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RESEARCH ARTICLE

A PROSPECTIVE STUDY TO EVALUATE THE EFFECTS OF CO₂ PNEUMOPERITONEUM ON HEPATIC ENZYMES IN LAPAROSCOPIC SURGERIES

Dr. B.P Sunil¹, Dr. Vasant Kumar V. Teggimani², Dr. Sachin M.B.³, Dr. Sajid Ibrahim Ali⁴ and Dr. Sachin R.⁵

1. Senior Resident Dept of Gen Surgery Jss Medical College Mysore.
2. Assistant Professor Dept of Gen Surgery Kimshubli.
3. Assistant Professor JSS MC MYSORE.
4. Assistant Professor Dept of Gen Surgery SDM College of Medical Sciences & Hospital, Dharwad.
5. Senior Resident Jss Medical College Mysore.

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Abstract

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Introduction:-

Minimally invasive surgery, especially laparoscopic surgery, has changed the face of general surgery. Laparoscopy provides access to the peritoneal cavity both for diagnosis and many surgical interventions that were previously possible only by laparotomy. Its advantages are well recognized and include reduced post-operative pain, shorter length of hospital stay and superior cosmetic results. And the magnifying factors in it have made it easy to identify the structures and thereby chances of injury. Some of the diseases, which were not tackled due to fear of damage to surrounding structures during access, are presently being treated easily with laparoscopic surgery. Laparoscopy has had a profound influence on management of patients with impalpable testes, gallbladder disease and Hirschsprung's disease.¹

Pneumoperitoneum is a crucial factor in laparoscopy. Insufflation with it helps to maximize the working space in the peritoneal cavity. Method of insufflation is usually intra-peritoneal, wherein the abdominal wall gets elevated and the viscera gets suppressed. Carbon dioxide (CO₂) is the preferred gas for establishing a pneumoperitoneum, and this method of creating pneumoperitoneum using CO₂ is referred to as capnoperitoneum. Although the mainstay for laparoscopic surgery, it has its own limiting factors. It produces elevated intra-abdominal pressure (IAP) and continuous compression on intra-abdominal organs with elevation of diaphragm, which might potentially influence the hepatic, cardio-pulmonary and renal functions.

However the operation time may be prolonged and the pneumoperitoneum produces elevated intra abdominal pressure with continuous compression of intra-abdominal organs, which potentially, influences hepatic microcirculatory perfusion.²⁻⁴ One of the important hemodynamic changes is the transient reduction in hepatic blood flow caused by a pneumoperitoneum.⁴ The pressure of the created pneumoperitoneum and its duration was shown to influence, the degree of hepatic ischemia. This results in elevations in liver enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase and bilirubin. Although laparoscopic surgeries are associated with transient elevation of liver enzymes, the disturbances after the procedure are self-limited and not associated with any morbidity in patients with normal liver function tests.

Corresponding Author:- Dr. Sajid Ibrahim Ali

Address:- Assistant Professor Dept of Gen Surgery SDM College of Medical Sciences & Hospital, Sattur Colony, Manjushree Nagar, Dharwad -580009.

Many studies have disclosed unexplained changes in postoperative liver function tests (LFTs) in patients, undergoing laparoscopic procedures. It has been noticed that, following laparoscopic surgery, level of certain serum liver enzymes rose markedly in most patients who had shown normal preoperative LFTs. This observation raised several questions - Are these changes, of any clinical significance? What is the mechanism responsible? These changes might be attributed to hepatocellular dysfunction, secondary to one or, combination of CO₂ pneumoperitoneum, diathermy extruding liver, branch of hepatic artery injured and general anaesthesia. The transient elevation of hepatic enzymes, showed no apparent clinical implication in most, patients who received laparoscopic surgery according to follow-up observations and feedback from these patients. However in patients with pre-operatively altered liver function tests, this may further worsen and for the same reason some surgeons use abdominal lift technique to avoid these effects of CO₂ pneumoperitoneum.

However, any increase in liver enzymes, is a matter of concern to the clinician and warrants further investigation to determine the underlying pathology, as laparoscopy, is gaining wide popularity all around the world. There have been no studies in our setting to evaluate the potential deleterious effects of laparoscopic surgery on hepatic function. This study aims to investigate the alterations in the serum levels of liver enzymes following laparoscopic surgeries performed under constant intra peritoneal pressure (12 – 14 mm Hg) at Tertiary care teaching hospital.

