Shall we use low-pressure CO_2 pneumoperitoneum in laparoscopic cholecystectomy?

Ann Ital Chir, 2022 93, 2: 217-223
pii: S0003469X22036193
Online ahead of print Jan. 10
free reading: www.annitalchir.com

Haci Bolat*, Mustafa Kaçmaz**

**Nigde Omer Halisdemir University, Faculty of Medicine, Department of General Surgery, Nigde, Turkey*
***Department of Anesthesiology, Ömer Halisdemir University Faculty of Medicine, Niğde, Turkey*

Shall we use Low-pressure CO_2 Pneumoperitoneum in Laparoscopic Cholecystectomy?

BACKGROUND E AIMS: *We aimed to determine whether intraabdominal pressure change caused by pneumoperitoneum created during laparoscopic cholecystectomy (LC) has effects on abdominal and shoulder pain, nausea, vomiting, bowel movements, time of first flatus and defecation, and biochemical parameters.*
METHODS: *Seventy patients that were diagnosed with cholelithiasis and would undergo LC, between the ages of 18-75, with the Society of Anesthesia Physical Status (ASA) I-III classifications were included in the study. Patients were divided into two groups as whose intervention was defined as low pressure (8-10 mm/hg) and whose intervention was defined as high pressure (14-16 mm/hg). Differences in the prognoses of patients in both groups were observed for statistical significance.*
RESULTS: *Shoulder pain- visual analogue scale (VAS) values in 6th and 24th hours were lower in Group 1($p<0.005$). There was no significant difference in abdominal pain-VAS values($p\geq0.05$). Mean intraoperative end-tidal carbon dioxide (ETCO2) values were higher in Group 2 ($p<0.005$). Differences in nausea and vomiting were not significant($p\geq0.05$). There was no significant difference in the first flatus times($p\geq0.05$). Bowel movements resumed earlier in Group 1($p<0.005$). Changes were not significant for biochemical blood parameters in the preoperative and postoperative periods($p\geq0.05$).*
CONCLUSION: *The use of low-pressure and high pressure carbon-dioxide (CO_2)-pneumoperitoneum created during LC does not cause a significant difference in terms of clinical and laboratory results. Therefore, the surgical team should prefer an easy-to-apply pressure level which they are used to and in which they have low complication rates.*

KEY WORDS: Cholecystectomy, Pneumoperitoneum, Low-pressure CO_2

Introduction

Nowadays, laparoscopic cholecystectomy method has commonly been used for cholecystectomy operations. It provides a faster recovery especially in interventions performed with small incisions and enables patients to tolerate the operation more easily. Moreover, it shortens the length of hospital stay during postoperative period and is tolerated by the patients as it decreases the need for analgesics in addition to decreasing the health costs [1-3].
Besides these advantages, this method may cause some problems. Laparoscopic cholecystectomy may cause postoperative nausea and vomiting (PONV). Moreover, it is thought that the compression of intraabdominal tissues by pressure created with pneumoperitoneum may cause intestinal ischemia as well as PONV [4].
In order to create a surgical intervention area during laparoscopic cholecystectomy, 10-15 mm/Hg intraabdominal pressure of CO_2 pneumoperitoneum is used as standard [5]. Intraabdominal (CO_2) insufflation induces cardiovascular, metabolic and respiratory changes due to the pressure created proportionally with the amount of intraabdominal CO_2 and may cause complications asso-

Pervenuto in Redazione Marzo 2021. Accettato per la pubblicazione Maggio 2021
Corresponence to: Nigde Omer Halisdemir University, Faculty of Medicine, Department of General Surgery, Nigde, Turkey (e-mail: hbolat01@yahoo.com)

ciated with laparoscopy. Postoperative pain is also one of the undesired results of laparoscopic interventions [6]. There are recent studies aiming to decrease abdominal and diaphragm distention with the use of low CO_2 insufflation pressures in order to decrease postoperative pain levels and changes caused by CO_2 pneumoperitoneum after laparoscopic interventions [7,8].

It was asserted that intraabdominal pressure created with CO_2 insufflation and laparoscopy performed at Trendelenburg position may also induce cardiovascular and respiratory functions by inducing metabolic and respiratory changes such as changes in acid-base balance and changes in arterial pH and pCO_2 [9,10].

