Does carbon dioxide intraperitoneal insufflation pressure affect coagulation status and laboratory liver function test after laparoscopic cholecystectomy? A clinical trial

Abstract

Background: It seems intraperitoneal CO2 insufflation, in these patients to be a risk factor for change in coagulation and liver function test (LFT) after Laparoscopic cholecystectomy, but there is conflict in studies about the effects of low-, and high-pressure level of CO2. Therefore, the present study was conducted with the aim of comparing the effect of low-pressure CO2 intraperitoneal insufflation (12-15 mm Hg), and high -pressure CO2 intraperitoneal insufflation (16-20 mm Hg) on the patient's coagulation status and liver function test after laparoscopic cholecystectomy.

Materials and Methods: This randomized clinical trial was consisted of 150 patients who were candidates for laparoscopic cholecystectomy and referred to Shahid Beheshti and Shahid Jalil Hospitals affiliated with Yasuj University of Medical Sciences, Iran. They were recruited using convenience sampling method and allocated to two different CO2 insufflation pressure levels, either 12-15 or 16-20 mmHg by random sampling method (each 75 patients in each group). Coagulation profile including prothrombin time (PT), partial thromboplastin time (PTT), International normalized ratio (INR), and bleeding time (BT), and liver function tests such as AST, ALT, ALP, total bilirubin (T.bili), and direct bilirubin (D.bili) were measured and recorded in the form the night before the operation and 24 hours after the operation. The data analyzed by SPSS 16 considering P-value<0.05.

Results: Results of the present study showed significant increasement in PT(P =0.035). , and decrease in BT (P=0.0001) in the group with pressure levels 16-20 compare to 12-15 mmHg after the intervention.

Conclusion: Given the lack of significant difference in INR, and LFTs between the two group and the normal range of PT and BT after laparoscopy, level of intraperitoneal CO2 insufflation had no effect on coagulation, and liver. Therefore, based on the results, CO2 pressure of 12-20 can be used safely in laparoscopic cholecystectomy surgeries, if confirmed the results in other study.

Keywords: CO2, insufflation, Blood **Coagulation** Factor, liver function test, laparoscopic cholecystectomy

Introduction

Gallstone disease is the manifestation of stones in the gallbladder or common bile duct. Chronic abnormal gallbladder motility and emptying may cause gallbladder stones leading to chronic cholelithiasis. Manifestations of the gallstone disease might be mild and non-specific or severe and painful. In the case of acute biliary colic recurrent pain attacks occur, and while the pain continues for more than a day, surgical intervention is inevitable [1, 2].

Approximately 700,000 people require gallbladder surgery every year, and 80-90% of them are candidates for laparoscopic cholecystectomy. Recent studies have shown that every year more than 500,000 Americans undergo laparoscopic cholecystectomy [3].

The adoption of laparoscopic cholecystectomy in the treatment of gallbladder diseases created a new range of intraoperative and postoperative complications. Minor complications (biliary and non-biliary) are usually treated conservatively. Major complications (biliary and vascular) are life-threatening and increase the mortality rate, so for their treatment, there is a need to convert to open surgery. The most serious complications associated with a high mortality rate include damage to the common bile duct with an incidence of 0.1-0.6%, and damage to large blood vessels 0.4-1.22%. The most common complication is iatrogenic perforation of the gallbladder with a shed gallstone with an incidence of 10-30% [4, 5, 6]. Considering the side effects of blowing CO2 gas and the mechanical effects of intraperitoneal CO2 insufflation and increased intraabdominal pressure (IAP), the veins may be compressed and cause hemodynamic consequences [7, 8].

A significant postoperative decrease in activated partial thromboplastin time (aPTT) and antithrombin III indicates the activation of coagulation, while the increase in d-dimer indicates the activation of fibrinolysis. Age, body mass index and duration of CO2 intraperitoneal insufflation are associated with significant activation of coagulation and fibrinolysis. CO2 intraperitoneal insufflation increases coagulation activation and fibrinolysis associated with laparoscopic cholecystectomy. Patients with risk factors such as old age, obesity, or with a long-expected duration of laparoscopic surgery are likely to have significant coagulation activation, making them a high-risk group for postoperative deep vein thrombosis [8, 9].