Methodology:-

This is a prospective cross-sectional study performed in the Department of General Surgery. KIMS, Hubli between December 2017 to December 2018

Patients admitted in department of General surgery at Karnataka institute of Medical sciences, Hubli and posted for elective laparoscopic surgeries.

This prospective controlled study was conducted to evaluate the effects of CO₂ pneumoperitoneum in laparoscopic procedures on hepatic enzymes. The study population constituted 53 consenting inpatients, selected by purposive sampling from those who underwent various laparoscopic surgeries in the department of General Surgery, Karnataka institute of medical sciences , Hubli in the above mentioned period.

Prior to selection, they underwent routine history taking, physical examination and investigations to exclude pre-existing liver diseases or generalized debility. Those selected had normal values of serum liver enzymes prior to surgery.

Approval from the ethical committee of the institution was taken. All the patients were explained about the basis of the study and informed consents were obtained.

Patients having normal pre-operative liver enzymes were included in our study. Those patients with pre operative abnormality in liver enzymes or deranged LFTs, suspected chronic liver diseases or co-existing liver disease, common bile duct pathology, conversion to open procedure, haematological disorders, intra-operative complications – hypotension, patients who had undergone endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy within one week before surgery, patients on long term use of hepatotoxic drugs, Patients who develop complications such as bile duct injury, obstruction, infection, leakage, patients not giving consent for being part of our study and those undergoing total extra peritoneal hernia repair.

Protocol:

The 53 patients selected for the study had pre-operatively tested liver functions and were within normal limits. These pre-operative values will be the baseline values to compare with values done post-operatively and to check for changes or trends in changes of hepatic enzymes.

Statistical Methods:

Data entry was done in Microsoft Excel spreadsheet and all the statistical analysis was performed in SPSS version 20.0.

All data were expressed as the mean ± standard deviation. P value less than 0.05 was considered to be statistically significant.

Results:-

in our study we found that majority of the study population was between 20-29 years, which is contradictory to universally performed studies. Unusually, we also found that 69.81% of study population was females. Mean age of the study population was 40.47 +/- 14.83 years.

In the present study, we analyzed the types of studies the patient underwent, as this would influence the duration of pneumoperitoneum that was maintained during the surgery. In our study we found that 86.79% patients had undergone laparoscopic cholecystectomy.

In our study, we found that there was a significant elevation in the total bilirubin levels before and after laparoscopic surgery. (p value <0.05)

However, the mean direct bilirubin and indirect bilirubin was not significantly elevated.

When we analyzed the effect of pneumoperitoneum on hepatic enzymes, we found that AST, ALT and ALP was significantly elevated post operatively.

Table 1:- Comparison of Pre OP and Post Op values of AST (U/L) scores by dependent t test.

Time points	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	P-value
Pre Op	29.68	14.28					
Post Op (First 24-48 hrs)	90.75	68.48	-61.08	69.67	-205.79	-6.3819	0.0001*

*p<0.05

Table 2:- Comparison of Pre Op and Post Op values of ALT (U/L) scores by dependent t test.

Time points	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	P-value
Pre Op	25.36	17.60					
Post OP (First 24-48 hrs)	90.32	70.51	-64.96	71.44	-256.18	-6.6200	0.0001*

*p<0.05

Table 3:- Comparison of Pre OP and Post Op values of ALP (U/L) scores by dependent t test.

Time points	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	P-value
Pre Op	90.14	55.57					
Post OP (First 24-48 hrs)	107.23	61.69	-17.08	32.93	-18.95	-3.7767	0.0004*

*p<0.05

The mean duration of surgery among those who had significant changes (more than the double of pre-operative values) in serum liver enzymes was higher was 86 minutes on an average. Whereas the mean duration among those who didn't show significant changes was 61.68 minutes on an average .

Discussion:-

Laparoscopic surgery has become the established method of treatment for many surgical conditions. The progress in laparoscopic procedures has largely been due to the technological advances in endoscopic optics, video cameras and endoscopic instrumentation. Smaller incisions, reduced postoperative pain, shorter hospital stay, early ambulation and return to work are some of the advantages that increased the popularity of laparoscopic procedures.⁶ Although laparoscopy offered many advantages over laparotomy, new concerns arose regarding the effects of

pneumoperitoneum on the cardiovascular and respiratory system. Many studies in the past decade, have disclosed unexplained changes in post-operative liver function in patients undergoing laparoscopic procedures. CO₂ pneumoperitoneum is the main reason for this change in serum liver enzymes, as this is the main difference between laparoscopic and open surgeries. Our study performed to assess the presence of clinical significance of unexplained alterations in liver enzymes subsequent to laparoscopic surgeries.