This study primarily aimed to determine whether intraabdominal pressure change created during pneumoperitoneum caused a difference in abdominal and shoulder pain seen as the most unpleasant clinical result during postoperative period of laparoscopic cholecystectomy and secondarily aimed to determine whether pneumoperitoneum caused nausea, vomiting, decrease in bowel movements, and significant delay in first flatus and defecation due to possible temporal ischemia and caused a significant change in routine laboratory tests.

Material and methods

This prospective, randomized, and controlled study examined 70 consecutive healthy patients who underwent elective LC with the diagnosis of symptomatic cholelithiasis between February 2020 and October 2020. After the approval was obtained from Clinical Research Ethics Committee of the Faculty of Medicine, Omer Halisdemir University (2020/08) 75 patients who were hospitalized to undergo a surgery due to symptomatic gallstone in general surgery clinic were prospectively included in this study with randomized sampling. The study was completely conducted according to the principles of Helsinki Declaration. The patients were determined with single-blind method by using sealed envelopes the day before and informed in detail about the study plan and informed consents were obtained from these patients. Five of the patients were excluded during the study due to various reasons and the study was completed with 70 patients (Fig. 1).

Inclusion criteria were as follows: patients in Society of Anesthesia physical status (ASA) I-III classifications, patients between the ages of 18-75, patients who approved the informed consent form, and patients who would undergo a surgery due to isolated gallstone were included in the study.

Patients with unstable hypertension which was not under control, diabetes mellitus, coronary arterial disease, chronic obstructive pulmonary disease and asthma, and patients who systemically had portal hypertension, coagulopathy, suspect of gallbladder carcinoma, cirrhosis, generalized peritonitis disease and acute cholecystitis, thickened gallbladder wall were not included in the study.

Based on the corporate standards of laparoscopic interventions, intraoperative stable CO_2 pressure was defined as low pressure for 9-11 mm/Hg and standard pressure (SP) for 14-16 mm/Hg [11]. According to the CO_2 pressure values used during 70 laparoscopic cholecystectomy, those who received low pressure (8-10 mm / Hg) were named as Group 1, and those who received high pressure (14-16 mg / Hg) were named as Group 2. recorded complications during surgeries.

A standard anesthesia protocol was used for all the patients included in the study. Patients underwent endotracheal intubation by receiving intravenous fentanyl (0.01 μg/kg body weight [BW]; B. Braun, Malsungen, Germany), propofol (1%, 1-2 mg/kg BW; Fresenius Kabi, Bad Homburg) and rocuronium (0.5-0.7 mg/kg BW; Hexal, Holzkirchen, Germany) and then anesthesia was maintained by administering Sevofluran 1.5-2.0 MAC; (Baxter, Unterschleissheim, Germany) and 0.1 mg/kg of rocuronium at 30 minute intervals. Controlled ventilation was maintained with 6-8 ml/kg of tidal volume, 14-16 breaths/min of respiratory rate, 1-1.5 of inspiration to expiration ratio and 10-20 mm/Hg of inspiration pressure. No change was made in other standard procedures that were routinely applied during the study.

Laparoscopic cholecystectomy was performed at 30° reverse trendelenburg position by using four-port technique and following a standard corporate approach. CO_2