Laparoscopic cholecystectomy disturbs liver function tests (LFTs) in many patients. Observation of postoperative changes in the level of LFTs after open cholecystectomy has been reported in various studies. Changes in postoperative LFTs reflect a hemodynamic disturbance in hepatic and abdominal visceral blood flow, anesthetic hepatotoxicity, and biliary injuries [10, 11, 12, 13, 14]. The sensitivity of LFTs in detecting bile obstruction is more than 90%. Aspartate aminotransferase (AST), and alanine transaminase (ALT) are generally considered a measure of liver cell function. Alkaline phosphatase (ALP) levels increase during obstruction of the bile duct system. Bilirubin levels can be elevated due to hemolysis or obstruction of bile flow. Very high levels of serum transaminases can also indicate common bile duct (CBD) stones [13, 14].

In the study by Aggrawal et al. high- pressure pneumoperitoneum (>14 mm of Hg) increased significantly serum Aspartate Aminotransferase (AST) and Alkaline phosphatase (ALP) compare to Low Pressure of pneumoperitoneum (<10 mm of Hg). However, in the study by Zagorac et al., there was no significant difference between low-pressure pneumoperitoneum (12 mm Hg; N = 78) and high-pressure pneumoperitoneum (14 mm Hg) in bilirubin, AST, GGT, LDH, albumin, and fibrinogen between [15]. However, ALT changed significantly on the 30th postoperative day, and there was a statistical difference for all hemato- parameters, independent of the level of pneumoperitoneum pressure [16]. Therefore, given the conflicting results of studies on the complications of laparoscopic cholecystectomy after CO_2 intraperitoneal insufflation, the present study was conducted with the aim of comparing the effect of low-pressure CO_2 intraperitoneal insufflation (12-15 mm Hg) , and high -pressure CO_2 intraperitoneal insufflation (16-20 mm Hg) on the patient's coagulation status and liver function test after laparoscopic cholecystectomy .

Materials and Methods

Design

The present study was randomized clinical trial that was registered in I*ranian Registry of Clinical Trial* with ID number: IRCT20220421054608N1. The study was conducted at Shahid Beheshti and Shahid Jalil Hospitals affiliated with Yasuj University of Medical Sciences, Yasuj, Iran.

Participants, and sampling

In this randomized clinical trial, the study population was the patients who were candidates for laparoscopic cholecystectomy in Shahid Beheshti and Shahid Jalil Hospitals affiliated with Yasuj University of Medical Sciences from 2022/12/20 to 2023/12/23.

Based on $\sigma_1=14.4$ $\sigma_2= 30.1$ $\mu_1= 36.8$ $\mu_2= 44$, $\alpha = 0.05$, $\beta = 0.2$, $1-\beta = 0.80$, $z_{1-\alpha/2} = 1.96$, and below statistical formula, the sample size was estimated 134 patients, that Considering a 20% dropout rate, the sample size increased to 150 patients (each group 75 patients) [17].

$$n = \frac{\left[\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2\right] \times (S_1^2 + S_2^2)}{(\mu_1 - \mu_2)^2}$$

They were recruited using convenience sampling method and allocated to two groups including two different CO_2 insufflation pressure levels, either 12-15 or 16-20 mmHg by random sampling method. Since patients come weekly for surgery, the first one is random. The patient will be considered as the group with CO_2 pressure between 12 - 15 mm Hg and the next patient as the group with CO_2 pressure 16-20 mm Hg.

One hundred and fifty patients who were candidates for laparoscopic cholecystectomy entered the study.

The inclusion criteria of the study were candidates for elective laparoscopic cholecystectomy, patient consent to participate in the study, age range 18-70 years, absence of blood coagulation problems, absence of pregnancy, absence of previous abdominal surgery, absence of heart problems, and not taking anticoagulant drugs.

The exclusion criteria of the study were the occurrence of any complications during the operation including bleeding, intra-abdominal pressure drop, conversion to open, the patient's lack of satisfaction, and noninformative or uncooperative patients.

Instruments, and Data gathering methods.

For evaluating the coagulation profile status, five milliliters (ml) of citrated blood (4.5 ml of blood + 0.5 ml of citrate) were used. The requested coagulation profile tests were PTT, PT, and INR. The normal range of PT is 10.8-13.3 seconds and PTT is 31.4-48 seconds [18]. The AST and ALT concentrations were measured with a Hitachi 7600 automatic analyzer (Hitachi, Tokyo, Japan)

Intervention

In the present study, the intervention was using carbon dioxide intraperitoneal insufflation pressure in low-pressure (12-15 mm Hg) and high- pressure (16-20 mm Hg) in patients with laparoscopic cholecystectomy.

