Effects of Different Intraperitoneal Pressure of Pneumoperitoneum on Liver Function Test During Laparoscopic Cholecystectomy: A Comparative Study

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ABSTRACT

Intra-abdominal pressure created by pneumoperitoneum during laparoscopic cholecystectomy is considered to compromise hepatic, splanchnic and cardiac perfusion. The objective of this study was to evaluate the effect of different pressures of pneumoperitoneum on hepatic perfusion by evaluating liver function test in post-operative period. This was a prospective comparative study. We studied 60 cases scheduled for laparoscopic cholecystectomy during March 2015 to August 2015. Alternate patients were allocated in two groups; Group 1: 7mmHg pneumoperitoneum pressure and Group 2: 14mmHg. Liver function test (total and direct bilirubin, serum glutamic oxaloacetic transaminase: SGOT, Serum glutamic Pyruvic Transaminase: SGPT, Alkaline Phosphatase: ALP) was done in every patient pre-operatively and repeated on 24-hour post-operative and 7th day post-operative day. Different findings were analyzed. Patient demographics, duration of symptoms and time of pneumoperitoneum in between the two groups were similar. Difference between the means of the parameters of liver function tests were analyzed within the group, as well as between the groups. There was slight increase in the levels of bilirubin and enzymes in 24 hours of surgery with decrease in day 7, irrespective of the groups. The findings did not show any statistical as well as clinical significance. Slight increase in the levels of bilirubin and enzymes occurred transiently in the post-operative period of laparoscopic cholecystectomy. This increase did not have statistical and clinical significance.Different intraperitoneal pressures did not seem to affect the post-operative liver function test.

Key words: Laparoscopic Cholecystectomy, Liver function test, Pneumoperitoneum, Post-operative.

INTRODUCTION

Laparoscopic surgery is the gold standard treatment for gall bladder stones. Working space in laparoscopic cholecystectomy is created by insufflating carbon dioxide into the peritoneal cavity to the pressure of 12-14 mm Hg, which is considered standard.[1,2] Despite many clinical advantages of laparoscopic surgery, the adverse effects of carbon dioxide (CO_2) pneumoperitoneum are cardiopulmonary, renal, splanchnic and hepato-portal ischemic effects.[3-6] But the studies have shown two conflicting reports about the effect of carbondioxide pneumoperitoneum on splanchnic and hepatic perfusion. Jakimowicz *et al* reported the decrease in portal flow by 53%, with increase in intraperitoneal pressure up to 14mmHg.[7] Meierhenrich *et al* observed the induction of CO2 pneumoperitoneum with intra-abdominal pressure of 12mmHg causing increase in hepatic per fusion due to compensatory increase of hepatic artery fl ow, the phenomenon known as "hepatic arterial buffer response (HABR)" in rat model. This phenomenon probably is yet to be proven in human.[8,9] Laparoscopic cholecystectomy under low pressure pneumoperitoneum (7-10mmHg) has also been reported to be feasible.[10-12]Generally, pneumoperitoneum is the standard pre-requisite for the laparoscopic surgery, although gas-less laparo-lift techniques have been practiced to avoid the adverse effects of the capno-pneumoperitoneum. But the exposure during surgery in laparo-lift cases is compromised.[13] We, in this study, have tried to evaluate the effect of different intra-abdominal pressure; highest and lowest possible recommended (7mmHg and 14mmHg), on hepatic dysfunction after laparoscopic cholecystectomy.

MATERIAL AND METHODS

The prospective comparative study was carried out in Kathmandu Medical College within a period of 6 months, from March 2015 to August 2015. All adult patients, posted for laparoscopic cholecystectomy for symptomatic gall stone disease in the age group of 19-60 years without any other co-morbid illness or deranged liver function test were included in the study. After getting approval from the Institutional Review Committee (IRC), every alternate patient was grouped as either group A or group B. Group