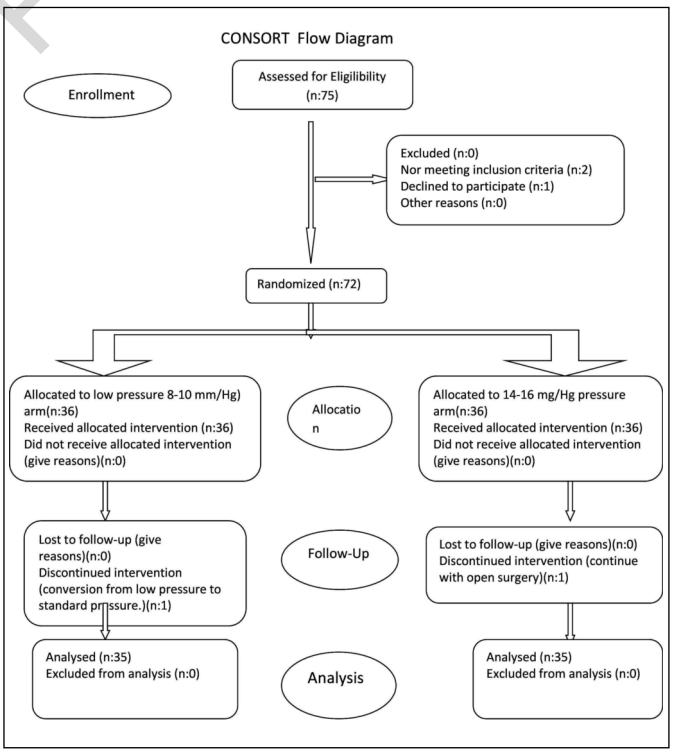

Fig. 1: Consolidated Standards of Reporting Trials statement flow diagram.

insufflation used in intraabdominal region according to preference of the surgeon was insufflated with a 2.1 mm of stainless steel Veress needle (Karl Storz SE & Co. KG, Tuttlingen, Germany) inserted through the abdominal midline by using an electronic endoflator (Karl Storz SE & Co. KG, Tuttlingen, Germany). Insufflation was performed at a standard temperature of 19-21°C and 0% relative humidity.

After standard cholecystectomy protocol was completed patients underwent a wake up procedure and waited in postoperative wake up room until sufficient recovery occurred.

Intraoperative end-tidal CO_2 value, SPO2, pulse, blood pressure and complications were recorded. VAS in abdominal and shoulder regions, nausea, vomiting, the time when bowel movements resumed, time of first flatus and defecation were recorded in postoperative 1st, 6th, 12th, 24th and 48th hours. Diclofenac 75 mg was administered to the patients by general surgery clinic in case their VAS score was measured as 4 or above at any period of their follow-ups after laparoscopic cholecystectomy and intramuscular tramadol 75 mg as additional analgesic was administered in case the pain was not relieved. Metoclopramide 10 mg was invasively administered to the patients in case they had nausea and vomiting at any period of their follow-ups. Therefore, only VAS value and the condition of nausea and vomiting were recorded. No intervention was done in routine medication. In addition, whether there was any statistically significant change in preoperative and postoperative laboratory tests of all the patients was recorded.

Statistical Analysis

Statistical analyses were performed on "SPSS for Windows version 22.0" software. Numerical variables were summarized with mean±standard deviation. Normal distribution of numerical variables was analyzed with Kolmogorov Smirnov and Shapiro Wilks tests. Independent t test was used for comparison of normally distributed variables between the groups. Mann-Whitney U test was used for non-normally distributed variables. Pearson's chi-squared test and Fisher's exact test were used for comparison of categorical variables between the groups. Mann-Whitney U test was used to analyze whether there was difference between the groups in terms of VAS and Friedman test was used to analyze whether there was a change in the group. Significance level was accepted as $p<0.05$.

The study called "Which intraperitoneal insufflation pressure should be used for less postoperative pain in transperitoneal laparoscopic urologic surgeries?" by Ali Akkoc et al. was used and while type error was 0.10, effect size was 0.5 and test's power was 0.80 the minimum sampling size required in both groups was calculated as 35 [12].

Findings

There was no statistically significant difference between the groups in terms of age, gender, weight, height and ASA score. No significant difference was recorded between the mean values of mean arterial pressure (MAP), pulse rate, and Oxygen saturation (SPO2) measured in minute 0, and 15th, 30th and 45th minutes during the surgery ($p\geq0.05$). There was no statistically significant difference between the groups in terms of discharge criteria, duration of surgery and duration of pneumoperitoneum ($p\geq0.05$) (Table I).

