CAUSES OF LIVER ENZYMES AND BILLIRUBIN LEVELS ELEVATION AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Liver enzymes ALT, AST, alkaline phosphatase and serum bilirubin show a transient elevation after laparoscopic cholecystectomy. The cause is not clear but it may be due to bile duct kink, use of electocautery on the liver surface, "squeeze" effect on the liver by upward traction on the gall bladder fundus or due to pneumoperitoneum created for the laparoscopic procedure. The enzymes return to normal within 72 hours. In this work we will study the effect of each factor on the liver enzymes level separately to detect the cause and significance of this enzymatic disturbances.

INTRODUCTION

Bile duct injury is the most feared complication of laparoscopic cholecystectomy. Some laboratory tests may be indicative of this complication, such as increase liver enzymes ALT, AST, alkaline phosphatase and serum bilirubin. Such increase of liver enzymes and bilirubin levels were noted incidentally after laparoscopic cholecystectomy (Halevy et al., 1994). The elevated liver enzymes levels were found to return to normal level; within 72 hours after surgery and was found to have no clinical significance (Lygidakis & Tytgat, 1989). Its cause is not clear, but it may be due to the increase of the intra-abdominal pressure by the pneumoperitoneum created for laparoscopic surgery or due the squeeze effect on the liver by gall bladder fundus traction in an upward direction which may free these enzymes into the blood stream (Shemel, 1976). Other causes may be the prolonged use of diathermy on the liver tissue, the kink of the common bile duct which occurs during surgery, or due to drugs used during anaesthesia such as halothan, nitros oxide, thiopentone or others.

However, this increase in liver enzymes and bilirubin levels were found to be two or three folds and it has no effect on the patient general condition (Pagana and Stahlgren 1980).

In the present study, we compared this enzyme levels elevation in laparoscopic cholecystectomy and in open cholecystectomy as well as in other laparoscopic procedure in which pneumoperitoneum is
created for pelvic surgery to study the effect of increased intra-abdominal pressure on the liver enzymes. Also, a study on an animal model was performed to show the effect of the liver "Squeeze" on the liver enzymes levels.

**MATERIALS AND METHODS**

In this controlled study, 91 patients were included. Their ages ranged from 22 to 56 years with a mean age of 39 years. 35 patients underwent laparoscopic cholecystectomy (group 1). 29 patients were females and 6 were males. Their mean age was 37 years.

Another 31 patient underwent open cholecystectomy (group 2), 23 were females and 8 were males. In this group we performed a standard technique in which traction was done on the gall bladder neck just like in laparoscopic cholecystectomy and the electrocautery was used in all cases to dessect the gall bladder from the liver bed.

A third group, 25 patients, underwent pneumoperitoneum for other reasons. Five patients were males who underwent repair of a groin hernia, and 20 patients were females subject to a pelvic laparoscopic surgery as ovarian cystectomy, tubolysis or removal of endometriotic cyst. All cases were admitted in Ain Shams University Hospital surgical and Gynecology departments between June 1993 and August 1995. For all patients in the study, blood samples were collected 24 hours before and after surgery and ALT, AST, serum alkaline phosphatase and serum bilirubin were measured and recorded. Another blood sample was collected 72 hours latter for measurement of the same enzymes levels.

All cases with high preoperative enzymes levels were excluded from the study. Also cases that needed conversion to open surgery were excluded. For each patient we recorded the time of the operation, the drugs used for anaesthesia and any drug used during or after surgery.

Another study was carried on at the same time on 11 Guinea pigs. We performed a midline incision and the suprahepatic venacava was sampled, then the liver of the animal was retracted in an upword and cephalad direction just like in laparoscopic cholecystectomy. This position was maintained for one hour and another blood sample was analysed for serum bilirubin, AST, ALT and serum alkaline phosphatase. The animals were anaesthized using thiopental and nitrous oxide.

**RESULTS**

In group 1 the mean preoperative level of ALT was 17 and this level increased significantly in 28 patients (80%) to a mean postoperative level of 37 which is 2.1 times the mean preoperative level. AST mean preoperative level was 24 and its postoperative level was 41. AST level increased significantly in 31 patients (88%) (Table 1).
The mean preoperative level of serum alkaline phosphatase was 132 U/L and it was increased in 15 patients in group 1 (42%). Its mean postoperative level was 156, an increase that is within the normal limits (Table 1).

Serum bilirubin was increased in 17 patients (48%) in this group to a mean value of 1.7 mg/dl, and it reached a level of 2.2 mg/dl in one patient. All these values returned to normal within 72 hours after surgery.

In group (2), there was a mild increase in ALT value in 9 patients (29%) with a mean postoperative value of 21. The increase in ALT level was 1.3 times the preoperative level. AST was increased only in 3 patients in this group (9.6%) and it was increased only 1.2 times the preoperative level. There was no increase in serum alkaline phosphatase in this group except in 2 patients and the increase was not significant. Serum bilirubin rise was detected only in one patient (Table II).

In group (3) in which pneumoperitoneum was performed for pelvic surgery, the ALT mean postoperative level was 1.2 times the preoperative level. AST also was raised to a mean value that is 1.3 times the mean preoperative level. There was no rise in serum alkaline phosphatase or serum bilirubin in this group (Table III).

