common bile duct stricture due to thermal damage (25).

In conclusion, transient mild abnormality in liver function tests is a usual finding after laparoscopic cholecystectomy without clinical significance. It is mainly attributed to the high intraabdominal pressure of carbon dioxide pneumoperitoneum, which may compromise the hepatic blood flow causing alterations in the microcirculation. Despite the fact that it has not any consequences in otherwise healthy patients, it could deteriorate the liver function in patients with severe liver disease who undergo long lasting pneumoperitoneum. In such cases the low-pressure pneumoperitoneum or gasless laparoscopy by abdominal wall lifting could be reasonable alternatives.

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References

1. Griniatsos J, Karvounis E, Isla AM. Limitations of fluoroscopic intraoperative cholangiography in cases suggestive of choledocholithiasis. J Laparoendosc Adv Surg Tech A 2005; 15: 312-317.
2. Lein HH, Huang CC, Huang CS, Shi MY, Chen DF, Wang NY, Tai FC. Laparoscopic common bile duct exploration with T-tube choledochotomy for the management of choledocholithiasis. J Laparoendosc Adv Surg Tech A 2005; 15: 298-302.
3. Koivusalo AM, Lindgren L. Effects of carbon dioxide pneumoperitoneum for laparoscopic cholecystectomy. Acta Anaesthesiol Scand 2000; 44: 834-841.
4. Hashikura Y, Kawasaki S, Munakata Y, Hashimoto S, Hayashi K, Makuuchi M. Effects of peritoneal insufflation on hepatic and renal blood flow. Surg Endosc 1994; 8: 759-761.
5. Elefteriadis E, Kotzampassi K, Papanotas K, Heliadis N, Sarris K. Gut ischemia, oxidative stress, and bacterial translocation in elevated abdominal pressure in rats. World J Surg 1996; 20: 11-16.
6. Gutt CN, Oniu T, Schemmer P, Kashfi A, Kraus T, Büchler MW. Circulatory and respiratory complications of carbon dioxide insufflation. Dig Surg 2004; 21: 95-105.
7. Elefteriadis E, Kotzampassi K, Botsios D, Tzartinoglou E, Farmakis H, Dadoukis J. Splanchnic ischemia during laparoscopic cholecystectomy. Surg Endosc 1996; 10: 324-326.
8. Jakimowicz J, Stultiëns G, Smulders F. Laparoscopic insufflation of the abdomen reduces portal venous flow. Surg Endosc 1998; 12: 129-132.
9. Schäfer M, Krähenbühl L. Effect of laparoscopy on intra-abdominal blood flow. Surgery 2001; 129: 385-389.
10. Schäfer M, Sägesser H, Reichen J, Krähenbühl L. Alterations in hemodynamics and hepatic and splanchnic circulation during laparoscopy in rats. Surg Endosc 2001; 15: 1197-1201.
11. Odeberg S, Ljungqvist O, Sollevi A. Pneumoperitoneum for laparoscopic cholecystectomy is not associated with compromised splanchnic circulation. Eur J Surg 1998; 164: 843-848.
12. Sakorafas G, Anagnostopoulos G, Stafyla V, Koletis T, Kotsifopoulos N, Tsiakos S, Kassaras G. Elevation of serum liver enzymes after laparoscopic cholecystectomy. N Z Med J 2005; 118: U 1317.
13. Al-Jaberi TM, Tolba MF, Dwaba M, Hafiz M. Liver function disturbances following laparoscopic cholecystectomy: incidence and significance. J Laparoendosc Adv Surg Tech A 2002; 12: 407-410.
14. Nesek-Adam V, Rasic Z, Kos J, Vnuk D. Aminotransferases after experimental pneumoperitoneum in dogs. Acta Anaesthesiol Scand 2004; 48: 862-866.
15. Halevy A, Gold-Deutch R, Negri M, Lin G, Shlamkovich N, Evans S, Cotariu D, Scapa E, Bahar M, Sackier JM. Are elevated liver enzymes and bilirubin levels significant after laparoscopic cholecystectomy in the absence of bile duct injury? Ann Surg 1994: 219: 362-364.
16. 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.
17. 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.
18. Morino M, Giraudo G, Festa V. Alterations in hepatic function during laparoscopic surgery. An experimental clinical study. Surg Endosc 1998; 12: 968-972.
19. Giraudo G, Brachet Contul R, Caccetta M, Morino M. Gasless laparoscopy could avoid alterations in hepatic function. Surg Endosc 2001; 15: 741-746.
20. Pavlidis T, Alexiadis D, Papanicolaou C, Kouvelas D. Effect of laparoscopic cholecystectomy on liver function tests. Comparative study. Arch Gastroenterohepatol 1995; 14: 26-27.
21. Campos LI, Mansfield D, Smith A, Kohli H, Sun D, Espinosa MH, Dy V. Carbon dioxide volume and intra-abdominal pressure determination before the creation of a pneumoperitoneum. Surg Laparosc Endosc 1995; 5: 100-104.
22. Glantzounis GK, Tselepis AD, Tambaki AP, Trikalinos TA, Manataki AD, Galaris DA, Tsimoyiannis EC, Kappas AM. Laparoscopic surgery-induced changes in oxidative stress markers in human plasma. Surg Endosc 2001; 15: 1315-1319.
23. Taura P, Lopez A, Lacy AM, Anglada T, Beltran J, Fernandez-Cruz L, Targarona E, Garcia-Valdecasas JC, Marin JL. Prolonged pneumoperitoneum at 15 mm Hg causes lactic acidosis. Surg Endosc 1998; 12: 198-201.
24. Sefr R, Puszkailer K, Jagos F. Randomized trial of different intraabdominal pressures and acid-balance alterations during laparoscopic cholecystectomy. Surg Endosc 2003; 17: 947-950.
25. Hochstadetr H, Bekavac-Beslin M, Doko M, Kopljar M, Cupic H, Glavan E, Mijic A, Zovak M, Salic D. Functional liver damage during laparoscopic cholecystectomy as the sign of the late common bile duct stricture development. Hepatogastroenterology 2003; 50: 676-679.

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