Laparoscopic cholecystectomies were performed successfully under general anesthesia. A standardized anesthesia protocol was used for all patients. Propofol 2–2.5 mg/kg and fentanyl 1 μg/kg were used for the induction of anesthesia. Muscle relaxation for endotracheal intubation was obtained with rocuronium 0.6 mg/kg. Patients were ventilated with volume-controlled ventilation (VCV) mode using an anesthesia device (Dräger Primus®; Dräger Medical Systems, Inc. Danvers, MA, USA). Tidal volume (Vt) was set as 6–8 ml per kg of ideal body weight and positive end-expiratory pressure (PEEP) was set as 5 cmH2O. The respiratory rate was adjusted to maintain normocarbia (PETCO2 = 32–36 mmHg). Maintenance of anesthesia was provided with sevoflurane (1.5–2%) with an oxygen-air mixture (FiO2 = 0.4). After the termination of the anesthesia procedure patients were placed in the Trendelenburg position, and the operation started with small infra umbilical incisions and the insertion of a Veress needle for CO2 intraperitoneal insufflation. Group 1 received low-pressure pneumoperitoneum (12-15 mm Hg, 75 patients) and group 2 received high- pressure pneumoperitoneum (16-20 mm Hg, 75 patients). Then, the patient was placed in the reverse Trendelenburg position with a slight left angle. All of the patients were operated on using a standard 4-port technique.

None of the patients received prophylactic Low Molecular Weight Heparin (LMWH). Elastic socks were used on each patient prior to surgery to prevent deep venous thrombosis.

Study Outcomes

Research outcomes included coagulation factors profile such as (prothrombin time (PT), partial thromboplastin time (PTT), International normalized ratio (INR), and bleeding time (BT), and liver function tests such as AST, ALT, ALP, total bilirubin (T.bili), and direct bilirubin (D.bili). The target tests of coagulation profile and liver function were measured and recorded the night before the operation and 24 hours after the operation.

Blinding

Neither the patient nor the analyst was aware of how the collected data was divided (double-blind).

Ethical considerations

The research followed the Tenets of the Declaration of Helsinki and was started after approval by the independent research ethics committee (the ethics committee of the Yasuj University of Medical Sciences (IR.YUMS.REC.1401.132)), and was completed based on and according to a plan (proposal). For the study participants, an informed consent form was completed. The confidentiality and privacy of the patients were respected. The information of the participants was coded from the beginning and only the researcher had access to the patient's profile. Patients did not deprive of usual treatment protocols and no additional cost was imposed on the patients and insurance organizations

Statistical analysis

Descriptive results were presented as mean ± standard deviation (SD), median and interquartile difference or percentage considering the type of data. An independent or paired t-test was used to compare the two means in variables with normal distribution, and in the case of non-normal data distribution, the Wilcoxon sign rank or Mann-Whitney test was applied. A P-value less than 0.05 was considered statistically significant. All data were analyzed using software SPSS version 16.

Results

150 patients participated in this research (75 patients in each group), however, only in low-pressure CO2 group one patient drop out due to dead. Therefore, data about 74 patients in low-pressure group, and 75 patients in high-pressure group analyzed. There was no significant difference between intervention and control groups in age, sex, and weight. (Table 1)

Table 1: comparing Demography characteristics between groups before intervention.

	Group less than 15	Group more than 15	P-value
Age mean±SD	48.55±13.56	49.34 ±12.49	0.675*

Weight	mean±SD	78.99±9.78	76.26±10.41	0.097*
sex	Female N(%)	30(40)	43(56.6)	0.051**
	Male N(%)	45(60)	33(43.4)	

*t-test
**chi-square test

Before the intervention, the normality of the variables as PT, PTT, INR, BT, AST, ALT, ALP, T.Bili, and D.Bili was checked in the separated two groups. The results of the Shapiro-Wilk test showed that at least for one of the groups, the distribution of PT, PTT, INR, BT, AST, ALT, ALP, T.Bili, and D.Bili was not normal before the intervention (P-value <0.05). Therefore, the Mann-Whitney test was used to compare the two groups. Results of comparing the two groups (Table 2) showed that the variables such as PT, AST, ALT, T.Bili, and D.Bili before the intervention had no statistically significant difference between the two groups (less than 15 and more than 15) (P-value>0.05). However, PTT (P-value=0.001), INR (P-value=0.001), BT (P-value=0.0001), and ALP (P-value=0.048) in the group more than 15 was significantly more than the group less than 15. (Table 2)

