

Changes in the level of serum liver enzymes after laparoscopic surgery

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Abstract

AIM: The purpose of this study was to investigate the effect of laparoscopic surgery on liver function in humans and the possible mechanisms behind such effect.

METHODS: Blood samples from 286 patients who underwent laparoscopic cholecystectomy (LC) and 40 patients who underwent open cholecystectomy (OC) were tested for liver function by measuring the level of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) before and after the operations. The same tests were also applied to 18 laparoscopic colorectal cancer resection (LCR) patients and 23 open colorectal cancer resection (OCR) patients to determine whether CO₂ pneumoperitoneum could alter the serum liver enzymes.

RESULTS: The level of serum ALT and AST increased significantly during the first 48 hours post operations in both LC and LCR patients. However, no significant change of the serum liver enzymes was detected in both OC and OCR patients. As a result, there was statistically significant difference in change of both ALT and AST levels between LC and OC patients and LCR and OCR patients, respectively. By the 7th day post operation, the level of both enzymes returned to normal values in LC, OC and OCR patients except LCR patients whose enzymes remained at a higher level.

CONCLUSION: Transient elevation of hepatic transaminases occurred after laparoscopic surgery. The major causative factor seemed to be the CO₂ pneumoperitoneum. In most of the laparoscopic surgery patients, the transient elevation of serum liver enzymes showed no apparent clinical implications. However, if preoperative liver function was very poor, laparoscopic surgery may not be the best choice for the treatment of patients with certain abdominal diseases.

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INTRODUCTION

The introduction of laparoscopic surgery has profoundly

changed the way for the management of patients with both gallbladder disease and common bile duct stone, and the laparoscopic cholecystectomy (LC) has become the "gold standard" in the treatment of benign gallbladder diseases such as gallbladder stone and cholecystitis^[1-4]. However, little attention has been paid to effects on liver function by laparoscopic surgery. We noticed in clinical practice that, following laparoscopic surgery, the level of certain serum liver enzymes rose markedly in most patients who had shown normal preoperative liver function tests. This clinical observation raises several questions. Are these changes of any clinical significance? What is the mechanism responsible for these changes? Do other laparoscopic operations cause the same changes? To address these questions, we conducted a prospective study to compare changes in serum liver enzymes before and after operations between LC and open cholecystectomy (OC) and laparoscopic colorectal cancer resection (LCR) with open colorectal resection (OCR).

MATERIALS AND METHODS

A total of 286 patients (102 men and 184 women with mean age of 48.6 years and range of 21-89 years) underwent elective LC from February 2001 to April 2002. During the same period, 40 patients (18 men and 22 women with mean age of 51.2 years and range of 29-86 years) with symptomatic cholelithiasis, gallbladder stone or gallbladder polypus underwent OC and were included for the study. For comparison, 18 LCR (10 men and 8 women with mean age of 62.8 years and range of 43-85 years) and 23 OCR patients (16 men and 7 women with mean age of 61.6 years and range of 39-76 years) were also selected for the study. The LCR cases included 2 descending colon cancers, 7 sigmoid colon cancers and 9 rectal cancers. The OCR patients included 4 ascending colon cancers, 6 transverse colon cancers, 1 descending colon cancers, 6 sigmoid colon cancers and 6 rectal cancers.

All patients selected for the study had normal values of serum liver enzymes prior to the operations. The following patients were excluded from the study: those who had undergone endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (EST) within one week before laparoscopic operation. The cases who developed complications such as bile duct injury, obstruction, infection, leakage and high fever by any reason were also excluded. All colorectal cancer patients included for the study had no evidence of cancer metastasis to liver by B-ultrasonic and CT scan.

Serum liver enzymes alanine amino transferase (ALT) and aspartate aminotransferase (AST) were measured before operations and 1, 2 and 7 days post operation to assess liver function except for LC patients. The LC patients were randomly divided into two groups before the operation, with group A of 143 LC patients tested for the liver function postoperatively on days 1 and 7 and group B of 143 patients tested for the liver function postoperatively on days 2 and 7. All LC and LCR patients received operation by one surgeon. The OC operations were performed by 3 surgeons from the same Division. The OCR operations were performed by the same team of surgical

staff. All patients received general anesthesia except OC patients who received local anesthesia. The operations on LC and LCR patients were performed with four-cannula technique. During laparoscopic surgery, the intra-abdominal pressure (IAP) was maintained at a range of 12-14 mmHg. Monopolar diathermy was used in LC and OC patients to dissect the gallbladder from the liver beds. Ultrasonic scissors and bipolar diathermy were used in LCR to dissect the mesenteric vessels.