When visual analogue scale (VAS) values measured in postoperative hours 1, 6, 12, and 24 were evaluated shoulder pain-VAS values measured in 6th and 24th hours were found statistically significantly lower in Group 1 than in Group 2 ($p<0.005$). No significant difference was recorded between VAS values measured in the 1st and 12th hours ($p\geq0.05$) (Table II). Although VAS values measured in 1st, 6th,12th, and 24th hours were higher in Group 2 then Group 1 .No statistically significant difference was recorded between abdominal pain-VAS values measured in the 1st, 6th, 12th and 24th hours ($p\geq0.05$). The VAS values measured in postoperative hours 1, 6, and 24 were higher in Groups 2, while VAS value measured in 12th hour was higher in Group 1 (Fig. 2).

Table I - *Age, weight, height, ASA and gender characteristics of groups*

	Group (1) (8-10 mmHg)	**Group (2) (14-16 mmHg)**	**p**
Age[a] (years)	50.9 ± 11.8	53.2±14.3	0.477
Height[a] (cm)	163.6 ± 6.9	164.8 ± 7.6	0.414
Weight[a] (kg)	79 ± 10.4	84.7 ± 14.5	0.106
MAP[a] (mm/hg)	97.3 ± 9.2	95.2 ±13.4	0.459
PULSE[a]	81.0 ±9.3	81.2 ±10.6	0.687
ASA[c] (I/II/III)	8/21/6	5/22/8	0.606
Gender[c] (M/F)	10/25	47/33	0.568
SPO2[a] (%)	95.8±1.9	95.7±2.2	0.796
Duration of [a] surgery (Min)	40.03±4.3	38.3±4.0	0.104
Duration of [a] Pneumoperitoneum(Min)	35.20±4.1	34.4±4.0	0.412
Duration of Discharge(h)[b]	27.60±4.7	26.80±5.2	0.454

Data presented as mean SD or number of patients (%); [a] Student-T test; [b]Mann–Whitney U-test; [c]Pearson's 2 –test; [d]Fisher's exact test. Statistically significant between-group differences (P< 0.05) *; ASA, American Society of Anesthesiologists; f=female, m=male

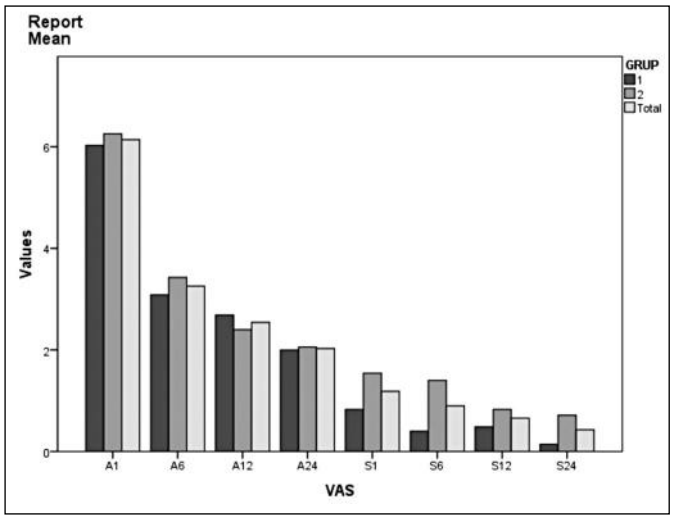

Fig. 2: Shoulder pain-VAS values and abdominal pain-VAS values in the 1st, 6th, 12th and 24th hours. Data were presented as mean. Group 1: Low Pressure (10(8-10) mm/Hg); Group 2: Standard(high) Pressure (15(14-16) mm/Hg). A: Abdominal, S: Shoulder

TABLE II - *Comparison of $EtCO_2$, Nausea, Vomiting, Bowel movement, Flatus in Postoperative Pain Scores in Laparoscopic Cholecystectomy Performed at Low Pressure (8-10 mm Hg) and Standard Pressure (14-16 mm Hg)*

