Rise in liver enzymes after laproscopic cholecystectomy: A transient phenomenon

R Koirala,[1] VC Shakya,[2] S Khania,[3] S Adhikary[3] and CS Agrawal[3]

Department of surgery, [1]Nepal Medical College and Teaching Hospital, Attarkhel, Jorpati, Kathmandu, Nepal, [2]Civil Services Hospital, Minbhawan Kathmandu, Nepal and [3]BP Koirala Institute of Health Sciences, Dharan, Nepal

Corresponding author: Dr. Rabin Koirala Associate Professor, Nepal Medical College and Teaching Hospital, Attarkhel, Jorpati, Kathmandu, Nepal

ABSTRACT

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. Blood samples from 30 patients who underwent laparoscopic cholecystectomy (LC) and 20 patients who underwent open cholecystectomy (OC) were tested for liver function by measuring the level of serum alanine aminotrasferase (ALT) and aspartate aminotrasferase (AST) before and after surgery. The level of serum ALT and AST increased significantly during the first 24 hours after surgery in laparoscopic cholecystectomy. However, no significant change of the serum liver enzymes was detected in open cholecystectomy patients. As a result, there was statistically significant difference in change of both ALT and AST levels between LC and OC patients. The effect was transient and reverted back to normal by the 7th day post operation. Transient elevation of hepatic transaminases occurred after laparoscopic surgery. The major causative factor seemed to be the CO_2 pneumoperitoneum. In most of the laparoscopic surgery patients, the transient elevation of serum liver enzymes showed no apparent clinical implications.

Keywords: Laparoscopic cholecystectomy, liver enzyme.

INTRODUCTION

Laparoscopic cholecystectomy is now considered the "Gold standard" in management of Gall stone disease. More than 90% of cholecystectomy today is done laparoscopically.[1] Creating a pneumoperitoneum is an integral part of the procedure. Pneumoperitoneum has its own physiological consequences. Some studies have reported an unexplained rise in liver enzymes post operatively. Other studies have pointed to hemodynamic changes and decrease in portal flow secondary to pneumoperitoneum.[2-4] Various other factors have also been blamed including traction to the liver and electrocautery. Our study tries to document the changes in liver enzymes and evaluate the possible causes behind it.

MATERIALS AND METHODS

This was a prospective comparative trial conducted after institutional ethical clearance in BP Koirala Institute of Health Sciences (BPKIHS). Thirty consecutive patients who opted for laparoscopic Cholecystectomy and twenty Patients who opted for open cholecystectomy were chosen and the consent obtained for the study. Patients with preoperatively deranged liver function tests, chronic cholecystitis, choledocholithiasis and chronic liver disease were excluded from the study.

Laparoscopic cholecystectomy was performed with four standard ports with pneumoperitoneum created using the open Hassan's technique and the insufflation pressure was kept at 10 mmhg. Open cholecystectomy was performed using an approximately 6 cm long subcostal incision two finger breadths below the costal margin from the midline running laterally.

Valley lab force FX cautery with coagulation power at 40 was kept for all the patients in the study. Liver function tests were repeated on postoperative day 1 and day 7 respectively.

Statistical analysis was done using SPSS 11.5 version. Chi^2 was applied and a p value of < 0.05 was considered significant.

RESULTS

Fifty patients were included in the study; thirty in the laparoscopic arm and twenty in the open arm. There were ten males and 40 females. The patient profiles were comparable (Table-1). The age ranged between 19- 65 years. Nine had a family history of gall stone disease. The duration of surgery lasted between 35- 90 minutes and the hospital stay was between 1- 4 days. There was no mortality or significant morbidity. There was no conversion and no morbidity in the laparoscopic group. Two cases of open cholecystectomy developed superficial wound infection which required partial suture removal and dressing.

There was no significant differences between the two groups in preoperative levels of AST, ALT, total bilirubin

Table-1: Basic patient characteristics

Variables	Open cholecystectomy	Laparoscopic Cholecystectomy	P value (t/U Test)
Age (years)	42.35 ±11.9	36.5±9.9	0.07
Duration of surgery (min)	48.25 ±12.3	53.8 ±14.0	0.15
BMI=kg/m^2	25.3 ±3.90	25.0 ±3.82	0.851
Hemoglobin (gm%)	12.5 ±1.79	12.9 ±1.89	0.47
TLC ($10^3/mm^3$)	9.27 ±3.68	8.53 ±2.33	0.39
Urea (mg%)	24.75 ±10.13	22.03 ±8.72	0.317
Creatinine(mg%)	0.77 ±0.30	0.90 ±0.27	0.084
Serum albumin (gm%)	4.58 ±0.64	4.2 ±0.72	0.054
PT (seconds)	13.59 ±1.63	14.53 ±1.74	0.06
Total Bilirubin (mg%)	0.65 ±0.29	0.77 ±0.25	0.119
ALT (IU)	26.3 ±8.94	24.5 ±7.45	0.444
AST(IU)	30.75 ±8.10	31.87 ±7.72	0.625
Alk PO4	158.75 ±65.56	157.4 ±47.26	0.933
Symptoms Duration (months)	22.57 ±17.89	20.61 ±18.12	0.709

or Alkaline phosphatase levels (Table-1). There was a significant rise in the levels of both AST and ALT levels in the postoperative day 1 and this was highly significant with a p value < 0.001. Total bilirubin levels and alkaline phosphatase levels also showed a significant rise (Table-2). When the liver enzymes were evaluated a week later the enzymes in the laparoscopic groups were still raised with AST and Total bilirubin being still significant but the difference was less marked (Table:3). All the liver enzymes and bilirubin show an upward trend postoperatively. This was especially marked in laparoscopic group and this was statistically significant. But by one week they seem to have almost come down to normal levels (Fig 1-3).

