Changes of liver enzymes and serum bilirubin after laparoscopic cholecystectomy

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ABSTRACT

Background: Laparoscopic cholecystectomy (LC) has become the standard treatment of benign gallbladder diseases. However, it has been noticed that following LC, the serum level of certain liver enzyme rises markedly in patients who had preoperatively normal liver enzyme values.

Objectives: The study is aimed to evaluate the effect of pneumoperitoneum in LC on liver enzymes and serum bilirubin in comparison with open cholecystectomy (OC).

Patients and methods: A prospective case control study involved 74 patients treated by LC, and, 30 patients treated by OC as a control group, during the period from October 2010 to October 2011 at the Department of Surgery, Surgical Unit Number One, Al-Jumhori Teaching Hospital, Mosul, Iraq. Blood samples were taken 24 hours preoperatively and 24 hours after operation for biochemical tests.

Results: There were significant increases in serum bilirubin, Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and Lactate dehydrogenase (LDH) levels in LC group postoperatively when compared with the OC group, while there were no significant changes in serum alkaline phosphatase (ALP).

Conclusion: It has been concluded that, serum bilirubin and liver enzymes elevation could be attributed to the negative effects of the pneumoperitoneum on the hepatic blood flow. Although these changes seem to be of no clinical importance, care should be taken before deciding to perform LC in patients with hepatic insufficiency.

Keywords: Laparoscopic cholecystectomy, pneumoperitoneum, liver enzymes.

تغيرات إنزيمات الكبد بعد عمليات رفع المرارة بالناظور

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الخلاصة

الخلفية والأهداف: لوحظ إرتفاع بعض إنزيمات الكبد في المصل بعد عملية إستئصال المرارة بالمنظار لبعض المرضى الذين كانت إنزيمات الكبد لديهم طبيعية قبل العملية. الهدف هو دراسة التغيرات الحاصلة في مصل الدم لهذه الإنزيمات للمرضى الذين أجريت لهم عملية إستئصال المرارة بالمنظار ومقارنة هذه التغييرات مع تلك التي تحدث بعد إستئصال المرارة عن طريق فتح البطن.

المرضى وطريقة العمل: أجريت هذه الدراسة المستقبلية في الردهة الجراحية الأولى في مستشفى الجمهوري التعليمي- الموصل خلال الفترة من تشرين الأول سنة ٢٠١٠ الى تشرين الأول سنة ٢٠١١. وشملت ٧٤ مريضا ممن أجريت لهم عملية إستئصال المرارة بالناظور، وكذلك ٣٠ مريضا خضعوا لعملية إستئصال المرارة عن طريق فتح البطن خلال نفس الفترة للمقارنة. عينات الدم أخذت قبل ٢٤ ساعة وبعد ٢٤ ساعة من العملية لإجراء الفحص المختبري عليهما.

النتائج: تبين التحاليل الإحصائية زيادة ملحوظة في مستويات الالانين اماينوترانسفريز، اسبارتيت اماينوترانسفريز، والاكتيت ديهايدروجينيز في المجموعة التي أجريت لهم عملية إستئصال المرارة بالمنظار مقارنة مع المجموعة التي أجريت لهم عملية إستئصال المرارة عن طريق فتح البطن.

الاستنتاج: نستنتج بأن إرتفاع مستويات الإنزيمات في الدم قد يكون سببه التأثير السلبي للغاز داخل الصفاق على جريان الدم للكبد. وعلى الرغم من أن هذه التغييرات لا تبدو ذات أهمية سريرية، ولكن يجب أن نكون حذرين قبل إتخاذ القرار لإجراء عملية إستئصال المرارة بالمنظار للمرضى الذين يعانون من قصور الكبد.

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. LC is entering an era where it is considered an outpatient procedure. 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] The pressure of a created pneumoperitoneum and its duration was shown to cause elevations in liver enzymes.[3,4] Any increase in liver enzymes is always a matter of concern for the clinician and warrants further investigation to determine the underlying pathology.

