ORIGINAL ARTICLE

The Effect of Carbon Dioxide Volume Insufflation on Postoperative Pain in Elective Laparoscopic Cholecystectomy: An Observational Study

ZAWAND ALRASHEED[1] , ALI AL-DABBAGH[2]
[1]MBChB (Iraq) , MSc (UK), Trainee Department of Surgery, Kurdistan Board of Medical Specialty, Ministry of Education, Erbil/-Iraq, https://orcid.org/0000-0001-7020-4154 , Email: zawand@yahoo.com
[2]MBChB (Iraq), FICMS(Iraq), CABS(Iraq), FRCS (UK), Department of Surgery, College of Medicine, Hawler Medical University, Ministry of Education, Erbil/Iraq. dabbagh69@yahoo.com.
[*]Corresponding author: zawand@yahoo.com

ABSTRACT
Background: Pneumoperitoneum plays an important role in introducing post-laparoscopic pain. Total gas volume insufflation might be more important and not related to the length of the procedure. It is an important factor that increases residual pneumoperitoneum and should be taken under consideration along pressure setting and flow rate.
Aim: To examine the effect of different total carbon dioxide volume insufflation on postoperative abdominal and shoulder tip pain in terms of severity and development time.
Methods: A prospective observational study was conducted on 119 patients who underwent elective laparoscopic cholecystectomy. Patients were allocated into four groups “low, moderate, high, and extremely high” volume carbon dioxide groups depending on the amount of gas used. Postoperative pain was measured using a numerical rating scales (NRS); no pain (0), mild pain (1,2,3), moderate pain (4,5,6) and severe pain (7,8,9,10) at 2, 6, and 24 hours postoperatively.
Results: Postoperative abdominal pain was significantly lower in the “low volume group” in early postoperative hours, although there was no significant difference (P=0.73) in late postoperative hours. There was no significant difference in postoperative shoulder pain in early hours (P=0.78); however, the shoulder pain started to increase 6 hours after operation more in “high volume groups”.
Conclusion: The total CO_2 volume insufflation can be regarded as an important factor in the etiology of post-laparoscopic pain.
Keywords: Pneumoperitoneum; insufflation, total volume; abdominal pain; shoulder pain

INTRODUCTION
Modern surgeries have been concurred by laparoscopic and robotic procedures owing to the increasing demand from patients for minimal scar and earlier recovery period.[1] Considering all the advances in laparoscopic surgery, this technique still has numerous side effects that some of them are partially known. [2] The side effects might occur due to pressure within the abdomen and from the composition of the gas used, generally CO_2[3] To establish sufficient space for vision and mobilize viscera, the pressure is raised to 10-15 mmHg during LC intra-abdominal. Gas insufflation results in stretching the intra-abdominal cavity and peritoneal inflammation and irritation. Irritation of peritoneum can be due to the effect of the gas on the phrenic nerve and peritoneum[3].

One of the theories states that irritation of peritoneum is by carbonic acid formed by the transformation of CO_2 by combing with fluid in the peritoneal cavity[4]. The total CO_2 volume used in laparoscopy increases the residual volume in laparoscopic surgery. Hence, it might be a contributing factor in the etiology of postoperative pain[5].

The pain pattern after laparoscopic procedures is multimodal. It is a combination of three separate entities: incisional pain (somatic pain), visceral pain (deep intraabdominal pain), and shoulder pain. Deep intra-abdominal pain is considered to be responsible for early postoperative discomfort. Upper abdominal and shoulder tip pain might be transient or persist for three days[6]. Laparoscopic shoulder pain rarely occurs in laparotomy procedures; however, its incidence is about 35% to 80%, and it might be severe[7].

Even with different strategies that have been applied by researchers to ease the pain and enhance recovery; such as non-steroidal anti-inflammatory drugs, worm gas, used of low pressure and nitrous oxide, use of anesthetics (skin and intraperitoneally), insertion of drain intra-operatively yet postoperative pain control has not been sufficiently established. In 1994 Fredman, Jedeikin et al[8] established the relation between residual pneumoperitoneum and postoperative pain after laparoscopic cholecystectomy.