Nine patients in the laparoscopic group and 3 patients in the open cholecystectomy group developed tachycardia, hypotension or both during the procedure but this was not statistically significant (P value 0.267)(Table-4).

DISCUSSION

Our study shows a transient increase in the postoperative liver enzyme levels in the laparoscopic group. This change in laparoscopic cholecystectomy vis a vis open cholecystectomy has been documented before.[3,5,6] The rise in liver enzymes was subclinical and approached normal limits within a week and none of the patients had hepatic dysfunction.

The effects of pneumoperitoneum on hepatic blood flow are poorly understood. Junghans and collegues in a pig model found decreased splanchnic and portal perfusion when intrabdominal pressures greater than 12 mmhg were used especially so in head up positions.[7] Sato *et al* had similar findings using transesophageal echo to monitor hepatic blood flow. Their study showed that head up position combined with pneumoperitoneum decreased hepatic perfusion.[8]

Table-2: Post-operative changes in liver enzyme levels Day 1

Day 1	Procedure	Mean change in Value in mg%	Two Standard deviation(SD)	P Value
Total Bilirubin (mg%)	OC	0.75	±0.27	0.007
	LC	1.0	±0.422	
ALT (IU)	OC	33.15	±10.97	0.001
	LC	69.6	±44.64	
AST (IU)	OC	38.75	± 16.28	0.001
	LC	79.1	±50.37	
ALK PO4	OC	154.6	±62.9	0.044
	LC	192.2	±63.13	

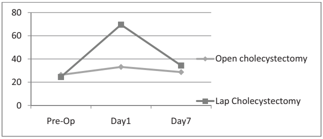

Fig. 1. ALT levels in IU/ml

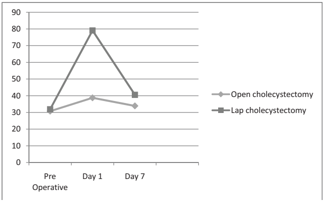

Fig. 2. AST levels in IU/ ml

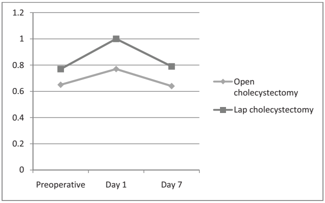

Fig. 3. Total bilirubin

In contrast Blobner et al demonstrated an increase in splanchnic and portal blood flow due to vasodilatory effect of CO_2 at pressures below16 mmhg.[9] Others have also demonstrated that induction of CO_2 pneumoperitoneum with intrabdominal pressures of 12mmhg was associated with increased hepatic perfusion in healthy individuals.[10]

In a recently published study the authors used 14 mmhg and 10 mmhg of intrabdominal pressures during laparoscopic cholecystectomy. They conclude that 10mmhg pressures in creating pneumoperitoneum to be superior to 14mmhg.[2,11] We used pressures of 10 mmhg during pneumoperitoneum and still got significant rise in liver enzymes.

To look into traction as a possible cause we used small incisions of around 6 cm for open cholecystectomy

Table-4: Hemodynamic complications

Procedure	n.		n.
LC	9/30	Fall in BP	5
		Tachycardia	2
		Both	2
OC	3/20	Fall in BP	1
Chi^2 Test		Tachycardia	0
P value: 0.267		Both	2

Table-3: Post-operative changes in liver enzyme levels: Day 7

Day 7	Procedure	Value	SD	P Value
Total Bilirubin (mg%)	OC	0.64	$\pm$0.19	0.016
	LC	0.79	$\pm$0.22	
ALT (IU)	OC	28.7	$\pm$7.17	0.06
	LC	34.39	$\pm$13.06	
AST (IU)	OC	33.9	$\pm$7.9	0.05
	LC	40.53	$\pm$13.28	
ALK PO4	OC	153.15	$\pm$51.5.9	0.726
	LC	158.43	$\pm$52.2	

but we found that the rise in liver enzymes could not be attributed to traction and squeeze pressure thus generated. Min T and collegues used a similar length of incision for open cholecystectomy and reached a similar conclusion.[3]

Use of electrocautery as a possible source of liver injury has been explored in previous studies.[12-15] While electrocautery as a mode for liver injury is a possibility it can be discounted when identical strenghths of cautery is used in both open and laparoscopic procedures. We used the same cautery in identical strengths for diathermy in both the open and laparoscopic groups thus diathermic injury appears to be an unlikely cause for rise in liver enzymes.