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are considered a measure of hepatocellular function.[5,6] Elevated liver function test (LFT) is commonly seen after surgery.[7] The elevation is usually transient, and the LFTs return to normal levels without any intervention.[8,9] Pneumoperitoneum is the essential component for laparoscopic procedures even though a gasless approach has been described utilizing an intra-abdominal lift, this approach was not superior than pneumoperitoneum in healthy patients.[10] The hemodynamic reaction to peritoneal insufflation has been well described, and depends upon the interaction of many factors.[11] Serum bilirubin, ALT, AST, and Lactate dehydrogenase (LDH) levels are true liver function tests, typically used to detect liver injury.[12-14] Alkaline Phosphatase (ALP) results are usually evaluated along with other tests for liver disease. When the bile ducts are blocked, ALP and bilirubin may be increased much more than AST or ALT.[15]

The aim of this study is to evaluate the effect of pneumoperitoneum on liver enzymes and serum bilirubin after LC in comparison with open cholecystectomy (OC).

PATIENTS AND METHODS

A prospective case control study, conducted at the Surgical Unit Number One, at AL-Jumhouri Teaching Hospital, during the period from October 2010 to October 2011. LC was performed on 74 patients, and 30 patients underwent OC as a control group. Both groups were anesthetized by the same protocol. Blood biochemistry for AST, ALT, ALP, LDH, and total serum bilirubin (TSB) were obtained both preoperatively and 24 hours after the operation from a superficial vein in the antecubital region. Patients with concomitant bile duct stones, high levels of liver 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.

LC was performed using four trochars with the standard American technique. 14 mmHg of pneumoperitoneum was created and maintained by intraperitoneal carbon dioxide (CO_2) insufflations with an automatic insufflator. OC was performed 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 (cephalosporin), and diclofenac sodium for postoperative pain control. All patients received intravenous fluid solutions for the first 24 hours. 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 TSB 5-17µmol/L, AST and ALT up to 20 IU/L, for LDH 25-190 IU/L and for ALP 22-91 IU/L. Patients were seen between an interval of one week and one month after the operation on an outpatient basis.

The statistical analysis

The results presented as a mean ± SD. The statistical analysis carried out by paired student (t) test to calculate the differences between two

means and by Chi square (χ^2). The p value was considered a significant if it is less than 0.05.

RESULTS

The mean age of patients was 45.1 years (range 22-76 years).

In LC and OC there were no significant differences in post-operative liver enzymes in relation to gender (as shown in **Table 1**).

The duration of pneumoperitoneum for LC lasted 30-65 minutes. In LC, the changes in post-operative liver enzymes showed significant increase in pneumoperitoneum more than 40 minutes, **Table 2.**

In OC, the changes in post-operative liver enzymes were significantly lower than those with LC, (as shown in **Table 3**).

In OC group, mean operation time was 47.22 minutes and only 2 patients of the thirty patients involved had changes in liver enzymes and serum bilirubin and these changes statistically were not significant.

In LC group there was significant increase postoperatively in total serum bilirubin, ALT, AST, LDH, while there was no significant changes in ALP (**Table 4**).

Table 1. Relation of gender to post-operative liver enzymes.

| Gender | Post-operative enzymes | | P– value |
	Changes No.	No changes No.	
Female	53	37	0.09
Male	11	3	

Table 2. Relation between duration of pneumoperitoneum and post-operative liver enzymes.