In all patients in the study, we did not notice any clinical adverse effect in those cases who showed increased liver enzymes postoperatively.

Similarly, in the animal group, we noticed a significant rise of the mean ALT value and its postoperative level was 2.1 that of the preoperative level. AST was raised also to a mean level that is 1.6 the preoperative level. Serum alkaline phosphatase rise was marked and its mean level 2.4 times that of the preoperative level. Serum bilirubin level increased to a mean value that is 1.2 that of the mean preoperative value (Table IV).

**DISCUSSION**

In this study done on 35 patients submitted to laparoscopic cholecystectomy, we noticed a significant rise of liver enzymes ALT and AST in 80% and 88% respectively. Serum bilirubin rise was detected in 48% of cases and was primarily of the unconjugated type. ALP rise was detected in 42% but still remained within normal limits. The enzymes rises were of no clinical significance and it returned to normal within 72 hours after the operation.

Similar results were obtained by Halevy et al., 1994. None of their cases had bile duct injury. They postulated several possible explanations, such as an increased intra-abdominal pressure due to pneumoperitoneum, the use of diathermy to remove the gall bladder from its bed and spread of heat to the liver parenchyma, the squeeze effect of the liver by traction on the gall bladder fundus in an upward direction which may free some enzymes to the bloodstream.

Another possible explanation is the kink of the common bile duct due to con-
Table (1)

<table>
<thead>
<tr>
<th>Group 1 (35 pts)</th>
<th>ALT</th>
<th>AST</th>
<th>SALP</th>
<th>S. BI L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean preop. level</td>
<td>17</td>
<td>24</td>
<td>132</td>
<td>1.1</td>
</tr>
<tr>
<td>Mean postop. level</td>
<td>37</td>
<td>41</td>
<td>156</td>
<td>1.7</td>
</tr>
<tr>
<td>% of pt.</td>
<td>28 (80%)</td>
<td>31 (88%)</td>
<td>15 (42%)</td>
<td>17 (48%)</td>
</tr>
</tbody>
</table>

Table (2)

<table>
<thead>
<tr>
<th>Group 2 (13 pts)</th>
<th>ALT</th>
<th>AST</th>
<th>SALP</th>
<th>S. BI L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean preop. level</td>
<td>17</td>
<td>24</td>
<td>132</td>
<td>1.1</td>
</tr>
<tr>
<td>Mean postop. level</td>
<td>37</td>
<td>41</td>
<td>156</td>
<td>1.7</td>
</tr>
<tr>
<td>No. of patients</td>
<td>28 (80%)</td>
<td>31 (88%)</td>
<td>15 (42%)</td>
<td>17 (48%)</td>
</tr>
</tbody>
</table>
## Causes of liver enzymes

### Table (3)

| Group 3  
(25 pts) | ALT | AST | SALP | S. BIL |
<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Mean preop. level</td>
<td>17</td>
<td>22</td>
<td>133</td>
<td>1.1</td>
</tr>
<tr>
<td>Mean postop. level</td>
<td>20.1</td>
<td>28.6</td>
<td>137</td>
<td>1.1</td>
</tr>
<tr>
<td>% of pt.</td>
<td>11 (14%)</td>
<td>9 (36%)</td>
<td>4 - 16%</td>
<td>---</td>
</tr>
</tbody>
</table>

### Table (4)

| Group 4  
(11 pigs) | ALT | AST | SALP | S. BIL |
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Mean preop. level</td>
<td>12.0</td>
<td>17.0</td>
<td>78</td>
<td>0.6</td>
</tr>
<tr>
<td>Mean postop. level</td>
<td>25.0</td>
<td>27.2</td>
<td>187</td>
<td>0.75</td>
</tr>
<tr>
<td>No. of G. pigs</td>
<td>9 (81%)</td>
<td>10 (91%)</td>
<td>11 (100%)</td>
<td>6 (55%)</td>
</tr>
</tbody>
</table>
tensive traction on the gall bladder neck, which increase the intraductal pressure and subsequently increase the serum levels of liver enzymes and bilirubin.

Another issue is the passage of small stone, during manipulating the gall bladder, to the common bile duct. However this could not explain this enzymed rise as the incidence of missed stones is 1.2% to 12.4% (Sackier et al., 1991). Also if it is the reason, it should occur in cases submitted to open cholecystectomy. Finally, inadvertant clipping of an aberrant right branch of the hepatic artery can not be in-crriminated for this enzymatic rise as it should be followed by a massive and clinically significant rise in all liver enzymes and bilirubin level (Sackier et al., 1991).

In this study, we tried to identify the main factor responsible for his enzymes elevation. We found that the effect of pneumoperitoneum done for pelvic surgery is minimal and it can not be only factor. Also we noticed that such elevated enzymes levels did not occur in open cholecystectomy inspire the use of diathermy to remove the gall bladder from its bed and the kink of the CBD during manipulating the gall bladder.

The study on the animal model showed a significant rise of liver enzymes and bilirubin when the liver of the animal was squeezed as in laparoscopic cholecystectomy and this may be the responsible factor in such enzymatic rise. Such enzymatic rise is of no significance on liver function in normally functioning liver but it may be harmful for patients with preoperative liver cell affection and may add further damage to the liver cells.

REFERENCES