Table 2. comparing the two groups according to variables before the operation

Variable	Group less than 15		Group more than 15		P-value**
	Median	IQR*	Median	IQR	
PT	13	1	12	1	0.272
PTT	32	2	34	1	0.001<
INR	1	0.1	1.1	0.2	0.001<
BT	1.3	0.5	2.3	0.4	<0.0001
AST	38	7	35.5	11	0.387
ALT	43	24	45	11	0.213
ALP	157.5	44	171.5	52	0.048
T.Bili	1.55	0.3	1.54	0.25	0.642
D.Bili	0.425	0.31	0.45	0.3	0.805

* Interquartile range
** Mann-Whitney test

Results of comparing the two groups after the intervention (Table 3) showed that the distribution of PT between the two groups of less than 15 and more than 15 had a statistically significant difference (P-value=0.035). Other variables, including AST, ALT, D.Bili, and T.Bili had no statistically significant difference between the two groups after the intervention (P-value>0.05).(Table 3)

Table 3. Results of comparing PT, AST, ALT, D.Bili, and T.Bili between the two groups after the intervention

Variable	Group less than 15		Group more than 15		P-value
	Median	IQR*	Median	IQR*	
PT	12	1	13	2	0.035**
AST	66	41	67.5	39	0.896**
ALT	45	44	45	43.75	0.972**
T.Bili	0.21	0.3	1.53	0.21	0.920***
D.Bili	0.30	0.31	0.45	0.30	0.841**

* Interquartile range
** Mann-Whitney test
***t-test

The variables including BT, PTT, INR, and ALP had a significant difference between the two groups before the intervention. So first, the differences (changes) before and after the intervention were calculated for these variables, then this difference before and after the intervention was compared between the two groups.

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Results of comparing the two groups according to the difference before and after the operation showed that the changes before and after the intervention of the BT variable between the two groups of less than 15 and more than 15 had statistically significant differences (P-value =0.0001). The changes before and after the intervention of INR, ALP, and PTT variables between the two groups had no statistically significant difference (P-value>0.05). (Table 4)

Table 4. Results of comparing the two groups according to the difference before and after the operation of BT, PTT, INR, and ALP

Variable	Group less than 15		Group more than 15		P-value**
	Median	***IQR**	**Median**	***IQR**	
BT difference	-1	0.38	0.98	0.35	<0.0001
PTT difference	-3	4	-2	3	0.783
INR difference	0	0.22	0	0.3	0.988
ALP difference	7	66	20	25.73	0.127

* Interquartile range

** Mann-Whitney test

In the low- pressure group, PT, ALP, T.Bili, and D.Bili variables before and after the intervention had no statistically significant difference (P-value>0.05). But PTT, INR, BT, ALT, and AST variables were significantly higher after the intervention than before the intervention (P-value <0.05).

In the high- pressure group, INR, T.Bili, and D.Bili before and after the intervention had no statistically significant difference (P-value>0.05). ALT, PT, PTT, and AST variables after the intervention were significantly higher than before the intervention (P-value <0.05). BT and ALP after the intervention were significantly lower than before the intervention (P-value <0.05). (Table 5)

Table 5. Intragroup comparison of the investigated variables before and after the operation in each group (less than 15 and more than 15).

Variable		Before intervention		After intervention		P-value
		Median	**IQR**	**Median**	**IQR**	
PT*	12-15	13	1	12	1	0.850
	16-20	12	1	13	2	0.004
PTT*	12-15	32	2	35	4	>0.001
	16-20	34	1	35.5	2.75	>0.001
INR*	12-15	1	0.1	1	0.2	>0.001
	16-20	1/1	0.2	1.2	0.3	0.056
BT*	12-15	1.3	0.5	2.3	0.4	>0.001
	16-20	2.3	0.4	1.25	0.17	>0.001
AST*	12-15	43	24	45	44	0.034
	16-20	45	11	45	43.75	>0.001
ALT*	12-15	38	7	66	41	>0.001
	16-20	35.5	11	66	41	>0.001
ALP*	12-15	157.5	44	145	48	0.330
	16-20	171.5	52	145	51	0.002
T.Bili**	12-15	1.51	0.21	1.54	0.21	0.498
	16-20	1.53	0.24	1.53	0.21	0.981
D.Bili**	12-15	0.44	0.19	0.49	0.21	0.088
	16-20	0.44	0.19	0.49	0.21	0.208