This study is to evaluate the potential deleterious effects of laparoscopic surgery on hepatic function and to assess the clinical significance of unexplained disturbances in liver enzymes following laparoscopic surgeries. The post-operative increase seen in the levels of serum bilirubin and liver enzymes was significant and occurred irrespective of the type of laparoscopic surgery they underwent. None of the patients presented with post-operative clinical hepatic dysfunction in the follow up period.

It was noticed that in the first 24-48 hrs, doubling of the pre-operative values was seen in significant number of cases.

1. 53% of patients had doubling of serum AST levels,
2. 57% had doubling of serum ALT levels,
3. 2.5% of patients in case of serum Bilirubin,
4. 9.4% had doubling of serum ALP levels.

All the patients in our study were subjected to carbon dioxide pneumoperitoneum and they showed changes in post-operative serum liver enzymes level. This is consistent with the results of other similar studies. The intra-abdominal pressure of 12 – 15 mmHg used in our study was higher than the normal portal venous pressure of 7 – 10mmHg. This might cause a reduction in portal blood flow and lead to alterations in liver function. During laparoscopic surgery, there is an elevation and depression of intra-abdominal pressure (IAP) in a short time, this sudden alteration of IAP could cause undulation of portal blood flow. This undulation in blood flow and re-irrigation of organs may give rise to ischemia and re-irrigation damage of tissues and organs, especially the Kupffer and endothelial cells of hepatic sinusoids.⁷ This can cause free radical generation.⁸ The role of reperfusion related mechanisms after laparoscopy and the production of free radicals are however smaller than the role of total surgical injury during open surgery.

Out of 53 patients in our study population, 16 were male patients and 37 were females. In the 10 year age distribution of patients in our study, maximum number of patients were in the age group of 20-29 years i.e. 16 out of the 53 patients (30% of the study population). 8 out of 53 patients (15% of the study population) were aged more than 60years. Mean age being 40 years. Our study included patients who underwent various types of laparoscopic surgeries. Most common indication being cholelithiasis and most common surgery among is laparoscopic cholecystectomy. 85% of the patients underwent cholecystectomy, 10% underwent appendectomy and 5% underwent laparoscopic procedures for pseudocyst of pancreas.

In all patients, liver function tests were done pre operatively and were found to be normal. Liver function tests especially for liver enzymes were repeated postoperatively in first 24-48 hours for all the patients.

12 patients out of 53 (who had elevated liver enzymes in the first 24-48 hrs), who followed up after discharge were followed up on post-op day 7 and further subjected for liver function tests to check the trends in post operative changes of liver enzymes.

Changes in serum AST

The mean value of serum AST pre-operatively was 29.68U/L. Mean value of serum AST done in first 24-48hrs post operatively is 90.75U/L. There was a significant increase in serum AST levels immediate post-operatively when compared to the pre-op values. The P value of which being statistically significant 0.0001.

Changes in serum ALT

The mean value of serum ALT pre-operatively was 25.36U/L. Mean value of serum ALT done in first 24-48hrs post operatively is 90.32U/L. There was a significant increase in serum ALT levels immediate post-operatively when compared to the pre-op values. The P value of which being statistically significant 0.0001.

Changes in serum ALP

The mean value of serum ALP pre-operatively was 90.14 U/L. Mean value of serum ALP done in first 24-48hrs post operatively is 107.23 U/L. There was a significant increase in serum ALP levels immediate post-operatively when compared to the pre-op values. The P value of which being statistically significant 0.0004.

Changes in serum bilirubin

The mean value of serum total bilirubin pre-operatively was 0.73 mg/dl. Mean value of serum total bilirubin done in first 24-48hrs post operatively is 0.78 mg/dl. There was a significant increase in serum total bilirubin levels immediate post-operatively when compared to the pre-op values. The P value of which being statistically significant 0.0104.

And there was no statistically significant changes in serum direct bilirubin after the laparoscopic surgery.

These significant changes in serum liver enzymes following laparoscopic surgery were not related to age and sex of the patient.

Among the 12 patients who followed up after discharge on post operative day 7, who were subjected to repeat liver function tests showed decrease in the serum liver enzymes towards pre-operative near normal values.

Considering duration of surgery to be the aggravating factor for these changes, the mean duration of surgery among those who had significant changes (more than the double of pre-operative values) in serum liver enzymes was higher (i.e. 86 minutes on an average) compared to those who didn't show significant changes (i.e. 61.68 minutes on an average).