A for pneumoperitoneum pressure of 7mm Hg and Group B for14mmHg. Informed consent was taken for the study and pre-operative workup was done, including pre-operative liver function test (LFT). LFT included total bilirubin (TB) in mg/dl, Direct bilirubin (DB) in mg/dl, serum glutamic oxalo-acetic transaminase (SGOT) [aspartate aminotransferase (AST)] in IU/L, serum glutamic pyruvic transaminase (SGPT) [alanine aminotransferase (ALT)] in IU/L and alkaline phosphatase (ALP) in IU/L. Laparoscopic cholecystectomy was performed as a three port procedure under general anesthesia. All patients got standard pre-anesthetic medication, similar induction technique and general anesthetic medication. For prophylaxis, single dose of injection ceftriaxone one-gram was given intravenously at the time of induction. Pneumoperitoneum was created with open Hassan technique. Pneumoperitoneum pressure was kept at 7 mmHg in group 1 patients and 14 mmHg in group 2 patients. Two other ports were made, one 10mm epigastric port and another 5mm right subcostal mid-clavicular port. Dissection of Calots triangle was done by Maryland dissector and gall bladder was grasped by Babcock forceps through the right subcostal port at Hartmann's pouch. After clipping and dividing the cystic duct and artery, gall bladder was dissected from the liver bed using monopolar hook diathermy. Gall bladder was removed from the umbilical port. Local anesthetic was instilled in the gall bladder fossa in all cases at the end of the surgery. The total time of pneumoperitoneum was recorded. All patients in post-operative period were given intravenous fluid and intravenous paracetamol injection as analgesics. Those who needed modifi cation in this treatment were excluded from the study. Liver function test was done in all cases at 24 hour of surgery and discharged form hospital either at 24 hours or at 48 hours and asked to follow up at the outpatient clinic after 7 days with repeat liver function test at day seven. Patient parameters, preoperative, 24 hour post-operative and 7th day liver function tests were recorded and analyzed using non-parametric t-test and one-way ANOVA using SPSS 20.

RESULTS

A total of 60 cases were studied. There were 30 patients in each group of different pneumoperitoneum pressures (Group1:7 mmHg and Group2: 14mmHg). Demographics of patients in both the groups were compared. Gender distribution showed that majority of the patients were females (>70%) and maximum number of patients were in the 31-40years old age group (30-40%) (Fig 1).

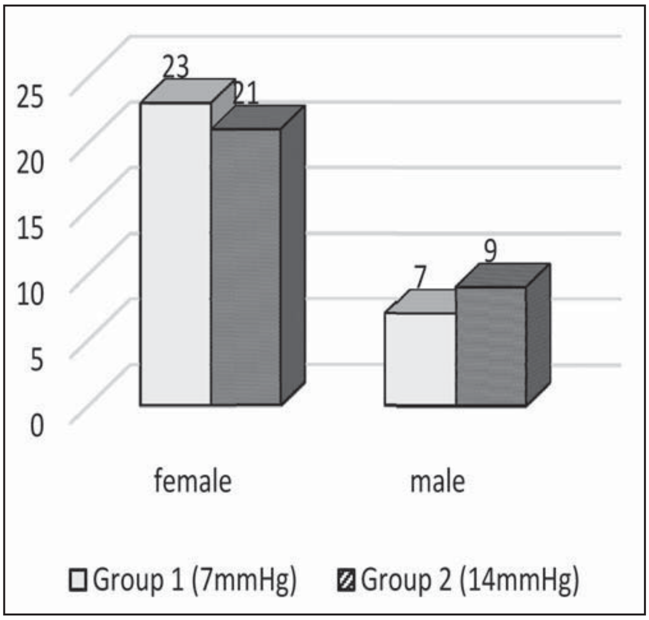

Fig 1. Gender distribution in both group

Patient parameters like mean age and duration of symptoms were almost similar. Mean duration of CO2 pneumoperitoneum created during surgery, which is the major component for effect on liver perfusion in either group was almost the same (approximately 30 minutes) with no statistically significant difference(p-value>0.05) asshown in Table 1.

Table 1. Comparison of patient parameters

Patient parameters	Group 1. (7mmHg)	Group 2. (14mmHg)	*P* value
Age (years) mean±SD	39.3±12.4	40.60±10.95	0.669
Duration of Symptoms (weeks) (mean±SD)	77.4±74.5	61.6±71.9	0.407
Total time of pneumoperitoneum (minutes)(mean±SD)	33.6±12.2	31.8±12.2	0.576

LFT at different times was compared between the two groups. Mean values of different parameters of LFT using t-test are shown in Table 2. There was slight increase in the levels in almost all tests (TB, DB, SGOT, SGPT and ALP) in 24hours post-operatively, which came near to pre-op levels in 7 days but the difference is not statistically significant. None of the patients show any clinical features of this difference. As these levels were done at different timings, the findings were compared within the same group and between the two groups at different times using the one-way ANOVA test (Table 3: p-value >0.05).