*Wilcoxon test

**t-test

Discussion

The present study was conducted with the aim of comparing the effect of low-pressure CO2 intraperitoneal insufflation (12-15 mm Hg), and high -pressure CO2 intraperitoneal insufflation (16-20 mm Hg) on the patient's coagulation status and liver function test after laparoscopic cholecystectomy. Results of the present study showed that, after laparoscopic cholecystectomy, in group with high-pressure carbon dioxide (16-20 mm Hg) compare to low-pressure (12-15 mm Hg) intraperitoneal insufflation, indexes of PT increased and BT decreased significantly. However, there was no significant change in AST, ALT, D.Bili, T.Bili, PTT, INR, and ALP between groups after intervention.

In the low- pressure CO2 group (12-15 mm Hg), PTT, INR, BT, ALT, and AST variables were significantly higher after than before the intervention. Also, In the group of high- pressure CO2 (16-20 mm Hg) , PTT, ALT, and AST variables after the intervention were significantly higher than before the intervention, and BT and ALP after the intervention were significantly lower than before.

The intraperitoneal insufflation of CO2 for laparoscopic cholecystectomy may lead to postoperative hypercoagulation (reduced coagulation activity and increased fibrinolytic activity) and LFT change in the patients, and thereby may increase the risks for the development of postoperative thrombosis and liver dysfunction; Patients may have risks for occurrence of thrombosis within 8 hours after the operation, to which attention should be paid in favor of preventing thrombosis and liver dysfunction [8, 19, 20]s and this may be attributed to surgical trauma and pneumoperitoneum effects on the portal vein flow [21]. However, in the present study, PTT increased after the intervention in two groups, Moreover, BT, INR, ALT, and AST increased in the group with low-pressure (12-15 mm Hg) intraperitoneal insufflation, and ALP and BT decreased and PT, ALT, and AST increased in the group with high-pressure (16- 20 mm Hg) after the intervention. Therefore, intraperitoneal insufflation of CO2 for laparoscopic cholecystectomy may lead to change in some coagulation factors and liver function tests.

According to the side effects of blowing CO2 gas and the mechanical effects of increased intraperitoneal insufflation pressure and intra-abdominal pressure (IAP), the veins may be compressed and cause an initial increase followed by a sustained decrease in cardiac preload. Cardiac vascular resistance (SVR) may be significantly reduced, and the magnitude of this effect is proportional to IAP [7]. In a study by Dexter et al., in healthy subjects who underwent laparoscopic cholecystectomy, using transesophageal Doppler, found that cardiac output decreased by up to 28% at a gas pressure of 15 mmHg, but the cardiac output was maintained at a gas pressure of 7 mmHg [22]. In an animal model, Ishizaki et al reported that the IAP threshold that had the least effect on hemodynamic performance was less than 12 mmHg and recommended this pressure limit to avoid cardiovascular risks during CO2 insufflation [23].

The adverse effects of persistently elevated IAP on hepatic circulation are well documented. Hepatic blood flow varies in relation to IAP. Jakimowicz et al. investigated the effect of increased IAP on portal vein flow using duplex Doppler ultrasound in patients who underwent laparoscopic cholecystectomy. Portal blood flow decreased by 37% at an IAP of 7 mmHg and by 53% when the IAP reached 14 mmHg [24]. Also, the way the patient is positioned affects the changes in hepatic blood flow. Reverse Trendelenburg position is associated with a decrease in total hepatic, hepatic arterial, and portal venous blood flow [7].

