STUDY OF CHANGES IN COAGULATION PROFILE OF PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY USING CARBON DIOXIDE PNEUMOPERITONEUM

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ABSTRACT

BACKGROUND
Laparoscopic cholecystectomy is now the gold standard procedure and with over 5,00,000 procedures being done annually, laparoscopic cholecystectomy assumes a great significance in general surgical specialty. This study aims to study the effects of carbon dioxide pneumoperitoneum on the coagulation system of patients undergoing laparoscopic cholecystectomy and make the surgeon aware of the detrimental effects.

MATERIALS AND METHODS
A prospective clinical observational study of 50 patients selected by systematic sampling method from January 2015 to September 2015 at our institution was conducted to determine the results of changes in coagulation profile of patients undergoing laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum.

RESULTS
The mean prothrombin time of the patients before surgery is 11.83 seconds. The standard deviation was 1.008 and standard error of mean was 0.143. The mean of prothrombin time 6 hours after surgery was 11.7 seconds. The standard deviation was 0.898 and the standard error of mean being 0.127. The difference in the mean between the two groups was 0.130. The p-value was 0.0109 (<0.05). Hence, the value was statistically extremely significant. The values for D-dimer were analysed. The mean value of D-dimer before surgery is 129.78. The standard deviation was 21.01 and standard error of mean was at 2.97. In the D-dimer values after surgery, mean was calculated to be 350.22 with the standard deviation at 73.21 and standard error of mean at 10.35.

CONCLUSION
Our study concluded that there is activation of both coagulation and fibrinolytic systems post laparoscopic cholecystectomy.

KEYWORDS
Laparoscopic Cholecystectomy, D-Dimer Levels, Prothrombin Time.


BACKGROUND
Laparoscopy is one of the widely used tools for diagnostic and therapeutic purposes in recent times. Laparoscopy offers the advantage of better cosmesis, lesser postoperative pain, shorter hospital stay and early return to normal life and work. With advancements in technology and instrumentation, laparoscopy has entered into every array of surgical field.

A working cavity is one of the requisites for laparoscopy. This cavity is commonly created by positive pressure pneumoperitoneum using carbon dioxide.

Carbon dioxide pneumoperitoneum affects normal physiology. It is easily absorbed from the peritoneal cavity into circulation. It may affect the cardiovascular, respiratory and coagulation system, to name a few.

Laparoscopy has its complications due to increased intra-abdominal pressure, carbon dioxide absorption from peritoneum during insufflation and reverse Trendelenburg position adopted during surgery.

Laparoscopic cholecystectomy is now the gold standard procedure and with over 5,00,000 procedures being done annually. Laparoscopic cholecystectomy assumes a great significance in general surgical specialty.

This study aims to study the effects of carbon dioxide pneumoperitoneum on the coagulation system of patients undergoing laparoscopic cholecystectomy and make the surgeon aware of the detrimental effects if any.
AIM OF THE STUDY
1. To determine the changes in coagulation profile of patients undergoing laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum.
2. Assess if there is an increased risk of thrombosis postoperatively.
3. To determine if patients undergoing laparoscopic cholecystectomy have to be started on prophylaxis for deep vein thrombosis to prevent complications.

Parameters to be evaluated

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<td>Prothrombin Time</td>
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<td>D-dimer</td>
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MATERIALS AND METHODS
Type of Study- This is a clinical observational study.
Size of the Study- 50 patients undergoing laparoscopic cholecystectomy.
Duration of the Study- January 2015 to September 2015.
Place of Study- Department of General Surgery, Government Kilpauk Medical College and Hospital.

Method of Collection of Data
- 50 eligible patients are chosen.
- Clinical assessment and examination done at the time of inclusion in the study.
- Basic routine investigations will be done for all patients.
- 3 cc of blood was drawn under strict aseptic precautions.
- One sample prior to surgery. One sample 6 hours after onset of pneumoperitoneum.
- Samples will be processed for prothrombin time and D-dimer.
- Duplex scan of legs was done to look for deep vein thrombosis.
- Consent was obtained for inclusion under study and for surgery.