PATIENTS AND METHODS
Study design and sampling: A prospective observational study was conducted on 119 patients who underwent elective LC in two governmental hospitals, between February 2018 and November 2019. The research data were collected by research nurses and resident doctors. The study was completely double-blinded since the patients and surgeons were masked to the aim of the study. The study included, patients who aged between 18 to 70 years old ; suffered from symptomatic gallbladder disease for more than one week with no significant cardiopulmonary, hepatic or renal impairment, and had ASA II and less were included in this study. The patients with acute cholecystitis, cholangitis, gallstone pancreatitis, acalculous cholecystitis, obstructive jaundice, morbid

obesity with a BMI of more than 35 kg/m2 were excluded from the study.

The initial data were collected from 123 patients who went through elective laparoscopic cholecystectomy. Only 119 patients were included because two patients had minor procedures carried on with laparoscopic cholecystectomy, one discovered to have acute cholecystitis during the operation, and one patient converted to open cholecystectomy due to severe adhesions procedure.

Patient preparation and surgical techniques: Patients were admitted to the hospital a day before the operation. The medical history was taken from all patients. The physical and clinical examination was done for all patients by abdominal ultrasound, hematological, and biochemical investigations. All patients fasted for six hours before the operation. The patients received a single prophylactic parental third-generation cephalosporin 1g half of the hour before surgery. Accordingly, they were anesthetized with fentanyl and Propofol intravenously (I.V), Atracurium (I.V) to facilitate tracheal intubation. After tracheal intubation, the patients were located on mechanical ventilation, the anesthesia procedure was maintained by Isophorone. Ventilation was adjusted to maintain an end-tidal CO_2 pressure below 38mmHg.

After endotracheal intubation, an orogastric tube was inserted to decompress the stomach. It was removed after the operation was terminated. The insufflator device was set according to the surgeon's preference (Pressure and Flow Rate). All gas insufflators used in the study were the same model by the same manufacture. Laparoscopic cholecystectomies were performed by an experienced surgeon in the American position. The optical laparoscopic cannula 10mm was inserted at the umbilicus or supra-umbilicus with either (Open or Veress) methods. The second laparoscopic cannula 10mm was inserted 2 cm below xiphisternum, the third laparoscopic cannula 5 mm was applied on the right mid-axillary line. The fourth laparoscopic cannula if the present was applied in the midclavicular line below the costal margin. Subsequently, the patient was turned into a reverse Trendelenburg position with slight tilting from the supine position. After diagnostic laparoscopy, cystic duct and artery were defined clipped; the gallbladder was separated from the liver bed. The cystic duct and artery were washed and sucked in the case of plausible bleeding or perforation of the gallbladder. The gallbladder was removed from the xiphisternum port, with no infiltration of peritoneum or wound made by local anesthesia.

After the operation, all patients received fluid, paracetamol bottle 1000 mg (I.V.), another dose of third general cephalosporins (IV), 100 mg of Tramadol (I.V.). Most patients were discharged on the same day. All patients received only paracetamol tab 1000 mg three times daily on their discharge.

Data collection: The information was obtained from the patients preoperatively were the date of admission, age, gender, body mass index (BMI), an indication of operation, preoperative medication, ASA grading. The trained nurses and residents who were masked to the study objectives collected the above-mentioned information and recorded in a pre-designed questionnaire.

The information of intraoperative surgery was medications used intraoperatively, flow rate and pressure setting of the insufflator, total carbon dioxide volume used, use of local anesthesia, the operation duration, complications encountered, the requirement of the additional port, whether suctioning conducted or not, insertion of the drain. The duration of the operation was calculated with the administration of carbon dioxide to the abdomen until the deflation of the gas at the end of the operation. The total carbon dioxide volume was recorded with the removal of the insufflation tube. Patients were divided into four groups according to the total CO2 volume used; an assumption was made on most frequent gas used the groups were divided accordingly (low 1-15L, moderate 15-50L, high 50- 100L and extremely high 100 and above L) volumes, included 24 low, 62 moderate, 22 high, and 11 extremely high volumes.