In some studies, it was proved that laparoscopy has no effect on liver enzymes [12, 25]. However, positioning of the patient during Trendelenburg laparoscopy and increasing the intra-abdominal pressure due to CO2 gas administration and its absorption can also be effective on the liver [26]. Also, in the present study, some liver function test in two groups increased. In a study by Donmez et al., intraperitoneal insufflation with 10 mmHg and 14 mmHg pressures had a significant increase in coagulation factors in both groups. According to increases in coagulation parameters, higher CO2 intraperitoneal insufflation pressure (14 mmHg) has a more negative effect on the coagulation cascade. Based on the results of this study, they suggest a lower intraperitoneal insufflation pressure (10 mmHg) during laparoscopic cholecystectomy because of the less pronounced effects on the coagulation status [27]. However, in the present study, PT, in high- pressure (16-20 mm Hg) increased more than low-pressure intraperitoneal insufflation (12-15 mm Hg), and BT index Vice versa decreased. There was no significant difference between two groups in INR and other indexes of coagulation and liver function test between low, and high- pressure. In a study by Vecchio et al., postoperative PT values elevated slightly after laparoscopic surgery, and causes activation of coagulation and fibrinolytic pathways However, there was no significant change after intervention compare to before [28]. In the present study, the results indicated significant increasement in PTT of both groups, and PT in high-pressure Co2 after intervention, although the range of them were normal, and INR was in normal range. The difference between the results of this study and other studies may be due to the fact that the laboratory tests were measured in different laboratories by different Technician with different normal range. In the present study, although in the low-pressure group, INR, ALT, and AST variables, and in high-pressure group, ALT, and AST variables after intervention increased, however, liver function tests no changed significantly between low-, and high- pressure groups. In a study by Giraudo, the gasless technique causes smaller alterations in serological hepatic parameters than intraperitoneal insufflation pressure of 14 mmHg. Therefore, the use of low-pressure intraperitoneal insufflation is recommended for patients with severe hepatic failure [29]. In a study done by Hasukić, ALT after 24 and 48 hours and AST after 24 h were increased in the patients who underwent high-pressure laparoscopic cholecystectomy. The AST levels after 48 hours were statistically unchanged from the baseline in both groups. T.bili and ALP levels remained unchanged from baseline in both groups, without a significant difference between the two groups [30]. Similar to the present study, although, in the present study, ALT, and AST increased after intervention in both groups, but there was no difference between low-, and high-pressure groups after 24 h post-operation. In a study by Morino et al., postoperative increases in AST, ALT, bilirubin, and PT were seen. The increase of AST and ALT was statistically significant and correlated both to the level (10 versus 14 mmHg) and the duration of CO_2 intraperitoneal insufflation. The duration and level of intraabdominal pressure are responsible for changes in hepatic function during laparoscopic procedures[31]. Maybe, differences between the present and above studies were due to the duration of pressure and time of follow up. In study of Aggrawal et al., there was no significant difference in bilirubin and ALP in both groups after surgery, but AST and ALT increased significantly after laparoscopic cholecystectomy in patients in high-pressure CO_2 (more than 14 mm Hg) group compare to low-pressure CO_2 (10- 14 mm Hg) [15]. However, In the present study, AST, ALT in low-, and high-pressure groups increased significantly, but ALP decreased in high-pressure group. Similar to the present study, Zagorac et al. in the study indicated that bilirubin, AST, and fibrinogen no changed significantly between low-, and high-pressure groups, but ALT changed between groups in 30th surgery day [16].

Transient elevation of hepatic transaminases might be attributed to hepatocellular dysfunction secondary to CO_2 intraperitoneal insufflation, diathermy, extruding liver, the branch of the hepatic artery injured, and general anesthesia [32].

The limitation of the study is that liver and coagulation tests were measured in different laboratories and had different normal ranges, and these were not taken into account. Another limitation is the short measurement time (24 hours) and it would have been better if laboratory tests had been measured 48 hours later.

Conclusion

The results of the present study revealed PT elevation and BT reduction in high-pressure CO_2 compare to low-pressure CO_2 intraperitoneal insufflation after laparoscopic cholecystectomy. Given the lack of significant difference in INR, and LFTs between the two group and the normal range of PT and BT after laparoscopy, level of intraperitoneal CO_2 insufflation had no effect on coagulation, and liver. Therefore, based on the results, CO_2 pressure of 12-20 can be used safely in laparoscopic cholecystectomy surgeries, if confirmed the results in other study.

Although, there was no significant change in liver function tests between two groups after laparoscopic cholecystectomy, however some liver tests, and coagulation factors changed in each group after intervention compare to before. This study indicated that laparoscopic cholecystectomy probably affects some coagulation factors and hepatic transaminases independent to CO_2 intraperitoneal insufflation pressure. However, due to probable change in coagulation, and liver indexes in patients after laparoscopy, factors should be checked before and after the operation, and if the patient's preoperative liver function and coagulation status were not suitable, laparoscopic surgery might not be the optimal choice.

It is suggested the similar study, that all laboratory tests measured by a laboratory, and by one technician. Moreover, the measurement repeat after 48 h.