Duration of pneumoperitoneum	changes No.	No changes No.	Total	P-value
Up to 30 minutes	14	8	22	0.3
31-40 minutes	7	3	10	0.2
>40 minutes	41	1	42	0.02
Total	62	12	74	

Table 3. Post - operative liver enzymes according to types of operation.

| Post op. enzymes | Type of operation | | P- value |
	LC No.	OC No.	
Change	62	2	0.000
No change	12	28	
Total	74	30	

Table 4. Mean values for postoperative enzyme changes after LC and OC.

| Test | LC group (n=74) | | OC group (n=30) | | P-value | 95% confidence interval |
	Preoperative	Post-operative	Preoperative	Post-operative		
TSB	9.36±2.79	19.31 ±4.09	10.33 ±2.68	15.37 ±2.44	0.000	2.64- 5.24
AST	11.21±2.60	32.32 ±8.38	11.23±3.047	17.43 ± 3.62	0.000	12.55- 17.22
ALT	11.48±2.15	32.37 ±8.4	11.53±3.048	17.57 ± 3.77	0.000	12.44- 17.18
LDH	106.27±24.13	199.1 ±52.5	112.60±20.7	158.4 ± 21.1	0.000	26.43- 55.04
AKP	47.62±12.33	49.0 ± 12.6	49.40±11.65	52.4 ± 11.4	0.183	-8.52 - 1.66

DISCUSSION

Elevation of liver enzymes after non-complicated LC has become a well-known fact. Although the clinical importance of these enzyme elevations has not been clarified.[5-7,16,17] In our study the female to male ratio was 6:1; this is in keeping with another study,[18] but at variance with other reports.[19-21] In our patients there were no significant change in post-operative liver enzymes levels between males and females. This is in agreement with other studies.[17,18]

In LC group we found that the prolonged duration of surgery is associated with higher levels of post-operative liver enzymes, while in OC the duration of surgery did not affect the post-operative levels of liver enzymes; also the duration of pneumoperitoneum was associated with the increase in the levels of post-operative liver enzymes. In contrast, OC patients who were under the same operation conditions to those of LC patients, except that they were not subjected to CO_2 pneumoperitoneum, 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 tests.[9,22] It is obvious that pneumoperitoneum and its duration are the causes of increased liver enzymes levels post-operatively.

In OC group, postoperative mean levels of studied enzymes remained within the normal limits,

while in LC group, increase in TSB, AST, ALT and LDH were significant. However, the changes in ALP levels were insignificant in both groups. These results are in accordance with most previously published literature on the subject.[3,11,12,18,23] In this study, changes in serum levels of liver enzymes occurred in 83.8% of patients. Disturbances in liver enzymes in patients undergoing LC have been already reported reaching up to 80% of cases in some studies.[15,24] It is known that 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 anesthesia are possible causes of elevation of certain liver enzymes. However, liver retraction for better exposure, manipulation of biliary tract for detecting possible common duct stones, and electrocauterization of the liver bed were routinely performed in OC as well.[7] We compared the enzyme alterations in LC patients with those in the OC group who were given the same anesthetic agents and same antibiotics. The only possible factor that might cause these alterations in this study was the elevated intraperitoneal pressure created during LC.

Knowing the fact that normal portal venous pressure is 7-10 mmHg and about half of the hepatic blood flow comes from the portal venous system, 14 mmHg of pneumoperitoneum created with CO_2 is stated to be the major cause of transient hepatic ischemia during LC.[2,8-10] Jakimowicz *et al* showed that 14 mmHg of intraperitoneal pressure reduced the portal blood flow by 53% using the Doppler technique.[10] During laparoscopic procedure, the sudden alteration of intraperitoneal pressure could cause the undulation of portal blood flow, which may give rise to ischemia and damage of tissues and organs, especially the Kupffer cells and the endothelial cells of the hepatic sinusoids.[25] 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 (14 mmHg) pneumoperitoneum.[6] In a study comparing hepatic enzyme alterations in LC, gasless LC and LC under low pressure pneumoperitoneum, 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 pressure on hepatic perfusion by means of enzyme level changes.[7]

We conclude that elevations in post-operative serum liver enzymes could be attributed to the negative effects of the pneumoperitoneum on the hepatic blood flow. These changes do not seem to be clinically important, but care should be taken before deciding to perform LC in patients with hepatic insufficiency.

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