Postoperatively, post-operative medications, pain (abdominal and shoulder pain) at two hours, and six hours were recorded. The abdominal pain and shoulder tip pain was based on a numerical rating scales (NRS) from 0 to 10 ; no pain (0), mild pain (1,2,3), moderate pain (4,5,6) and severe pain (7,8,9,10) at 2, 6, and 24 hours postoperatively, patient were given charge of pain for each hour assessment and the patients were assessed 2, 6, and 24 hours of operation. Since the nurses and doctors were masked to the study objectives to reduce the possible measurement bias, they were trained by the investigators about how to measure the pain of patients. The pain was categorized as (no pain, mild pain, moderate pain, severe pain). Nausea and vomiting were recorded as well two and six hours after the operation. Although most of the patients got discharged on the same day, 24 hours follow up was done by phone. Also, discharge medication, prolonged stay at the hospital, and readmissions were recorded.

Ethics Committee and Patients Approval: The ethical approval of this protocol was gained from the health ethics committee of the College of Medicine/ Hawler Medical University /Ministry of Higher Education and Scientific Research. The study was performed according to the modified principles of the Helsinki declaration. All patients filled up informed consent for the surgery and follow-up without giving any information about the study objectives. Permission was taken from administrative units of the hospitals, and informed consent was taken from all patients.

Statistical analysis: The descriptive characteristics of patients were presented in mean and Standard deviation or number and percentage. The comparison of age and BMI among study groups were examined in ANOVA-one way. The difference in the prevalence of abdominal and should tip pain severity of patients in different groups at different time follow-up was examined in Fishes' exact test. The significant level of difference was determined in a P-value of less than 0.05. The statistical calculations were performed using SPSS ® Version 23 for IOS ®.

RESULTS

The study showed that there were no statistical differences in the age and BMI of the different groups (Table 1). The patients were males (n=17, 14.3%) and females (n=102, 85.7%; P=0.071). There was no statistically significant difference between "total carbon dioxide insufflation volume" groups seen in all factors likely to increase postoperative abdominal and shoulder tip pain, including age mean, (P=0.357), BMI (P=0.667), Insufflator device measurements [Table1]. There was no statistical difference between perioperative analgesia, the requirement for readmission to hospital, use of drain, suction, complications (bleeding and perforation), prolonged stay for more than 24 hours. There was a significant difference (P=0.000) between duration and total volume used, there was an increase in volume with a longer period of procedure time [Table1].

Table 1: Comparison of factors among different groups of patients

Patients' characteristics (n=119)	Total CO_2 Volume Mean (SD)				P-value (two-sided)
	1-15 L	15-50 L	50-100 L	≥100 L	
	n=24 %=20.2	n=62 %=52.1	n=22 %=18.5	n=11 %=9.2	
Age (yrs.)	41.04 (14.58)	41.42 (14.58)	35.95 (1.91)	43.64 (13.40)	0.357
BMI	30.05 (6.60)	31.84 (3.768)	30.90 (5.133)	33.09 (3.60)	0.677
Drain	n/a	2 (3.17)	1 (5.00)	n/a	0.673
Bleeding	n/a	6 (9.52)	3(15.00)	3 (27.27)	0.074
Perforation	1(4.00)	4 (6.35)	3 (15.00)	2 (18.18)	0.324
Suction	2 (8.00)	7(11.11)	4 (20.00)	3 (27.27)	0.368
Flow	4.00± 2.54	4.93±2.156	5.87± 2.156	6.73 ± 2.611	0.31
Pressure	11.65±1.641	11.52±2.078	12.14±1.457	12.09±1.868	0.851
Duration	10±3.99	20.59±7.66	26.75±8.93	56.82±30.19	0.000
Additional Analgesia	n/a	n/a	n/a	n/a	n/a
Readmission	n/a	n/a	n/a	n/a	n/a
Local anesthesia	n/a	n/a	n/a	n/a	n/a
One-way ANOVA was used for statistical differences over time. and chi-square test for BMI, drain, bleeding, perforation suction, Flow and pressure Presented as mean ± standard deviation. (n) is the number of patients					