All data were expressed as the mean \pm standard deviation. Student *t* test was used to analyse the difference in level of serum liver enzymes before and after LC, OC, LCR and OCR. The *P* value less than 0.05 was considered to be statistically significant.

RESULTS

Postoperative liver failure or mortality did not occur in any of the patients studied, and all the patients were hemodynamically stable during the perioperative period.

The level of serum ALT and AST increased significantly within 24-48 hours following operations in LC and LCR patients compared with those in OC and OCR patients (Table 1). In details, the mean pre- and post operation serum levels of ALT were respectively 23.3 U·L⁻¹ and 38.8 U·L⁻¹ in LC patients of group A (*P*<0.05), 21.5 U·L⁻¹ and 44.2 U·L⁻¹ in LC patients of group B (*P*<0.01), and 22.6 U·L⁻¹ and 45.7 U·L⁻¹ in LCR patients (*P*<0.01). In contrast, ALT only increased from a preoperative mean of 21.8 U·L⁻¹ to 28.2 U·L⁻¹ in OC patients (*P*>0.05) and from 22.2 U·L⁻¹ to 30.6 U·L⁻¹ in OCR patients (*P*>0.05). The degree of change in ALT following the operations was greater in LC patients than that in OC patients (*P*<0.05, D1), *P*<0.01, D2), so was the change between LCR and OCR patients (*P* <0.05, D1 and D7), *P*<0.01, D2).

Similar changes were observed in the mean value of serum AST. The AST increased significantly after operation in LC patients (from 28.4 to 41.5 U·L⁻¹, *P*<0.05, D1) and 27.1 up to 48.7 U·L⁻¹, *P*<0.01, D2) and LCR patients (from 27.3 to 40.7 U·L⁻¹, *P*<0.05, D1) and to 45.5 U·L⁻¹, *P*<0.01, D2). In OC and OCR patients, however, the AST showed only a small degree of increase (Table 1). The change of AST due to the operations was also greater in LC patients than that in OC patients (*P*<0.05, D1), *P*<0.01, D2), and so was the change between LCR and OCR (*P*<0.05, D1 and D7), *P*<0.01, D2).

Seven days following the operations, both enzymes returned to normal value in LC, OC and OCR patients except in LCR patients whose enzymes, although lower than day 2 level, remained higher (ALT 37.2 U·L⁻¹, D7, *P*<0.05) and AST 38.6 U·L⁻¹ (D7, *P*<0.05) (Table 1).

Table 1 Preoperative and postoperative level of serum liver enzymes

	<i>n</i>	Preoperation	D1	D2	D7
ALT					
LC(a)	143	23.3±11.6	38.8±15.2 ^{ac}		25.1±14.3
LC(b)	143	21.5±12.9		44.2±14.5 ^{bc}	26.3±11.7
OC	40	21.8±16.7	28.2±13.7	27.3±18.3	24.2±11.1
LCR	18	22.6±10.9	39.3±13.4 ^{ac}	45.7±17.2 ^{bd}	37.2±18.1 ^{ac}
OCR	23	22.2±17.3	29.6±11.8	30.6±15.5	27.1±11.2
AST					
LC(a)	143	28.4±20.2	41.5±24.7 ^{ac}		29.1±18.7
LC(b)	143	27.1±18.8		48.7±20.8 ^{bd}	29.6±15.4
OC	40	25.2±17.6	31.8±22.1	32.6±21.1	27.9±16.6
LCR	18	27.3±16.1	40.7±27.3 ^{ac}	45.5±22.2 ^{bc}	38.6±20.3 ^{ac}
OCR	23	26.8±19.5	30.2±25.1	32.9±24.6	28.5±18.6

n=cases, Preo-=Preoperative, ^a*P*<0.05, ^b*P*<0.01 vs Preo-; ^c*P*<0.05, ^d*P*<0.01 vs OC; ^e*P*<0.05, ^f*P*<0.01 vs OCR.

In this study, we also tested other liver function indice such as total bilirubin (TBIL), direct bilirubin (DBIL), alkaline phosphatase (ALP), lactic dehydrogenase (LDH), total protein (TP) and gamma glutamyl transferase (GGT) (data not shown). In general, TBIL and DBIL showed a slight increase within 24-48 hours following operation in some patients, but the changes were within normal range, and these values returned to preoperative levels. Other liver function test indice did not show significant alteration.