	Group (1) (8-10 mmHg)	Group (2) (14-16 mmHg)	p
Shoulder Pain[a]			
VAS 1 h	0.83 (0-5)	1.54 (0-6)	0.720
VAS 6 h	0.40 (0-5)	1.40 (0-4)	0.020*
VAS 12 h	0.49 (0-5)	0.83(0-4)	0.254
VAS 24 h	0.14 (0-4)	0.71 (0-4)	0.018*
Abdominal Pain[a]			
VAS 1 h	6.03 (3-8)	6.26 (2-7)	0.454
VAS 6 h	3.09(2-6)	3.43 (0-6)	0.172
VAS 12 h	2.69 (0-6)	2.40 (0-4)	0.394
VAS 24 h	2.00 (0-4)	2.06 (0-4)	0.817
$ETCO_2$ [a]	32.4±3.3	34.6±3.0	0.007*
CO_2 Preop[b]	33.34±4.4	34.05±6.7	0.466
CO_2 Postop[b]	43,14±9.1	42.45±11.0	0.285
Nausea[c]	10/25	15/20	0.212
Vomiting[c]	9/26	11/24	0.597
Bowel Movement(h) [b]	10.11±4.05	12.57±4.6	0.008*
Flatus (h) [b]	15.63 ±10.6	15.03±9.0	0.925

Data presented as mean SD or number of patients (%); [a] Student-T test; [b] Mann–Whitney U-test; [c] Pearson's 2 -test; [d] Fisher's exact test; *VAS, Visual Analogue Scale; h: hour; Statistically significant between-group differences (P< 0.05); * h: hours

Patients' mean intraoperative ETCO2 values measured in minutes 0, 15, 30 and 45 were significantly higher in Group 2 (p<0.005). No statistically significant difference was recorded between the development of nausea and vomiting monitored during the first postoperative 24 hours (p≥0.05). While no statistically significant difference was recorded between the two groups in terms of the time of first flatus bowel movements resumed significantly earlier in Group 1 (p<0.005) (Table II).

TABLE III - *Laboratory values of Group 1 (8-10 mmHg) and Group 2 (15mmHg)*

	Group (1) (8-10 mmHg)	Group (2) (14-16 mmHg)	p
Lactate Preop [b]	1.31±0.5	1.37±0.5	0.559
Lactate Postop [b]	1.99±0.4	1.21±0.4	0,001*
CK-MB Preop [b]	2.18 ±2.7	1.84 ±1.1	0.920
CK-MB Postop [b]	4.1 ±4.8	2.98±1.9	0.643
AST Preop [b]	21.54±6.9	20.31±5.9	0.693
AST Postop [b]	43.85±29.1	41.37±39.8	0.368
ALT Preop [b]	25.74±18.8	20.00±6.8	0.778
ALT Postop [b]	36.88±21.3	28.17±11.8	0.125
CRP Preop	5.79±7.0	8.80±16.4	0.516
CRP Postop	8.16±10.2	9.95 ± 13.6	0.726
LDH Preop	215.45± 52.2	210.48±45.7	0.892
LDH Postop	225.94±49.7	221.82±71.1	0.445

Data presented as mean SD; [a] Student-T test; [b] Mann–Whitney U-test; Statistically significant between-group differences (P< 0.05) *

According to laboratory tests of the patients in preoperative 24 hours and postoperative 24 hours, there was no statistically significant difference between creatine kinase (CK-MB), aspartate aminotransferase (AST), alanine aminotransferase. (ALT), c-reactive protein CRP, lactate dehydrogenase (LDH) and CO_2 values measured in blood gas in preoperative and postoperative periods (p≥0.05). While there was no significant difference between lactate values measured during preoperative period lactate values measured during postoperative period were significantly higher in Group 1 (Table III).

Discussion

It has been reported for many years that laparoscopic cholecystectomy has various side effects such as cardiovascular changes, acid-base imbalances, deterioration in respiratory function and postoperative pain due to CO_2 pneumoperitoneum. Diaz-Cambronero O et al. asserted that these side effects could be minimized by using low intraperitoneal pressure between 7 mm/Hg and 10 mm/Hg especially in elders and in patients with cardiovascular and respiratory comorbidities [13].

Increase in intraabdominal pressure proportionally with the level of CO_2-pneumoperitoneum created during laparoscopic cholecystectomy induces small bowel ischemia and thereby may cause nausea and vomiting due to the release of emetic agents including serotonin. Bowel ischemia may potentially increase as a result of compression of the bowel with surgical manipulations and retractions during surgery. Bowel tissues are metabolically quite active and have a weak tolerance even for short ischemia periods [14].