Table 2. Analysis of parameters of Liver function test between two group

Liver function test parameters		Group 1. (7mmHg) (mean±SD)	Group 2. (14mmHg) (mean±SD)	P-value
Total Bilirubin (mg/dl)	Pre-op	0.603±0.23	0.620±0.37	0.83
	24hr post-op	0.879±0.27	0.939±0.38	0.48
	7days post op	0.391±0.16	0.460±0.18	0.12
Direct bilirubin (mg/dl)	Pre-op	0.152±0.11	0.139±0.17	0.73
	24hr post-op	0.353±0.29	0.354±0.31	0.99
	7days post op	0.097±0.05	0.111±0.89	0.47
SGOT (IU/L)	Pre-op	30.43±14.10	28.93±13.90	0.68
	24hr post-op	39.87±11.53	39.50±15.34	0.92
	7days post op	26.33±9.82	27.00±11.35	0.52
SGPT (IU/L)	Pre-op	28.77±13.75	31.07±13.80	0.52
	24hr post-op	40.56±11.22	41.47±13.85	0.78
	7days post op	30.27±15.11	31.23±13.52	0.78
ALP (IU/L)	Pre-op	70.80±48.91	60.53±46.35	0.41
	24hr post-op	83.03±48.23	74.53±48.57	0.50
	7days post op	76.60±54.60	78.47±44.51	0.88

Table 3. One-way ANOVA of different parameters of Liver function test showing relation within and between different pneumoperitoneal pressure groups

Liver function test parameters		Grouping according to intra peritoneal pressure (7mmHg&14mmH)	Sum of Squares	Mean Square	*P* - value
Total Bilirubin (mg/dl)	Pre op	Between Groups	0.004	0.004	0.832
		Within Group	5.551	0.96	
	At 24 hours	Between Groups	0.055	0.055	0.483
		Within Group	6.352	0.110	
	On 7th day	Between Groups	0.072	0.072	0.125
		Within Group	1.723	0.030	
Direct bilirubin (mg/dl)	Pre op	Between Groups	0.002	0.002	0.733
		Within Group	1.190	0.021	
	At 24 hours	Between Groups	0.000	0.000	0.990
		Within Group	5.191	0.089	
	On 7th day	Between Groups	0.003	0.003	0.472
		Within Group	0.325	0.006	
SGOT (IU/L)	Pre op	Between Groups	33.750	33.750	0.680
		Within Group	11375.233	196.125	
	At 24 hours	Between Groups	2.017	2.017	0.917
		Within Group	10682.967	184.189	
	On 7th day	Between Groups	6.667	6.667	0.809
		Within Group	6538.667	112.736	
SGPT (IU/L)	Pre op	Between Groups	79.350	79.350	0.520
		Within Group	11007.233	189.780	
	At 24 hours	Between Groups	12.150	12.150	0.783
		Within Group	9214.833	158.876	
	On 7th day	Between Groups	14.017	14.017	0.795
		Within Group	11915.233	205.435	
ALP (IU/L)	Pre op	Between Groups	1581.067	1581.067	0.407
		Within Group	131676.267	220.280	
	At 24 hours	Between Groups	1083.750	1083.750	0.499
		Within Group	135872.433	2342.628	
	On 7th day	Between Groups	52.267	52.267	0.885
		Within Group	143948.667	2481.874	

None of the cases had to be converted to open surgery due to difficulty created by low pressure pneumoperitoneum and none of them needed to switchover to the higher pressure group.