Inclusion Criteria
- All patients operated for cholecystectomy laparoscopically was included in the study.
- Patient of both sexes.
- Age from 18 years to 60 years.
- Patients with gallstones or gallbladder polyps.
- Patients with chronic cholecystitis, relief stages of acute cholecystitis was included.
- Surgery time between 90-180 minutes

Exclusion Criteria
- Patients below age of 18 and above the age of 60.
- Surgery time exceeding 3 hours.
- Procedures converted to open surgery.
- Associated hypertension.
- Patients on anticoagulant therapy.
- Patients with known malignancies.
- Patients with known history of bleeding and clotting disorders.
- Deep venous thrombosis.
- Pregnancy
- Patients who didn’t give consent.

Method of Surgery
- Procedure was done under general anaesthesia.
- Surgery was done with standard laparoscopic equipment for all patients using carbon dioxide pneumoperitoneum.
- The pressure of pneumoperitoneum was maintained at 13 mmHg ± 1 mmHg.

Surgical Steps
- Patients were put in classical supine position with table given a 30 degrees head up position and 15 degrees right up position to allow better visualisation of gallbladder and Calot’s triangle as it allows the colon and duodenum to fall away from the liver edge.
- Surgeon stands on the left of the patient with monitor placed near the right shoulder.
- A nasogastric tube and Foley’s catheter were inserted to deflate the distended stomach and empty the urinary bladder.
- Pneumoperitoneum was created by open Hasson’s method. A 1 to 1.5 cm incision is made in the umbilicus. Dissection is carried out and rectus sheath and peritoneum are opened in layers.
- After confirming entry into the peritoneal cavity, a 10 mm port was inserted and carbon dioxide was insufflated to a pressure between 12-14 mmHg at a flow rate of around 3 to 3.5 litres per minute.
- A 0 degree 10 mm telescope was attached to light source and endocamera and inserted through the 10 mm port.
- Laparotomy was done to exclude injury to structures during port insertion to exclude other suspected or associated pathologies and assess the feasibility of laparoscopic procedure.
- Rest of the ports were inserted under vision. A 10-mm working port is created in the epigastrium to the right of falciform ligament. Two 5-mm port one each in the midclavicular line and another in the anterior axillary line are created to retract the gallbladder and to visualise the Calot’s triangle.
- The cystic pedicle is exposed and dissection is carried out to create a window all around the cystic duct. Three clips are applied and cystic duct cut in between. Cystic artery is then isolated and clips applied and cut.
- The gallbladder is then removed from the liver bed by dissection in the loose fibrous layer, which separates the gallbladder from the fascia covering the bed of the liver.
- The gallbladder was then delivered through the epigastric or the umbilical port.
- Haemostasis was ascertained and ports are removed under vision and pneumoperitoneum was released.
Sages (American Gastro and Endoscopic Surgeons Society) 1 recommended that “Basic philosophy is that prophylaxis has to be tailored for each patient based on their estimated risk. All laparoscopic procedures carry a risk of hypercoagulability. Short and less complicated or less complex procedures like laparoscopic appendectomy and laparoscopic cholecystectomy carry a low risk of venous thromboembolism.”

“Patient positioning during surgery may alter the DVT risk. But, the evidence is not significant enough to suggest that DVT prophylaxis should be changed based only on body position.”

“Laparoscopic procedures that extend beyond one hour may need venous thromboembolism prophylaxis. Compression dressing, unfractionated heparin, low molecular weight heparin maybe used to this effect.”

Sages recommends that the risk factors for deep vein thrombosis are duration of surgery greater than 1 hour, previous history of venous thromboembolism, age more than 40, myocardial infarction in the past, features of congestive cardiac failure, immobilisation, patients undergoing hormone replacement therapy, varicose veins, oral contraceptive use, diagnosed malignancy, multiparous women, history of chronic renal failure, known case of inflammatory bowel disease, severe infection and obesity.

Sages recommends that each of the factors are given one point. If the total of positive factors is 0 or 1, then the patient need not be given prophylaxis or the patient may be subjected to one method, either pneumatic compression dressings or Unfractionated Heparin (UH) or Low Molecular Weight Heparin (LMWH).

If the sum of the factors is 2 or greater than 2, then the patient has to be put on unfractionated heparin or low molecular heparin in addition to pneumatic compression dressing to prevent deep vein thrombosis.

