J Med Sci
Vol. 42, No. 1, March 2010: 10-15

Comparison of serum aminotransferase between gas and gasless laparoscopy cholecystectomy

Imam Sofii*, Hendro Wartatmo, Agus Barmawi
Division of Digestive Surgery, Department of Surgery, Faculty of Medicine, Gadjah Mada University/Dr.Sardjito Hospital, Yogyakarta

ABSTRACT

Carbondioxide (CO_2) insufflations in laparoscopy with gas will increase intraabdominal pressure that influences the hemodynamic, lungs, and kidneys. One of important hemodynamic changes is temporary reduction of hepatic blood flow because of pneumoperitoneum. Pressure caused by pneumoperitoneum can influence ischemia degree of hepatic cell and cause hepatic enzymes increase. Enzyme that includes in hepatic enzyme is aminotransferase, which consists of: transaminase (AST) or glutamic oxaloacetic transaminase serum and alanine transaminase (ALT) or glutamic pyruvic transaminase serum. Laparoscopy method by lifting abdomen wall (gasless laparoscopy) without CO_2 insufflations can decrease the damaging effects of high intraabdominal pressure. This research was an experimental research with single blind randomized clinical trial (RCT) plan, with observation of symptomatic cholelithiasis patients who underwent cholecystectomy laparoscopic cholecystectomy with gas or CO_2 (pneumoperitoneum) or without gas (gasless). Hepatic function tests were then held at 24 hours and 72 hours after operation. Research subjects were symptomatic cholelithiasis patients who fulfilled inclusion and exclusion criteria. Samples needed were 24 people in each group. The independent variable was patients with symptomatic cholelithiasis who underwent cholecystectomy laparoscoped with gas compared to those being cholecystectomy laparoscoped without gas. The dependent variable was aminotransferase enzyme value before operation, and 24, 72 hours postoperation. The data were analyzed using Kolmogorov Smirnov, independent t-test, pair t-test, and Mann Whitney test. It was obtained 21 cases for men (43.75%), 27 cases for women (56.25%). The average age of the group laparoscopy with gas was 47.16 ± 10.76 years old and the group laparoscopy without gas was 45.3 ± 11.48 years old ($p > 0,05$). The average values of AST and ALT 24 hours postoperation of the group laparoscopy without gas were 21.9 ± 7.6 U/L (increase 24%) and 26.3 ± 5.2 U/L (increase 46%) compared to 65.8 ± 18.4 U/L (increase 206%) and 62.8 ± 14.3 U/L (increase 280%) in the group laparoscopy with gas ($p < 0,05$). The average values of AST and ALT 72 hours postoperation of the group laparoscopy without gas were 24.7 ± 8.3 U/L (increase 33%) and 28.9 ± 7.3 U/L (increase 17%) compared to 71,5 ± 28,6 U/L (increase 250%) and 75.8 ± 16.9 U/L (increase 360%) in the group laparoscopy with gas ($p < 0,05$). In conclusion, there were significantly increases of serum aminotransferase values (AST and ALT) in cholecystectomy laparoscopy with gas compared to in cholecystectomy laparoscopy without gas.

Key words: cholecystectomy laparoscopy – pneumoperitoneum - gasless – serum aminotransferase

INTRODUCTION

In the last 25 years, laparoscopic cholecystectomy has replaced the open cholecystectomy procedure for managing diseases of the gallbladder and has become gold standard for symptomatic cholelithiasis cases. Even though laparoscopic cholecystectomy has many advantages compared with laparotomy, there are several things to consider related to the effect of pneumoperitoneum to the cardiovascular and respiratory system.[1,2]

One important hemodynamic change is the temporary reduction in hepatic blood flow caused by pneumoperitoneum. The depression caused by pneumoperitoneum can influence the degree of hepatocyte ischemia and cause elevation of liver enzyme. Tan *et al*[3]. suggested that some factors contribute in the elevation of transaminase serum