DISCUSSION

Changes in serum levels of liver enzymes in LC rather than OC patients had been reported before^[5-9]. In order to understand whether or not CO₂ pneumoperitoneum could cause these changes, we tested the liver function of patients who received LCR or OCR. Our present studies suggest that these transient postoperative hypertransaminases in LC and LCR patients might be attributed to the following possible factors.

The first factor of consideration was CO₂ pneumoperitoneum. Both LC and LCR patients were subject to CO₂ pneumoperitoneum during the operations and they showed significant changes in serum liver enzymes after operation. In contrast, both OC and OCR patients were under the operation conditions similar to those of LC and LCR patients except that they were not subject to CO₂ pneumoperitoneum and they showed no apparent change in the level of serum liver enzymes. This finding is consistent with other studies that showed similar changes in liver function clearance test after pneumoperitoneum^[10-16]. Because an intra-abdominal pressure (IAP) of 12-14 mmHg used in the present laparoscopic surgery was higher than the normal portal blood pressure of 7-10 mmHg, this operation might, therefore, reduce portal blood flow and cause alteration in liver function^[17-20]. On the other hand, the elevation and depression of IAP in a short time during laparoscopic operation might be causative as well. During laparoscopic procedure, the sudden alteration of IAP could cause the undulation of portal blood flow. This undulation and "re-irrigation" of organs blood flow may give rise to "ischemia and re-irrigation" damage of tissues and organs, especially the Kupffer and the endothelial cells of the hepatic sinusoids^[21]. The mesothelial cells were bulging up and the intercellular clefts thereby increased in size, and the underlying basal lamina became visible^[22]. During LC, an IAP of 8 mmHg was found to decrease the hepatic microcirculation significantly^[23,24]. Therefore, the elevation of IAP caused by CO₂ pneumoperitoneum may be the main reason behind these changes.

A second possible mechanism for alterations of serum liver enzymes after LC is the "squeeze" pressure effect on the liver. The traction of the gallbladder may free these enzymes into the blood stream. But in our study, 40 OC were performed with a small wound within 6 cm. There should be the same or more "squeeze" pressure effect on the liver in these patients, yet the change of serum liver enzymes was different between LC and OC patients. In addition, the same changes occurred in LCR patients. This mechanism remains to be determined in animal models.

The third possibility may be the local effect of prolonged use of diathermy to the liver surface and spread of heat to liver parenchyma. This hypothesis is supported by some other studies^[25-31]. However, similar type and intensity of diathermy were used in both OC and LC patients and it remains to be explained why the serum liver enzyme level increased in LCR patients whose focus was far from liver. While the thermal damage to liver by diathermy is generally recognized, there are no references available in the literature that compared the postoperative enzyme levels between cholecystectomies performed with and without the use of diathermy in humans.

In addition, transient liver dysfunction occurs in patients after some general anesthesia^[32-41]. This complication is associated with anesthesia-induced changes in splanchnic blood flow and oxygen consumption. However, the anesthesia-induced hepatic hypoperfusion may not be the cause of elevation of transaminases after LC and LCR as the same anesthesia protocols was used in our 23 OCR patients who did not show marked postoperative change in serum liver enzymes. It seems that the anesthesia could not acted exclusively to cause these changes. Other studies have also shown similar liver function test results in both LC and OC cases with general anesthesia^[42].

Another possible mechanism of alterations of serum liver enzymes that had been considered was the inadvertent clipping of the right branch of the hepatic artery or any other aberrant arterial branch supplying blood to the liver. When Calot's triangle has dense or cicatricial adhesion, the related arterial branch could be easily injured. This, however, should be followed by a massive increase in liver enzymes and usually has clinical implications^[43-45]. Nevertheless, the LCR hardly gave rise to any chance to injure the right branch of the hepatic artery, yet the LCR patients showed marked elevation of ALT and AST postoperatively. Therefore, arterial branch injury could be ruled out in almost LC patients.

In summary, our present studies demonstrated that transient elevation of hepatic transaminases could occur after laparoscopic procedures. These changes might be attributed to hepatocellular dysfunction secondary to one or combination of CO₂ pneumoperitoneum, diathermy, extruding liver, branch of the hepatic artery injured and general anesthesia. Based on our findings, the CO₂ pneumoperitoneum might be one of the main reasons for the change of serum liver enzymes. However, the transient elevation of hepatic transaminases showed no apparent clinical implication in most patients who received laparoscopic surgery according to follow-up observations and feedback from these patients. Nevertheless, these results indicate that, if the patient's preoperative liver function was very poor, laparoscopic surgery might not be the optimal choice for treating certain abdominal diseases^[46].

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