M. Koc et al. compared normal and low pressure levels during laparoscopic cholecystectomy performed on 53 patients with gallstone and asserted that there was no correlation between high- and low-pressure laparoscopy and postoperative pain. They concluded that this had less effect on intensity of shoulder pain and abdominal pain caused by peritoneal distention. Routine use of low-pressure pneumoperitoneum was recommended to relieve postoperative pain after LC [15]. Findings obtained in our study support this.

Duck-Kyoung Kim et al. asserted that intraoperative pressure reduced to 8 mm/Hg in laparoscopic procedures performed during gynecological operations did not contribute to preventing postoperative nausea and vomiting compared to normal pressure level [14]. In our study, no difference occurred in low-pressure group in terms of nausea and vomiting. Occurrence of this effect is possible in case the difference between intraabdominal pressures is higher between the groups.

Beuk RJ et al. revealed that mesentery ischemia created in rats contributed to the ischemia to occur in intestinal region as a result of decrease in blood flow and thereby serious and fatal effects may develop as a result of decrease in time-dependent blood flow. Since high pressure levels decrease blood flow and affect circulation by putting pressure on mesentery, increase in intraabdominal pressure may be among the factors contributing to mesentery ischemia [16].

Corke C et al. assert that clinical results of intestinal ischemia in early period may be seen as decrease in bowel sounds and delay in time of physiological functions that are flatus and defecation as a result of the delay in return of gastrointestinal system to its normal function [17]. In our study, mean times when bowel movements resumed were earlier in low-pressure group, however, no significant difference was recorded between the time of first flatus. Not only intraabdominal pressure changes but also some other factors such as mobilization duration may have contributed to the time of first flatus.

Apoory Goel et al. evaluated shoulder pain in patients who underwent laparoscopic cholecystectomy at low and normal pressure and observed that VAS value was lower in low pressure group between 12th and 24th hours and that there was no significant difference between the groups in 24th hour [18]. HK Bhattacharjee et al. observed in patients who underwent laparoscopic cholecystectomy with 9 mm/hg and 14 mm/hg in two different groups that shoulder pain measured in the 8th and 24th hours was lower in the low pressure group [19]. In our study, shoulder pain-VAS values measured in the 6th and 24th hours were lower in low pressure group. There was no significant difference between the groups in terms of abdominal pain.

No difference was found between surgical durations in laparoscopic cholecystectomy performed under two different pressures in the study by Apoorv Goel et al.[18] and between surgical durations and hospital stays in laparoscopic surgery performed under different intraperitoneal pressures in the study by Ali Akkoc et al. [12] In our study, no difference was found between surgical duration, pneumoperitoneum durations, and hospital stays either and this result support the previous studies.

JC Radosa et al. observed that although the first flatus after two different intraabdominal CO_2 pneumoperitoneum was earlier in low pressure group no significant difference was recorded in the times when bowel movements resumed and shoulder and abdominal pain were less in low pressure group [20].

In their study comparing nausea and vomiting rates in patients who were divided into three groups according to their CO_2 levels and in whom intraabdominal pneumoperitoneum was created, Ji-Seon Son et al. observed that there was no significant difference within 24 hours [21]. In our study, $ETCO_2$ levels were found significantly higher in the group in which 14-16 mm/Hg of pressure was used compared to low pressure group. This suggests that the amount of CO_2 in respiration increases in direct proportion to the amount of CO_2 insufflated into the intraabdominal region.

H Chen et al. revealed an increase in the levels of AST and ALT, which were liver function tests, after laparoscopic cholecystectomy in normal pressure group compared to low pressure group, however, they asserted that this increase got back to normal on the 3rd day [22]. In our study, AST and ALT levels increased in both groups within postoperative 24 hours when compared with preoperative values, however, no statistically significant difference was recorded between the two groups.

Plasma CK-MB and CRP levels have been used as indicators of tissue damage for many years [23]. Although Kyeong A So et al. revealed that there was an increase in CRP levels in laparoscopic operations in which they used multiport and single port they did not analyze its relationship with pressure. In our study, there was no difference between the groups in terms of CRP levels.