* coresponding author: *imam_djawa@yahoo.com*

after laparoscopic cholecystectomy and colorectal, first the carbon dioxide pneumoperitoneum shows a significant elevation in the serum liver enzyme after surgery. A different situation was found in post cholecystectomy and colorectal laparotomy patients which did not experience a change in the serum liver enzyme. Intraabdominal pressure in laparoscopy is between 12-14 mmHg, the normal portal blood pressure is 7-10 mmHg, this means that laparoscopy can reduce the portal blood flow and cause disturbance in the liver function.[3,4]

Sudden fluctuation in the intraabdominal pressure during laparoscopy can cause undulation in the portal blood flow. The undulation and re-irrigation from the organ blood flow can cause ischemia and re-irrigation damage, especially to the Kuffer cells and hepatic sinusoid endothelial cells. The second possible cause of post laparoscopic cholecystectomy serum liver enzyme elevation is the liver squeeze effect. Traction in the gallbladder can cause excretion of this enzyme into the bloodstream; this mechanism was found in animals. The third possible cause is the local effect of using diathermy in the hepatic surface and the heat extension to the hepatic parenchyma. This hypothesis was supported by many studies, using the same diathermy type and intensity between laparoscopy and open surgery. No reference has compared the post cholecystectomy enzyme in diathermy users and non users in the clinical application.[4,5]

An additional cause experienced by the patient is temporary liver dysfunction after general anesthesia. This complication was related to the effect of general anesthesia to the splanchnic blood flow and oxygen consumption. Other mechanism that is probably related to the elevation of serum liver enzyme is the possibility of clipping the right branches of the hepatic artery or additional arterial branches which supply blood to the liver.[6]

Every laparoscopy surgery needs enough room in the peritoneal space to achieve the diagnostic and therapeutic purposes. This space can be reached using mechanical traction from the abdominal wall (gasless laparoscopy) or distending the peritoneal space using carbon dioxide gas (pneumoperitoneum). Carbondioxide is often used for pneumoperitoneum because it is safe and quickly cleaned by the lungs, does not produce optical distortion, reduces the burn wound, not expensive and easy to get. To prevent the disadvantage from carbondioxide insufflations, a device to move the anterior abdominal wall surface is used to achieve "gasless laparoscopy". Some of these devices move the anterior abdominal wall surface by skin or subcutaneous traction (U retraction or subcutaneous wire), intraperitoneal retractor can also be used. The advantages are preventing the physiological changes caused by carbon dioxide; minimize the risk of gas emboli, using a conventional device which is relative save for high risk patients. Other technique to be considered is the hybrid system with low pressure pneumoperitoneum (< 8 mmHg) combined with anterior abdominal wall traction using conventional devices.[5,7]

Aminotransferase enzyme includes AST or glutamic oxaloacetic transaminase serum and alanine transaminase (ALT) or glutamic pyruvic transaminase. Aminotransferase is a mitochondrial enzyme found in the heart, liver, muscle, and kidney. The serum level will rise if the body experiences acute damage caused by excretion of damaged cells. AST is a cytozolic enzyme in the liver. Increase in this serum level is more spesific in liver impairment than ALT, even though the amount of AST is smaller than ALT.[6]

The purpose of this research is to evaluate the changes of the liver because of pneumoperitoneum laparoscopy cholecistecytomy and without pneumoperitoneum (gasless). This research is very important to identify high risk patient in increasing intraabdominal pressure. It can be used for preoperative optimalizing and monitoring, also for finding the save operation technique, for example with laparoscopy gasless or open cholecystectomy technique.

MATERIALS AND METHODS

Subject was symptomatic cholelithiasis patient in several hospital at Yogyakarta. Subject should fulfil the inclussion and exclussion criterias. The inclussion criterias were age 20-60 years old, diagnosed by symtomatic cholelithiasis, operated by cholecystectomy laparoscopic with CO_2 or without CO_2, and patient with cholecystitis chronic. The

exclussion criteria were, patient with chirrosis, liver metastatic tumor, liver primary tumor, and liver function impairment before operate.