The rise in the mean values of serum liver enzymes in our study following laparoscopic surgeries, compared to pre operative values is consistent with results of similar studies conducted.

In a similar study to evaluate the changes in the level of serum liver enzymes after laparoscopic surgery conducted by Min Tanet al⁵ blood samples from 286 patients who underwent laparoscopic cholecystectomy (LC) and 40 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 the operations. The same tests were also applied to 18 laparoscopic colorectal cancer resection (LCR) patients and 23 open colorectal cancer resection (OCR) patients to determine whether CO₂ pneumoperitoneum could alter the serum liver enzymes. The level of serum ALT and AST increased significantly during the first 48 hours post operations in both LC and LCR patients. However, no significant change of the serum liver enzymes was detected in both OC and OCR patients. As a result, there was statistically significant difference in change of both ALT and AST levels between LC and OC patients and LCR and OCR patients, respectively. By the 7th day post operation, the level of both enzymes returned to normal values. And it was concluded that Transient elevation of hepatic transaminases occurred after laparoscopic surgery. The major causative factor seemed to be the CO₂ pneumoperitoneum.

Another study by Srikantaiah Hiremath⁹, which was conducted in 50 patients who underwent laparoscopic cholecystectomy Bilirubin (total) pre-operative was 0.510 ± 0.286 mg/dl, increased 24 h after surgery to 0.684 ± 0.239 mg/dl by 134% (P = 0.000). Bilirubin (direct) increased by 168% from 0.221 ± 0.129 mg/dl to 0.372 ± 0.203 mg/dl. Gamma-glutamyl transferase (GGT) increased from 45.13 ± 19.14 U/l to 46.37 ± 19.08 , (P = 0.046). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) was found to be significantly elevated from 22.68 ± 7.031 U/l to 32.74 ± 7.731 U/l (P = 0.000) and from 33.61 ± 10.40 U/l to 56.10 ± 15.08 U/l (P = 0.000), respectively. Alkaline phosphatase did not show any elevation, pre-operative values were 72.62 ± 14.36 U/l, and after 24 h was 71.81 ± 12.60 U/l (P = 0.350).

Rikki singal et al¹⁰ in 2015 conducted study including 200 patients diagnosed with cholelithiasis and randomly divided them into two groups consisting 100 each, who underwent laparoscopic cholecystectomy and open cholecystectomy respectively and similar pre-op and post-op comparison of serum liver enzymes was done. Pre-op mean value of AST being 27 U/L was found to be elevated to 73 U/L post operatively and ALT had increased from 26 U/L to 72 U/L. These values are near close to our study results and trend of gradual reduction also noted in the late post-operative period.

Another similar study by Gauven et al¹¹ showed similar rise of hepatic enzymes. Mean value of AST increased from 22.76U/L to 61.72 U/L after the laparoscopic surgery. And mean value of ALT increased from 21.55 U/L to 60.30 U/L after the surgery. This was conducted in 86 patients who underwent laparoscopic cholecystectomy and concluded that the differences between elevations of liver enzymes were statistically significant.

Tauro LF, Sheethal CM et.al¹² Evaluation of effects of laparoscopic surgery on hepatic function in the year 2008, concluded that all types of laparoscopic procedures can cause transient elevation of hepatic enzymes and serum bilirubin for which CO₂ pneumoperitoneum is the causative factor.

Halevy et.al¹³ studied alterations in liver enzymes after laparoscopic surgeries. The possible mechanism included increased intra- abdominal pressure, squeeze pressure effect on the liver, pulling on the gall bladder, excessive use of diathermy". Many investigations were done to evaluate the causes of this elevation and concluded that low pressure pneumoperitoneum was combined with lesser side effects on liver function.

Evaluation of the effects of laparoscopic surgeries by Syed Ibrahim et al¹⁴ conducted over 60 patients undergoing various types of laparoscopic surgeries by similar protocol as our study concluded that CO₂ pneumoperitoneum is the major causative factor responsible for transient elevation of serum liver enzymes which showed no apparent clinical manifestations.

In a study of alterations in liver function tests following laparoscopic surgery by Rama Rao et al¹⁵ the level of serum AST, ALT, bilirubin and alkaline phosphatase increased significantly during the immediate post-operative period. Doubling of pre-op values of AST was seen in 28.3% and of ALT was seen in 25%. By the 3rd post-operative day, levels of AST, ALT, bilirubin and alkaline phosphatase returned to near pre-operative values. Therefore, transient elevation of hepatic enzymes occurred after all types of laparoscopic procedures.