Neogi Probal et al. asserted that AST, ALT and LDH levels were lower in low pneumoperitoneum levels. In our study, although LDH levels increased in both groups compared to preoperative levels no significant difference was recorded between the groups.

Lactate is a product of anaerobic metabolism and used as an indicator of tissue damage caused by hypoxia especially in tissues of critical patients [24]. No significant difference was recorded between preoperative lactate values, but they were lower in normal pressure group in postoperative period. However, lactate levels under 2 nMol/L are accepted as normal. Therefore, we think this difference has no meaning as preoperative and postoperative lactate levels measured in both groups were normal [25].

In our study, we used 8-10 mm/Hg of CO_2 pneumoperitoneum because of the experience of surgical team, their usage habit and the thought that sufficient level of intraabdominal imaging could not be obtained in lower pressure values. A pressure level under this lev-

el may clinically have more significant effects. This is the limitation of our study. However, in this case, we think that unpleasant results of intraoperative complications such as trocar injury and traumatic lacerations in intraabdominal organs as a result of insufficient level of imaging required to be overcome.

Conclusion

Decreasing the pressure created for CO_2 pneumoperitoneum in laparoscopic cholecystectomy from 14-16 mm/Hg to 8-10 mm/Hg does not build a significant difference in terms of clinical results and laboratory values. Therefore, the surgical team should prefer easy-to-apply pressure levels in which they are experienced, in which they have the lowest complication rate and in which they obtain the best intraabdominal imaging during intraoperative period.

Riassunto

Scopo dello studio era quelo di determinare se la variazione della pressione intraaddominale causata dal pneumoperitoneo creato durante la colecistectomia laparoscopica (LC) ha effetti su dolore addominale e alla spalla, su nausea, vomito, movimenti intestinali, tempo del primo flatus e, della defecazione e sui parametri biochimici.
Nello studio sono stati inclusi settanta pazienti a cui è stata diagnosticata la colelitiasi e che sarebbero stati sottoposti a LC, di età compresa tra 18 e 75 anni, con le classificazioni I-III della Society of Anesthesia Physical Status (ASA). I pazienti sono stati divisi in due gruppi: per intervento a bassa pressione (8-10 mm/hg) e intervento ad alta pressione (14-16 mm/hg). Sono state osservate le differenze nelle prognosi dei pazienti in entrambi i gruppi per la significatività statistica.

References

1. Chui P, Gin T, Oh T: *Anaesthesia for laparoscopic general surgery.* Anaesthesia and intensive care, 1993; 21; 2:163-71.

2. Mcmahon AJ, Russell IT, Baxter JN, et al.: *Laparoscopic versus minilaparotomy cholecystectomy: A randomised trial.* Lancet, 1994; 343; 8890:135-38.

3. Gelmini R, Franzoni C, Saviano M: *Day surgery laparoscopic cholecystectomy: initial experience in 43 consecutive patients.* Ann Ital Chir, 2013; 84; 6:631-36.

4. Gan TJ, Diemunsch P, Habib AS, et al.: *Consensus guidelines for the management of postoperative nausea and vomiting.* Anesthesia & Analgesia, 2014; 118; 1:85-113.

5. Neudecker J, Sauerland S, Neugebauer E, et al.: *The european association for endoscopic surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery.* Surgical endoscopy, 2002;16; 7: 1121-143.

6. Galizia G, Prizio G, Lieto E, et al.: *Hemodynamic and pulmonary changes during open, carbon dioxide pneumoperitoneum, and abdominal wall-lifting cholecystectomy.* Surgical endoscopy, 2001; 15; 5: 477-83.

7. Özdemir-van Brunschot DM, van Laarhoven KC, Scheffer GJ,et al.: *What is the evidence for the use of low-pressure pneumoperitoneum? A systematic review.* Surgical endoscopy, 2016; 30; 5:2049-65.

8. Diaz-Cambronero O, Flor Lorente B, Mazzinari G, et al.: *A multifaceted individualized pneumoperitoneum strategy for laparoscopic colorectal surgery: A multicenter observational feasibility study.* Surgical endoscopy, 2019; 33; 1:252-60.