This study was an experimental research with single blind randomized clinical trial (RCT) for cholecystitis and cholelithiasis patient with normal liver function. Testing of liver function was performed at 24 and 72 hours postoperation. The number of sample was based on CI=95% and power test 80%. In each group contained 24 cases.

The independent variable was symptomatic cholelithiasis patient operated by laparoscopy cholecystecytomy either with or without gas. The dependent variable based on aminotransferase value before operation, and 24, 72 hours postoperation. Data analysis used Kolmogorov Smirnov, independent T-test, Pair T-test and Man Whitney Test version 13 for windows.

The study has been approved by the Health Research Ethics Committee of Faculty of Medicine, Gadjah Mada University, Yogyakarta.

RESULTS

This study consisted of 48 cases that operate with pneumoperitoneum laparoscopy cholecystecytomy or with gasless laparoscopy technique. The 21 cases (43.75%) of man subject, consisted of 11 (52.38%) gasless and 10 (47.61%) pneumoperitonium. The 27 cases (56.25%) of woman subject consisted of 12 (44.44%) gasless and 15 (55.56%) pneumoperitonium. The characteristics of gender, age and operation duration were not significantly different (TABLE 1). There was no significance sex difference between this group ($p > 0.05$). Average age of gasless group was 45.33±14.779 years old and pneumoperitoneum group was 45.27±13.108 years old. There was no significance age difference between this group ($p > 0.05$). The average operation duration time in gasless operation was 1.083±0.093 hours, and pneumoperitoneum operation was 1.2±0.189 hours. There was no significance operation duration difference between this group ($p > 0.05$).

TABLE 1. The gender, age, and operation duration characteristics of subjects

Variable	Gasless	Pneumo-peritoneum	p	RR	95%CI
Male	11	10	0.06	1.18	(0.33 – 4.17)
Female	12	15			
Age					
Mean	45.33	45.27	0.992		(-12.100-12.221)
SD	14.779	13,108			
Duration					
Mean	1.083	1.200	0.072		(-0.244-0.018)
SD	0.093	0.189			

TABLE 2 presented the comparison result of AST and ALT value preoperation in both of groups. The value of AST and ALT gasless laparoscopic group preoperation were 25.06±8.544 U/L and 17.83 (9.514) U/L, whereas in pneumoperitoneum laparoscopic group were 19.27±5.648 U/L and 12.27±5.179 U/L. The AST and ALT value preoperation in both of group were not significantly different ($p > 0.05$).

TABLE 2. Comparison of AST and ALT value preoperation between pneumoperitoneum laparoscopic choleicystectomy with gasless laparoscopic cholecystectomy

variable	Type of operation		p	95% CI
	Pneumo-ritaneum	gasless		
AST (U/L)				
Mean	19.27	25.06	0.071	(-0.538 – 12.159)
SD	5.648	8.544		
ALT (U/L)				
Mean	12.27	17.83	0.101	(-1.174 – 12.295)
SD	5.179	9.514		

The AST and ALT values preoperation and 24 hours postoperation on gasless cholecystectomy laparoscopic group were presented on TABLE 3, whereas on pneumoperitoneum cholecystectomy laparoscopic group were presented on TABLE 4. The increase of liver enzyme 24 hours postoperation on gasless laparoscopic group (24% for AST and 46% for ALT) was not significantly different ($p > 0.05$), whereas on pneumoperitoneum laparoscopic group (206% for AST and 280% for ALT) was significantly different ($p < 0.05$).

TABLE 3. Comparison AST and ALT value between preoperation with the 24 hours after gasless cholecystectomy laparoscopic

variable	preoperation (mean±SD)	24 hours postoperation (mean±SD)	p	95% Cl
AST (U/L)	25.08±8.544	31.79±9.466	0.194	(-15.755 – 3.588)
ALT (U/L)	17.83±9.514	26.08±21.030	0.277	(-24.113 – 7.613)

TABLE 4. Comparison AST and ALT value between preoperation with 24 hours after pneumoperitoneum holecystectomy laparoscopic