RESULTS
The paired Student’s t-test was used to analyse the values collected before and after the surgery. The software tools used for the purpose were downloaded from the internet. The values obtained were confirmed using another similar software to check the validity.

The mean of the two groups, the standard deviation, standard error of mean and the p-value were calculated. The results were again converted into pie charts, bar diagrams and scatter map for the sake of easy understanding and are presented as follows.

Of the 50 patients operated, 31 were females and 19 were male patients. The most common age group was 41-50 years among both female and male groups, followed by the age group of 51-60.

The duration of the surgery ranged from 1 hour 25 minutes to 2 hours 50 minutes. The reasons for prolonged surgical time were dense adhesions in the Calot’s triangle and gallbladder adherent to the liver bed.

There were no major peroperative complications. There was wound infection at the umbilical site in 3 patients, which settled with conservative treatment with a course of antibiotics.

There were no major postoperative complications in the operated patients during hospital stay and during the follow up period. The mean hospital stay was 4 days.

The prothrombin time of the patients before surgery ranged from 10 to 13.5 seconds with the mean at 11.83 seconds. The standard deviation was 1.008 and standard error of mean was 0.143.

The prothrombin time of patients 6 hours after surgery ranged from 10.5 seconds to 14 seconds. The mean of prothrombin time after surgery was 11.7 seconds. The standard deviation was 0.898 and the standard error of mean being 0.127.

The difference in the mean between the two groups was 0.130. The confidence interval at 95% was between 0.031 to 0.229. The p-value was 0.0109 (<0.05). Hence, the value was statistically extremely significant.

The values for D-dimer were analysed. The D-dimer value before surgery for the 50 patients ranged from 99 to 178 with the mean at 129.78. The standard deviation was 21.01 and standard error of mean was at 2.97.

The D-dimer values after surgery varied between 199 and 506. The mean was calculated to be 350.22 with the standard deviation at 73.21 and standard error of mean at 10.35.

The D-dimer of all the patients showed a drastic increase post-surgery. The difference in mean of the two groups was 220.44 and the confidence interval of 95% lay between 240 to 200.83. The p-value of the D-dimer analysis was at 0.001 was meant it was extremely significant statistically.

On follow up, none of the patients developed signs of deep vein thrombosis clinically when they turned up for follow up to 2 weeks post-surgery.
Figure 2. Age Distribution in Females

Figure 3. Age Distribution in Males

Figure 4. Duration of Surgery

Figure 5. Complications

Figure 6. Prothrombin Time of 50 Patients

Figure 7. Prothrombin Time in Seconds

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<thead>
<tr>
<th>Prothrombin Time</th>
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<tr>
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DISCUSSION

The values of prothrombin time and D-dimer of the 50 patients were analysed. The inferences derived from them were compared with other similar studies.

There was a higher incidence of female patients undergoing cholecystectomy, 62% compared to males 32%. This matches the global rates and rates in India, which also shows a higher female predisposition towards gallbladder pathologies.

The majority of the patients who underwent surgery were in the age group of 41-50 years in both the sexes. The second highest was seen in the age group of 51-60 years. These two groups constituted 76% of the cases showing that the disease incidence increased after the age of 40 years.

The duration of surgery varied between 1 hour 25 minutes to 2 hours 50 minutes. This shows the unpredictability of the duration of the surgery, the longest taking twice the time for the shortest procedure.

The prothrombin times of patients when analysed showed that the results were not uniform for all patients, while some showed an elevation in prothrombin time indicating hypocoagulability. There were a few who had decreased prothrombin time after surgery showing hypercoagulability.

The prothrombin time was not altered in most of the patients 62% (31 out of 50). This gave the appearance that there was not much difference in the coagulation profile with respect to prothrombin time.

The mean of the prothrombin time before surgery was 11.83 and the one after surgery was 11.7. The standard error of mean was 0.143 and 0.127. This small value showed the accuracy of the mean and that a similar mean would have been obtained with a study with a larger sample.

These values when charted showed that the decrease in the mean was statistically significant. Hence, the prothrombin time can be considered to decrease and there is hypercoagulability of blood.
The study goes in line with other studies by Hans et al, Garg et al who also support the fact that there is a state of hypercoagulability.

When the D-dimer values are analysed, all the patients are seen to have an increase in the D-dimer values with many showing a two-fold increase in the D-dimer values before and after surgery.