The relation between abdominal pain and total CO_2 volume used: Two hours after the operation, most of the patients had moderate pain levels in low volume group (54.2%), moderate volume group (58.1%), while most of the patients had a severe level of pain in the high-volume group (54.4%) and extremely high volume (90.9%). The prevalence of patients with severe abdominal pain was increased from the low to high volume CO2 group six hours after the operation. Half of the patients had mild levels of pain in low volume group (50.0%), moderate volume group (54.8%), and high-volume group (45.5%), while most of the patients had a moderate level of abdominal pain in the extremely high-volume group. At 24 hours post-surgery, most of the patients in all groups had no pain or a mild level of abdominal pain (P=0.73). The prevalence of mild pain in low volume, moderate volume, high volume, and extremely high groups was 37.5%, 45.2%, 59.1%, and 63.6%, respectively. The distribution of abdominal pain was not the same across groups of total CO_2 volume for two hours and six hours after the operation (P<0.001). The patients with higher volume group were significantly more likely to have severe pain. However, most of the patients at 24 hours of operation were more likely to have mild severity of pain with no significant difference between the group (Table 2).
Two hours after the operation, most of the patients had moderate pain levels in low volume group (54.2%), moderate volume group (58.1%), while most of the patients had a severe level of pain in the high-volume group (54.4%) and extremely high volume (90.9%). The prevalence of patients with severe abdominal pain was increased from the low to high volume CO2 group six hours after the operation. Half of the patients had mild levels of pain in low volume group (50.0%), moderate volume group (54.8%), and high-volume group (45.5%), while most of the patients had a moderate level of abdominal pain in the extremely high-volume group. At 24 hours post-surgery, most of the patients in all groups had no pain or a mild level of abdominal pain (P=0.73). The prevalence of mild pain in low volume, moderate volume, high volume, and extremely high groups was 37.5%, 45.2%, 59.1%, and 63.6%, respectively. The distribution of abdominal pain was not the same across groups of total CO_2 volume for two hours and six hours after the operation (P<0.001). The patients with higher volume group were significantly more likely to have severe pain. However, most of the patients at 24 hours of operation were more likely to have mild severity of pain with no significant difference between the group (Table 2).

The relation between shoulder pain and total CO_2 volume used: Most of the patients at two hours of surgery had no pain or a mild level of shoulder pain across study groups (P=0.78). The prevalence of mild pain in low volume, moderate volume, high volume, and extremely high groups was increased gradually and was 29.20%, 51.60%, 45.50%, and 63.60%, respectively. The prevalence of more severe shoulder pain was gradually increased from the low to high CO2 volumes six hours after the operation. The mild level of pain was the most common in low volume (16.70%), moderate volume (61.30%), high volume (50.0%), and extremely high volume (54.50%). The prevalence of pain severity was increased from low to high CO**2** volume 24 hours after the operation. The prevalence of mild pain severity was 8.30%, 61.30%, 63.60%, and 72.70% in low volume, moderate volume, high volume, and extremely high groups, respectively. The distribution of the shoulder tip pain across the groups of total CO2 volume was not the same in six hours and twenty-four hours after the operation (P<0.001). Patients with higher volume group were more likely to have more severe pain. However, at two hours of operation, there was no statistically significant difference in the prevalence of the shoulder tip pain in the group (Table 3).

Table 2: Comparison of abdominal pain among different groups of patients

Abdominal Pain	Total Volume (Liters); n v (%)				P-Value
Time and pain severity	Low 1-15	Moderate 15-50	High 50-100	Extremely high ≥100	
2 Hr.					<0.001
No pain	1 (4.2)	1 (1.6)	0 (0.0)	0 (0.0)	
Mild Pain	9 (37.5)	12 (19.4)	2 (9.1)	0 (0.0)	
Moderate Pain	13 (54.2)	36 (58.1)	8 (36.4)	1 (9.1)	
Severe Pain	1 (4.2)	13 (21.0)	12 (54.5)	10 (90.9)	
6 Hr.					<0.001
No pain	7 (29.2)	5 (8.1)	0 (0.0)	0 (0.0)	
Mild Pain	12 (50.0)	34 (54.8)	10 (45.5)	2 (18.2)	
Moderate Pain	4 (16.7)	19 (30.6)	9 (40.9)	8 (72.7)	
Severe Pain	1 (4.2)	4 (6.5)	3 (13.6)	1 (9.1)	
24 Hr.					0.73
No Pain	15 (62.5)	29 (46.8)	8 (36.4)	4 (36.4)	
Mild Pain	9 (37.5)	28 (45.2)	13 (59.1)	7 (63.6)	
Moderate Pain	0 (0.0)	5 (8.1)	0 (0.0)	0 (0.0)	
Severe Pain	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	
Fishers' exact test was performed for statistical analyses.					