Variable	preoperation (mean±SD)	24 hours postoperation (mean±SD)	p	95% CI
AST (U/L)	19.272±5.658	59.090±14.583	0.001	(-51.156 - -28517)
ALT(U/L)	12.272±5.178	46.636±22.200	0.001	(-50.970 - -17.756)

The AST and ALT values preoperation and 72 hours postoperation on gasless cholecystectomy laparoscopic group and on pneumoperitoneum cholecystectomy laparoscopic group were presented on TABLE 5 and 6. The increase of liver enzyme 72 hours postoperation on gasless laparoscopic group (33% for AST and 17% for ALT) was not significantly different ($p > 0.05$), whereas on pneumoperitoneum laparoscopic group (250% for AST and 360% for ALT) was significantly different ($p < 0.05$).

TABLE 5. Comparison AST and ALT value between preoperation and 72 hours after gasless cholecystectomy laparoscopic

Variable	preoperation (mean±SD)	72 hours postoperation (mean±SD)	p	95% CI
AST (U/L)	25.08±8.544	33.33±17.691	0.223	(-22.307 – 5.807)
ALT (U/L)	17.83±9.514	20.92±10.077	0.450	(-11.757 – 5.588)

TABLE 6. Comparison AST and ALT value between preoperation and 72 hours after pneumoperitoneum cholecystectomy

Variable	preoperation (mean±SD)	72 hours postoperation (mean±SD)	p	95% CI
AST (U/L)	19.272±5.658	68.000±28.284	0.001	(-70,764 - -26.690)
ALT (U/L)	12.272±5.178	57.454±43.144	0.001	(-76.679 - -13.692)

The average percentage increased in serum AST and ALT level 24 hours postoperation of pneumoperitoneum laparoscopy were 206% and 280%, whereas gasless laparoscopy were 24% and 46% (TABLE 7). The increased in serum AST and ALT level 24 hours postoperation in both of group were significantly different ($p < 0.05$). The average percentage increased in serum AST and ALT level 72 hours postoperation of pneumoperitoneum laparoscopy were 250% and 360%, whereas gasless laparoscopy were 37% and 17% (TABLE 8). The increased in serum AST and ALT level 72 hours postoperation in both of group were significantly different ($p < 0.05$).

TABLE 7. Comparison of AST and ALT value 24 hours postoperation between pneumoperitoneum choleicystectomy laparoscopic with gasless cholecystectomy laparoscopic.

Variable	Pneumoperitoneum		Gasless		p	95% CI
	preoperation	24 hours	preoperation	24 hours		
	(mean±SD)	(mean±SD)	(mean±SD)	(mean±SD)		
AST (U/L)	19.272±5.658	59.090±14.585	25.08±8.544	31.17±9.466	0.001	(-47,267 - -19,482)
ALT (U/L)	12.272±5.178	46.636±22.200	17.83±9.514	26.08±21.030	0.02	(-47,684 - -4,542)

TABLE 8. Comparison of AST and ALT value 72 hours postoperation between pneumoperitoneum laparoscopic choleicystectomy with gasless laparoscopic cholecystectomy

Variable	Pneumoperitoneum		Gasless		p	95% CI
	Preoperation	72 hours	Preoperation	72 hours		
	(mean±SD)	(mean±SD)	(mean±SD)	(mean±SD)		
AST (U/L)	19.272±5.658	68.000±28.284	25.08±8.544	33.33±17.691	0.002	(-64,546 - -16,408)
ALT (U/L)	12.272±5.178	57.454±43.144	17.83±9.514	20.92±10.077	0.007	(-71.456 - -12.740)

The comparison aminotransferase serum (AST and ALT) between pneumoperitoneum choleicystectomy laparoscopic with gasless choleicystectomy laparoscopic preoperation, 24 and 72 hours postoperation was discribed in FIGURE 1. The aminotransferase serum (AST and ALT) of pneumoperitoneum choleicystectomy laparoscopic at both 24 and 72 hours postoperation were hingher than of gasless choleicystectomy laparoscopic.