The mean of the D-dimer before and after surgery were calculated to be 129.78 and 350.22 and the standard error of mean was 2.97 and 10.35. The difference in the mean was 220.44. This increase clearly indicates the undergoing fibrinolytic process.

Statistically too, the values were found to be extremely significant with a p value of 0.001. Thus, this increase in D-dimer suggests the high risk of thrombosis leading to activation of fibrinolytic systems.

The high values of D-dimer post-surgery were also seen in many studies like the study by Amin Buhe et al where postoperative D-dimer values have been shown to get elevated by close to 5 times the preoperative values.

The findings of the study though contradicts the studies by Yan MJ et al, Martinez et al who report hypoocoagulability of blood postoperatively or no change in coagulation profile.

The change in the coagulation profile can be attributed to be due to surgery and is not specific to laparoscopy with carbon dioxide pneumoperitoneum as other studies by Jens Fromholt et al have shown similar rise in values after open surgery and gasless laparoscopic surgeries too.

D-dimer is not specific for pulmonary thrombosis or deep vein thrombosis. Values greater than 250 ng/mL are indicative of fibrinolytic activity.

These changes in coagulation factors cannot be attributed to the position of patient alone. Not all patients showed a similar change in coagulation profile.

The effect of position can only be studies if studies are done comparing laparoscopic procedures that adopt a Trendelenburg position to procedures that employ reverse Trendelenburg position.

The effect of increased abdominal pressure may have a role to play in the alteration of coagulation profile. Stasis of blood is a component of Virchow’s triad and could trigger the coagulation pathway. Intra-abdominal pressures of 12-14 mmHg are maintained for a period of few hours during laparoscopic surgery. In patients suffering from chronic liver disease with ascites, abdominal pressures ranging from 15 mmHg to as high as 80 mmHg have been recorded. But, these patients are not at increased risk for thrombotic phenomenon.

While Custendil et al in their studies found increased incidence of thrombosis on the first and third days following surgery, no such observations were made during the study.

None of the patients in the study were put on prophylaxis of any form because there were no added risk factors that indicated their need.

On the contrary to many studies that reported the incidence of thrombosis postoperatively, there were no cases who developed signs of thrombosis though the patients showed increased coagulation profile. This was probably due to the small size of the population under study. The incidence of postoperative thrombosis was placed at 0.02% (1 in 5,000) in the larger studies done elsewhere.

The analysis of these factors show that causation of deep vein thrombosis is multifactorial and only carbon dioxide pneumoperitoneum cannot be held responsible in patients undergoing laparoscopic cholecystectomy. But, laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum does play a role in altering the coagulation profile of patients and hence may need the use of prophylactic measures for thrombosis in high-risk individuals.

CONCLUSION

The study was done with the objective to find if there was a change in the coagulation profile in laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum and if there is an increased risk of thrombosis.

The study shows a marked increase in the D-dimer values and a significant decrease in the prothrombin time. This goes to prove that there is activation of both coagulation and fibrinolytic systems post laparoscopic cholecystectomy.

This activation of coagulation system could spell a disaster if the patients were to face a thromboembolic phenomenon post cholecystectomy. But, none of the 50 patients operated by us had any thromboembolic problems postoperatively. This could mean that the body has effective counter mechanisms to deal with this change in coagulation profile.

When assessed, if there is a need for prophylaxis against thrombosis, the study shows that regular need for thrombosis prophylaxis is questionable despite the gross change in the coagulation profile. A watchful eye and monitoring of the clinical picture could do the trick in most cases who are amenable to follow up.

Laparoscopic cholecystectomy is now being considered as an outpatient surgery. This means that the opportunity for postoperative follow up decreases. Hence, it is better that in those patients undergoing laparoscopic cholecystectomy and having lesser follow up opportunities are put on some form of deep vein thrombosis prophylaxis.

The choice of which patient has to be started on which method of prophylaxis could well be left to the surgeon considering that the risk varies on patient-to-patient basis.

The presence of even a single risk factor should necessitate the surgeon to start the patient on prophylaxis to avoid dire consequences.

Finally, larger and detailed studies are required to throw more light on these changes in the coagulation system and quantitatively determine the risk associated for laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum.

REFERENCES

[1] SAGES guidelines