Table 3: Comparison of shoulder tip pain among different groups of patients

Shoulder tip Pain	Total Volume (Liters)				P-value
Time and pain severity	Low 1-15	Moderate 15-50	High 50-100	Extremely high ≥100	
2 Hrs.					
No Pain	15 (62.50)	14 (22.60)	7 (31.80)	3 (27.30)	
Mild Pain	7 (29.20)	32 (51.60)	10 (45.50)	7 (63.60)	0.78
Moderate Pain	2 (8.30)	15 (24.20)	5 (22.70)	1 (9.10)	
Severe Pain	0 (0.00)	1 (1.60)	0 (0.00)	0 (0.00)	
6 Hrs.					
No pain	17 (70.80)	8 (12.90)	4 (18.20)	2 (18.20)	
Mild Pain	4 (16.70)	38 (61.30)	11 (50.00)	6 (54.50)	<0.001
Moderate Pain	2 (8.30)	16 (25.80)	7 (31.80)	3 (27.30)	
Severe Pain	1 (4.20)	0 (0.00)	0 (0.00)	0 (0.00)	
24 Hrs.					
No Pain	21 (87.50)	17 (27.40)	2 (9.10)	0 (0.00)	
Mild Pain	2 (8.30)	38 (61.30)	14 (63.60)	8 (72.70)	<0.001
Moderate Pain	1 (4.20)	7 (11.30)	6 (27.30)	3 (27.30)	
Severe Pain	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	
Fishers' exact test was performed for statistical analyses.					

DISCUSSION

Postoperative pain after laparoscopic procedures can be due to various etiologies including irritation of diaphragmatic irritation by high intra-abdominal pressure, caused by pneumoperitoneum or by CO_2 or absorption from the peritoneal cavity, patient's demographic factors, the volume of residual gas.[9]

Many research has been conducted to find out the ways to reduce the frequency and severity of postoperative abdominal and shoulder tip pain after elective LC.[10-12] There have been studies on the relationship between residual pneumoperitoneum and postoperative LC pain intensity that been measured by standard method [7] and studies on the effect of low pressure on postoperative abdominal and shoulder tip pain.

The study showed patients who had received a lower amount of CO_2 had lower scores of abdominal and shoulder tip pains without having any difference in demographic data statistically with an exception to gender "female predominance" there was no difference between male and female. Some studies have shown that the incidence and intensity of postoperative abdominal and shoulder tip pain were less in low-pressure, low flow rate, and duration of operation.[7, 13]

Dey and Malik [14] has also demonstrated in his study intra-abdominal pressures and shorter duration of surgery were factors irrelevant to the occurrence of shoulder tip pain after LC. This might indicate that total CO_2 volume used is a contributing factor in the etiology of the postoperative abdominal and shoulder tip pain, considering the demographic data, duration of the operation, and insufflator measurements are regarded as factors that might take part in etiology of postoperative abdominal and shoulder tip pain. Hence high pressure and high flow rate had little or no effect on the total volume will be used, nor the residual volume.

The first thing in LC is the creation of pneumoperitoneum. During LC, flow decreases when pressure is stabilized, and if there is a decrease in pressure for a reason for the instant gas leak, or suction during operation, the flow will increase again to stabilize the pressure. These maneuvers increase the total CO_2 volume used when more gas goes inside the abdomen i.e. when there is an increase of total CO_2 there will be an increase in the residual volume. Jackson et al.[13] showed that residual pneumoperitoneum volume is related to postoperative pain in gynecological laparoscopic procedures.[13] Another research by Sarvestani and Zamiri [7] founded the same relationship between residual pneumoperitoneum and postoperative abdominal and shoulder tip pain.