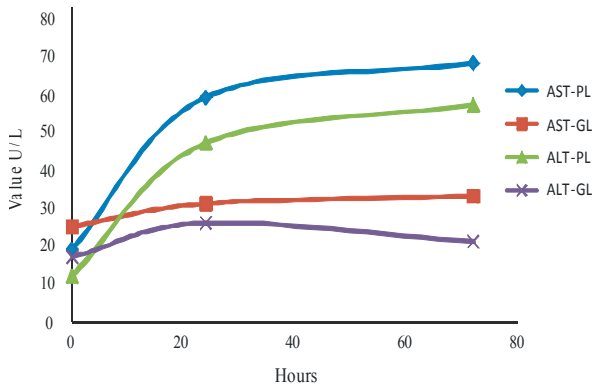

FIGURE 1. Comparison aminotransferase serum (AST and ALT) between pneumoperitoneum choleicystectomy laparoscopic (PL) with gasless choleicystectomy laparoscopic (GL)

DISCUSSION

Sakorafas, *et al*[8]. reported that AST and ALT value increased significantly at 24 and 72 hours after conventional (pneumoperitoneum) cholecystectomy laparoscopic and decreased to the normal value at 10 days postoperative. However, the increasing value did not caused incresing of morbidity and mortality. The increased of liver enzyme after conventional (pneumoperitoneum) laparoscopic cholecystectomy incidentally have been known. The clinical importance of it is not clear yet, but this temporary alteration of liver function could be a concideration before performing conventional (pneumoperitoneum) laparoscopy.

The normal porta vein pressure is 7-10 mmHg and half of hepatic blood flow coming from porta vein, so pressure of pneumoperitoneum to 14 mmHg could cause transient ischemic in hepatocytes. Jakimovics said that intraperitonel pressure to 14 mmHg could decreased portal blood flow to 53% using Doppler technique.[7]

To prevent further hepatocyte damage, conventional (pneumoperitoneum) choleicystectomy laparoscopic was adviced to avoided for somtomatic cholelithiasis patient with alteration of liver function. Gasless laparoscopic choleicystectomy, hybrid system (low pressure pneumoperitoneum technique

combined with anterior abdominal wall traction), and opened choleicystectomy were as alternative.

ACKNOWLEDGMENT

We would like to thank Prof. Dr. dr. Basarul Hamafi, SpBK-BD for his suggestions to improve this manuscript.

CONCLUSION

There were significantly increases of serum aminotransferase values (AST and ALT) in cholecystectomy laparoscopy with gas compared to in cholecystectomy laparoscopy without gas.

REFERENCES

1. Guven EH, Oral S. Hepar enzyme alterations after laparoscopy cholecystectomy. J Gastrointestin Liver Dis 2007; 16(4): 391-4.
2. Szold A, Weinbroum AA. Carbon dioxide pneumoperitoneum-related hepar injury is pressure dependent: a study in an isolated-perfused organ model. Surg Endosc 2008; 22(2): 365-71.
3. Tan M, Xu FF, Peng JS, Li DM, Chen LH, Ly B et al. Change in level of serum hepar enzim after laparoscopic surgery. World J Gastroenterol 2003; 9(2): 364-7.
4. Marakis G, Pavlidis TE, Ballas K, Rafailidids S. Alterations in hepar function test following laparoscopic cholecystectomy. Int J Surg 2006; 8(1): 84-9.
5. Bickel A, Drobot A, Aviram M. Validation and reduction of the oxidative stress following laparoscopic operation. Ann Surg 2007; 21:31-5.
6. Sherlock S, Dooley J. Disease of hepar and billiary system. 11th ed. Oxford. Blackweil Publishing Company. 2002.
7. Hasukio S, Kosuta D, Muminhodzic. Comparison of postoperative hepatic function between laparoscopic and open cholecystectomy. Med Princ Pract 2005; 14(3): 165-8.
8. Sakorafas G, Anagnostopoulos G, Satafyla V. Elevation of serum hepar ezymes after laparoscopic cholecystectomy. N Z Med J 2005; 118:1210-20.