Limitations Of Our Study

1. Sample size is smaller to conclude on duration of surgery as the aggravating factor for these significant changes in serum liver enzymes following laparoscopic surgeries, which requires studies on large scale to prove the same.
2. And all the patients who had changes in liver enzymes in the first 24-48 hrs couldn't be followed up till post operative day 7 to conclude on reduction of these elevation of serum liver enzymes to normal values as there were loss to follow up.

Conclusion:-

Serum bilirubin and liver enzymes (AST, ALT & ALP) were found to be significantly elevated following laparoscopic surgery in the first 24-48 hours.

These significant changes in liver function tests were not related to the age and sex of the patient.

Whereas the mean duration of surgery was slightly higher in the group who had significant changes in liver enzymes compared to those who didn't show the significant changes. This gives the inference that increased duration of surgery could be an aggravating factor for these changes as shown in similar studies. This further requires studies on large numbers to conclude on the duration of surgery as aggravating factors for these significant changes in liver enzymes.

Other attributing factors to hepato-cellular dysfunction thereby causing elevation of hepatic enzymes could be a combination of CO₂ pneumoperitoneum, diathermy on liver and general anaesthesia.

These changes in hepatic enzymes showed no clinical manifestations and no patients developed complications or adverse events in the post-operative period. These changes showed no outcomes on post operative wound healing or no patients had port site infections. No post-operative morbidity or mortality was found in our study. This signifies that these changes in hepatic enzymes are only transient and recovered without any sequelae.

References:-

1. Kiely JM, Brannigan AE, Foley E, Cheema S, O'Brien W, Delaney PV. Day case laparoscopic cholecystectomy is feasible. *Med Sci.* 2001; 170(2):98–99.
2. Odeberg-Werner S. Laparoscopic surgery - effects on circulatory and respiratory physiology: an overview. *Eur J SurgSuppl* 2000; 585:4-11.
3. Hasukić S. Postoperative changes in liver function tests: randomized comparison of low- and high-pressure laparoscopic cholecystectomy. *SurgEndosc* 2005 Nov; 19(11):1451-55.
4. Schmandra TC, Kim ZG, Gutt CN. Effect of insufflation gas and intraabdominal pressure on portal venous flow during pneumoperitoneum. *SurgEndosc* 2001; 15: 405-8.
5. Tan M, Xu FF et. al. "Changes in the level of serum liver enzymes after laparoscopic surgery." *World J Gastroenterol* 2003 Feb 15; 9(1;2):364-367.
6. Sood J, Kumra VP. Anaesthesia for laparoscopic surgery. *Indian J Surg* 2003; 65: 232-240.
7. Volz J, Koster S, Spacek Z, Paweletz N. Characteristic alterations of the peritoneum after carbon dioxide pneumoperitoneum. *SurgEndosc* 1999; 13: 611-614.
8. Sare M, Yilmaz I, Hamamci D, Birincioglu M, Ozmen M, Yesilada O: The effect of carbon dioxide pneumoperitoneum on free radicals. *SurgEndosc* 2000; 14:649-652.
9. Dr Srikantiah Hiremath: "effects of CO₂ pneumoperitoneum on liver function tests following laparoscopic cholecystectomy" *IJSS journal of surgery*, 10.17354/SUR/2016/49.
10. Singal R, Singal R P, Sandhu K, Singh B, Bhatia G, Khatri A et al. Evaluation and comparison of postoperative levels of serum bilirubin, serum transaminases and alkaline phosphatase in laparoscopic cholecystectomy versus open cholecystectomy. *J GastrointestOncol* 2015; 6(5): 479-486.
11. Guven HE, "Liver enzymes alterations after laparoscopic cholecystectomy. *J Gastro intestine liver Dis.*2007;16(4):391-4.
12. Tauro LF, Sheethal CM, Aithala PSM, Shetty SR, D'souza CS, Rao BSS, Evaluation of Effects of Laparoscopic Surgery on Hepatic Function. *Journal of Clinical and Diagnostic Research* [serial online] 2008 December [cited: 2013 Aug 26]; 2:1155-1162.
13. Halvey A, Negri M, Are elevated liver enzymes and bilirubin levels significant after laparoscopic cholecystectomy in the absence of bile duct injury? *Ann Surg.*1994;219(4):362-364.
14. Ibrahim A M S, evaluation of the effects of laparoscopic surgeries on hepatic enzymes, *IOSR-JDMS* Aug 2017, PP 22-28.
15. Rao P R, Study of alterations in liver function tests following laparoscopic surgery, *IOSR-JDMS* March 2017, PP 48-54.