DISCUSSION

The intraabdominal pressure created by pneumoperitoneum during laparoscopic cholecystectomy elevates the diaphragm and decreases the lung compliance.[14, 15] Decrease in venous return to the heart decreases the stroke volume and cardiac output which further decreases the renal, splanchnic and hepato-portal blood flow.[16] This effect in splanchnic and hepatic perfusion due to pneumoperitoneum is yet to be understood in detail.[17] There may be 40-80% increase in the level of liver function tests due to several reasons: First, Hepatic hypo-perfusion induced by pneumoperitoneum. Second, duration of pneumoperitoneum at constant pressure. Third, is general anaesthesia itself. Fourth, traction on the gall bladder that induces squeeze pressure on the liver with release of enzymes into the circulation. Fifth, prolonged and extensive use of diathermy induced hepatocyte damage. Sixth, transient kink of biliary tree, which may release enzymes into the circulation. Seventh, passage of small stone into the common bile duct. Eighth, inadvertent clipping of the right branch of the hepatic artery and hepatic ischemia. Ninth, combination of more than one cause and tenth is bile duct injury. [18, 19] As the normal portal venous pressure is 7-10 mm Hg, the pneumoperitoneum pressure above this level may decrease intraoperative portal venous flow. The decrease of hepatic microcirculation during laparoscopic cholecystectomy done under 12mm Hg has been shown by Eleftheriadis *et al* with abrupt elevation after de-suffl ation. [16] Observation of signifi cant elevation of SGOT and SGPT has been suggested by Hasukic in patients operated under high pressure of 14mmHg of pneumoperitoneum rather than those operated under low pressure of 7 mm Hg. [20] Because of these ischemic effects on hepatocytes, gasless and low pressure laparoscopic procedures were recommended.[21] According to Morino *et al*, if the duration of operation with a constant pneumoperitoneum is more than 60 minutes, there is signifi cant elevation in AST and ALP levels.[22] The pressure and duration of pneumoperitoneum are the only factors that are unique in laparoscopic cholecystectomy in comparison to open cholecystectomy, among other reasons for the changes in liver function test in post-operative period.

To minimize the effect of all other determinant factors including the factors given above, we established strict inclusion criteria and followed similar standard anaesthetic, operative and post-operative protocol. Surgery was performed by the surgeons with the experience of good volume of laparoscopic cholecystectomies. The technical procedure was also similar in almost all cases. Mean duration of pneumoperitoneum was less than 60 minutes. We operated with three ports, this obviated the probable compression of the liver by the fourth port while retracting the fundus of the gall bladder upward and outward. We included the 7th day liver function test to see both the early (24 hour) and late (7 day) effects.

There was no significant difference in patient demographics, and operative parameters like duration of symptoms and duration of pneumoperitoneum in between the two groups. We observed slight difference in the mean value of Liver function tests (LFT) done pre-operatively, early post- operative (24 hour) and late post-operative (7 day), but it was not statistically significant between the two groups and within the same group at different time periods. The liver receives approximately 25 % of the total cardiac output directly and 75% of blood flow to the liver is from the portal venous system. Since, the liver does not have direct regulation of portal flow, it regulates the flow indirectly by impacting in the flow of splanchnic blood supply. Being an organ with high vascular capacitance and vascular compliance it can affect the cardiac load and subsequently cardiac output and splanchnic circulation, hence affecting the portal flow. The other mechanism of hepatic perfusion control is hepatic arterial buffer response (HABR) i.e. the reduced portal flow activates the system to increase the hepatic arterial flow secondary to reduced-washout of adenosine from the space of Mall around the terminal branches of the portal vein and hepatic artery.[23] Many studies have shown that under physiologic and pathophysiologic conditions, hepatic oxygenation is preserved by regulating the hepatic arterial flow counteracting the portal blood flow alteration. Contrary to this, the experimental study in rats showed that the hepatic arterial flow does not compensate for reduction of portal venous inflow induced by the increase in intra-abdominal pressure. There is decrease in liver perfusion, inadequate oxygen supply and hepatocyte injury in higher pressure pneumoperitoneum surgery in comparison to low pressure surgery. [9]In our study, although the data could not show any significant change in LFT, mean value of bilirubin and enzymes increased slightly in 24-hours, which came down on the 7th day in both the groups. These effects did not have statistical relation and clinical impact as well. When the value of LFT is compared in between the groups during different time periods, the study failed to show the assumption that the difference in pneumoperitoneum pressure affects the function of the liver. Findings in this study support the probability of an important role of "hepatic arterial buffer response (HABR) system" in maintaining hepatic oxygenation and perfusion during compromised portal pressure. Although it is difficult to explain the cause, there may be many other reasons apart from pneumoperitoneal pressure for the rise of liver function parameters, especially in other studies mentioned above.

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