Carbonic acid is formed when CO_2 is dissolved in water, absorption of carbonic dioxide into intravascular space, and interaction with carbonic anhydrase will convert carbonic acid to bicarbonate. Bicarbonate is converted back to CO_2 and it will be expelled in the lungs. The carbonic acid that is formed is suggested to be one for the reasons of diaphragmatic irritation and cause abdominal and shoulder tip pain, as peritoneal acidosis has been proposed as one of the most important factors accountable for destroying of the mesothelial lining of the peritoneum and consequence peritoneal irritation. The phrenic nerve could be damaged by carbonic acid and that might cause referred pain in the C4 dermatome.[15,16] Moreover entrapped gas between liver and right diaphragm, irritating the diaphragm, also causes upper abdominal pain. Absorption of CO_2 affect acid-base balance, and it might lead to an increase of CO2 excretion load, and prolong exposure to CO_2 might lead to hypothermia which has diverse adverse side effects.[17]

The study showed that the distribution of abdominal pain severity between groups was not the same in 2 hours and 6 hours after the operation P=0.00. On the other hand, distribution of shoulder tip pain was not the same in 6 and 24 hours postoperatively (P=0.01, P=0.00). In the early postoperative period (two hours) abdominal pain was severe in patients who received high “volume” or “extremely high volume” 54.5%, 90.9% respectively, the severity tended to decrease in later hours. However, in “low volume group” and in “moderate volume group” pain was mainly moderate 54.2%,58.1% respectively. Twenty-four hours after the operation there was no significant difference between the severity of the pain; all the groups had no or mild pain. Thus, the study showed that abdominal pain tends to develop in the early hours of the postoperative period. The abdominal pain after the operation has a convoluted course and it might be due to various pain mechanisms such as surgical trauma to the abdominal wall, intra-abdominal disturbance (Cholecystectomy), abdominal distention due to gas insufflation and the impacts of the gas; therefore why it’s intensity is peaked in the early postoperative period.[18.19.23] A study on Port site and intraperitoneal Infiltration of local anesthetics by Alam, Hoque et al [11], showed that abdominal pain intensity after LC is highest in 6 hours after the operation, similar to our study. Shoulder pain tip pain mostly becomes obvious on the day after surgery when the visceral pain component has decreased [9], in our study shoulder pain was peaked in its severity 24 hours after the procedure.

The present study showed that should tip pain intensity recorded by the NRS also is more in groups with a “high volume” group, but with a different pattern from abdominal pain. In the early postoperative period, there was no significant difference between the total volumes and shoulder pain, most of the patients had mild pain. However, shoulder pain started to increase in all groups (with exception to low volume group) 6 hours after the operation and tend to increase throughout the patient's stay in the hospital, in low volume group there was a slight decrease in pain. Since the research was limited to 24 hours we were not able to assess patients after 24 hours as shoulder pain tends to say up to 3 days.[6] Postoperative shoulder pain is most frequent and severe on the early mobilization of the patient it’s suggested that mobilization of the patient increase traction on the peritoneum reflections of the heavy viscera, which then lose suction support for their weight owing to the creation of peritoneal spaces by the CO_2.[19,20.21.22]

Dey and Malik [14] observed the time of development of abdominal and shoulder tip pain, and it was noted that visceral pain (abdominal) gradually weans of the following day, the shoulder tip pain may become more obvious and necessitate treatment. It seems that shoulder tip pain takes time to develop and since the abdominal pain is more severe in the early postoperative hours, and multimodal factors are contributing to etiology of abdominal pain it might obscure the shoulder tip pain even if developed and ignored by patient.[9] We did observe a similar pattern of severity and time of development of abdominal and shoulder tip pain.

Limitations of the study: This study has certain limitations, pain assessment of the study was only done within 24 hours, shoulder tip pain remains up to three days, and since our study was limited to 24 hours, patients were not assessed after 24 hours. We have not found any similar study on total CO_2 volume insufflation. Therefore, some of the parts of the study have been assumed on frequency; for example, the total volume of CO_2 used in the study was set per observation of operations before initiation of the study.

CONCLUSION

The present study showed that the abdominal and shoulder tip pain is more intense with increasing CO_2 volume in elective LC surgeries. Hence the study concluded that total volume insufflation might be a contributing factor in the etiology of postoperative (shoulder tip and abdominal pain). Further studies on total CO_2 volume are warranted. Meanwhile, measures should be carried out to decrease the total volume of CO_2 used in LC and other laparoscopic procedures.

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