Inadvertent right hepatic artery or other major vascular injuries are associated with massive postoperative rise in liver enzymes and they usually have significant clinical repercussions.[16,17] None of our patients had massive rise in liver enzymes it is unlikely to be a causative factor in our study.

The rise in liver enzymes associated with laparoscopic colorectal surgeries mirrors the rise in laparoscopic cholecystectomy seen in a study by Tan *et al* points towards the pneumoperitoneum as the causative factor.[3] Whether it is the neurohumorally mediated transient hepatocyte dysfunction related to surgical stress or ischaemia and reirrigation due to reduced portal flow and microcirculation remains a conjecture.[3,4,18]

To conclude, laparoscopic cholecystectomy is associated with transient rise in liver enzymes. The absence of similar rise in open cholecystectomy which was matched to negate the effects of traction and squeeze pressure on the liver and injury due to diathermy suggests that pneumoperitoneum was associated with subclinical hepatic injury. Whether it is due to neurohumoral response to surgical stress or due to alteration in portal flow causing ischemic reperfusion injury is still conjectural. Further studies are warranted to shed light on this phenomenon.

REFERENCE

1. Gurusamy KS, Davidson BR. Surgical treatment of gallstones. *Gastroenterology Clin North Amer* 2010; 39: 229-44.
2. Eryılmaz HB, Dilek M, Atakan S, Mehmet TI. The Effects of Different Insufflation Pressures on Liver Functions Assessed with LiMON on Patients Undergoing Laparoscopic Cholecystectomy. *Sci World J* 2012; 2012: 172575. doi: 10.1100/2012/172575.PMCID: PMC3349322
3. Tan M, Xu FF, Peng JS *et al*. Changes in the level of serum liver enzymes after laparoscopic surgery. *World J Gastroenterol* 2003; 9: 364-7.
4. Kotake Y, Takeda J, Matsumoto M, Tagawa M, Kikuchi H. Subclinical hepatic dysfunction in laparoscopic cholecystectomy and laparoscopic colectomy. *Brit J Anaesthesia* 2001; 87: 774-7.
5. Giraudo G, Brachet Contul R, Caccetta M, Morino M. Gasless laparoscopy could avoid alterations in hepatic function. *Surg Endosc* 2001; 15: 741-6.
6. Morino M, Giraudo G, Festa V. Alterations in hepatic function during laparoscopic surgery. An experimental clinical study. *Surg Endosc* 1998; 12: 968-72.
7. Junghans T, Böhm B, Gründel K, Schwenk W, Müller JM. Does pneumoperitoneum with different gases, body positions, and intraperitoneal pressures influence renal and hepatic blood flow? *Surg* 1997; 121: 206-11.
8. Sato K, Kawamura T, Wakusawa R. Hepatic blood flow and function in elderly patients undergoing laparoscopic cholecyst ectomy. *Anesth Analg* 2000; 90: 1198-1202.
9. Blobner M, Bogdanski R, Kochs E, Henke J, Findeis A, Jelen-Esselborn S. Effects of intraabdominally insufflated carbon dioxide and elevated intraabdominal pressure on splanchnic circulation: an experimental study in pigs. *Anesthesiol* 1998; 89: 475-82.
10. Meierhenrich R, Gauss A, Vandenesch P, Georgieff M, Poch B, Schütz W. The effects of intraabdominally insufflated carbon dioxide on hepatic blood flow during laparoscopic surgery assessed by transesophageal echocardiography. *Anesth Analg* 2005; 100: 340-7.
11. Morino M, Giraudo G, Festa V. Alterations in hepatic function during laparoscopic surgery: an experimental clinical study. *Surg Endosc* 1998; 12: 968-72.
12. Barrat C, Capelluto E, Champault G. Intraperitoneal thermal variations during laparoscopic surgery. *Surg Endosc* 1999; 13: 136-8.
13. Shameiyeh A, Schernk P, Tulipan L, Vattay P, Bogner S, Wayand W. A new bipolar feedback-controlled sealant system for closure of the cystic duct and artery. *Surg Endosc* 2002; 16: 812-3.
14. Berger M, Junemann K, Schramm H. Danger of monopolar cautery in laparoscopic gall bladder surgery. *Zentralbl Chir* 2001; 126: 591-5.
15. Capelluto E Champault G. Variations in intraperitoneal temperatures during laparoscopic cholecystectomy. *Ann Chir* 2000; 125: 259-62.
16. Balsara KP, Dubash C, Shah CR. Pseudoaneurysm of the hepatic artery along with common bile duct injury following laparoscopic cholecystectomy.a report of two cases. *Surg Endosc* 1998; 12: 276-7.
17. Mathisen O, Soreide O, Bergan A. Laparoscopic cholecystectomy:bile duct and vascular injuries: management and outcome. *Scand J Gastroenterol* 2002; 37: 476-81.
18. Himal HS. Minimally invasive (laparoscopic) surgery. *Surg Endosc* 2002; 8: 265-70.