9. Sefr R, Puszkailer K, Jagos F: *Randomized trial of different intraabdominal pressures and acid-base balance alterations during laparoscopic cholecystectomy.* Surg Endosc, 2003; 17; 6:947-50.

10. Gándara V, de Vega DS, Escriú N, et al.: *Acid–base balance alterations in laparoscopic cholecystectomy.* Surgical endoscopy, 1997; 11; 7:707-10.

11. Hypólito OH, Azevedo JL, de Lima Alvarenga Caldeira FM, et al.: *Creation of pneumoperitoneum: noninvasive monitoring of clinical effects of elevated intraperitoneal pressure for the insertion of the first trocar.* Surgical endoscopy, 2010; 24; 7:1663-669.

12. Akkoc A, Topaktas R, Aydin C, et al.: *Which intraperitoneal insufflation pressure should be used for less postoperative pain in transperitoneal laparoscopic urologic surgeries?* Int Braz J Urol, 2017; 43; 3:518-24.

13. Berg K, Wilhelm W, Grundmann U, et al.: *Laparoscopic cholecystectomy. Effect of position changes and CO2 pneumoperitoneum on hemodynamic, respiratory and endocrinologic parameters.* Zentralbl Chir, 1997; 122; 5:395-404.

14. Kim, D K, Cheong I L, Lee GY, et al.: *Low pressure (8 mmhg) pneumoperitoneum does not reduce the incidence and severity of postoperative nausea and vomiting (ponv) following gynecologic laparoscopy.* Korean Journal of Anesthesiology, 2006; 50; 6:36-42.

15. Koc M, Ertan T, Tez M, et al.: *Randomized, prospective comparison of postoperative pain in low-versus high-pressure pneumoperitoneum.* ANZ journal of surgery, 2005; 75; 8:693-96.

16. Beuk RJ, Heineman E, Tangelder GJ, et al.: *Effects of different durations of total warm ischemia of the gut on rat mesenteric microcirculation.* J Surg Res, 1997; 73; 1:14-23.

17. Corke C, Glenister K: *Monitoring intestinal ischaemia.* Critical Care and Resuscitation, 2001; 3; 3:176.

18. Goel A, Gupta S, Bhagat TS, et al.: *Comparative analysis of hemodynamic changes and shoulder tip pain under standard pressure versus low-pressure pneumoperitoneum in laparoscopic cholecystectomy.* Euroasian J Hepatogastroenterol, 2019; 9; 1:5-8.

19. Bhattacharjee HK, Jalaludeen A, Bansal V, et al.: *Impact of standard-pressure and low-pressure pneumoperitoneum on shoulder pain following laparoscopic cholecystectomy: a randomised controlled trial.* Surg Endosc, 2017; 31; 3:1287-295.

20. Radosa JC, Radosa MP, Schweitzer PA, et al.: *Impact of different intraoperative CO2 pressure levels (8 and 15 mmHg) during laparoscopic hysterectomy performed due to benign uterine pathologies on postoperative pain and arterial pCO 2: a prospective randomised controlled clinical trial.* BJOG: An International Journal of Obstetrics & Gynaecology, 2019; 126; 10:1276-285.

21. Son JS, Oh JY, Ko S.: *Effects of hypercapnia on postoperative nausea and vomiting after laparoscopic surgery: A double-blind randomized controlled study.* Surgical endoscopy, 2017; 31;11: 4576-582.

22. Chen H: *Effects of different pneumoperitoneum pressure on liver, kidney and respiratory function during laparoscopic cholecystectomy.* Chinese Journal of Primary Medicine and Pharmacy, 2018; 25; 7:915-19.

23. Tabatabai M, Segal R, Amidi M, et al.: *Serum creatine phosphokinase, lactic dehydrogenase, and their isoenzymes in the perioperative period.* Journal of clinical anesthesia, 1989; 1; 4:277-83.

24. Brooks GA.: *The science and translation of lactate shuttle theory.* Cell Metab, 2018; 27; 4:757-85.

25. Husain FA, Martin MJ, Mullenix PS, et al.: *Serum lactate and base deficit as predictors of mortality and morbidity.* 2003; 185; 5: 485-91.