Cardiac and Liver Marker Alterations After Laparoscopic Gynaecologic Operations

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Objective: In our study, we aimed to investigate the effect of laparoscopic procedures in which the abdominal cavity at a Trendelenburg position of 15 degrees was insufflated with CO₂ on cardiac and liver markers.

Methods: Forty patients scheduled for laparoscopic gynaecological surgery were included in the study. Venous blood samples were taken the day before operation and 6 hours after surgery, and later, lactate dehydrogenase (LDH), creatine kinase (CK), creatine kinase-MB (CK-MB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), myoglobin (MY) and d-dimer (d-D) were measured.

Results: There was no statistically significant difference in the values of preoperative and postoperative ALT (16.8±9.4 and 17.8±9.3; p=0.579), AST (19.4±7 and 20.9±7.6; p=0.361) and ALP (65.2±16.2 and 63.3±16.9; p=0.609), but LDH (385.1±117.3 and 460.6±156.3; p=0.003), CK (113.8±138.5 and 247.9±283.5; p=0.0001), CK-MB (22.8±13.3 and 28.7±16; p=0.011), MY (28.1±12.9 and 138.8±129; p=0.0001) and d-D (509.5±815: 1026±1054; p=0.0001) increased significantly.

Conclusion: After laparoscopic operations in the Trendelenburg position, postoperative serum ALT, AST and ALP levels, remained unchanged, when compared to preoperative values, but LDH, CK, CK-MB, myoglobin and d-dimer values increased significantly.

Keywords: Gynaecological laparoscopic surgery, Trendelenburg, cardiac enzymes, liver enzymes

Introduction

Laparoscopic surgery replaced the open approaches in many surgical branches in the recent years because of a reduced hospitalization period due to the quick recovery of patients, less postoperative pain, preferred by patients aesthetically and reduced morbidity compared to open surgery. In laparoscopic surgeries, abdomen is inflated with various gases to provide better visualization of the surgical area. CO₂ is the most commonly used gas for this purpose because it is not flammable; it melts in water easily, leading to no gas accumulation and it is colourless and cost-effective (1).

Furthermore, various positions are applied to the patient depending on the surgery area to ease the access to the area that the surgery will be performed. The position that is applied in most gynaecological laparoscopic surgical interventions is the 15–20 degrees Trendelenburg (upside down) position.

During the Trendelenburg position, the diaphragm moves upward and limits the expansion capacity of the lungs, which causes a decrease in the respiration volume. Hydrostatic pressure increases and bradycardia may also be observed. It has been demonstrated in studies that the Trendelenburg position increases the pulmonary artery pressure, central vein pressure and pulmonary capillary wedge pressure (2).

Filling the abdominal cavity with CO₂ causes the upward replacement of the diaphragm, which may lead to a decrease in lung volumes and compliance, atelectasis, increase in airway resistance and ventilation perfusion mismatch (3, 4).

It is demonstrated that pneumoperitoneum increases systemic vascular resistance (5), increases central vein pressure (6), decreases venous return, increases the heart rate and mean arterial pressure, increases the intra-abdominal pressure increase by 15 mmHg and increases the cardiac output by 15%–30% (7). The European Association for Endoscopic Surgery states, in

a guideline published in 2001, that intra-abdominal pressure not exceeding 15 mmHg in healthy people causes a decrease in cardiac output in a manner without showing any clinical effects. The same guideline states, only in patients that have American Society of Anaesthesiologists (ASA) scores of III and IV, that insufflations can disrupt the stability of the cardiovascular system, blood supply of the lung and corresponding peripheral tissue oxygenation (8).

During laparoscopic interventions, hypercarbia can occur because of CO₂ absorption from the peritoneum, the Trendelenburg position, hypoventilation and diaphragm damages caused by pneumoperitoneum (9). Although the haemodynamic effect of 45–50 mmHg hypercarbia is small in healthy people, when partial carbon dioxide pressure exceeds 55 mmHg, it may lead to myocardial depression by directly or, via the autonomic nervous system, indirectly affecting the cardiovascular system (10).

When all these components are combined with the anaesthesia that will be used during the laparoscopic intervention, there is a possibility of affecting cardiac and pulmonary markers.

Therefore, our study attempts to study the effects on the cardiac and pulmonary markers of the gynaecological laparoscopic interventions in which the abdominal cavity is inflated with CO₂ in 15 degree Trendelenburg position.

Methods

This study was conducted in the Anaesthesiology and Reanimation Clinic of the Bağırcılar Training and Research Hospital after obtaining approval from the Ethics Committee of the same hospital. Every patient that will participate in the study was informed and their written consents were obtained prior to participating in the study.

The study was planned as a prospective one and 40 female patients who underwent laparoscopic gynaecological interventions with the following criteria were included: ASA I–II, 18–65 years of age and body mass index (BMI) <35. Every patient that was planned to participate in the study underwent physical examination, and their routine tests were examined a day prior to the intervention.

Patients with known cardiovascular pathologies, histories of previous hepatitis B and C occurrences, a trauma experience in the past week and inflammatory gallbladder disease were excluded from the study. Patients were rendered hungry for at least 6 h prior to surgery and they were intramuscularly administered with, as a premedication, 0.07 mg kg⁻¹ midazolam, after being admitted to the operating room. After the patient is admitted to the operating room and after standard electrocardiogram (EKG), non-invasive blood pressure and pulse oximetry monitorization is performed, vascular access is established in one of the forearm veins via 18 Gauge IV cannula to administer fluid and medicine. Prior to the in-

tervention, blood samples are collected for measurements of lactate dehydrogenase (LDH), creatine kinase (CK), creatine kinase-MB (CK-MB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), myoglobin (MY) and d-Dimer (d-D).

Anaesthesia inductions of the patients were established by 1 µg kg⁻¹ fentanyl and 2 mg kg⁻¹ propofol vs. 0.6 mg kg⁻¹ rocuronium, and endotracheal intubation was performed. In the maintenance of the anaesthesia, 50% oxygen/air mixture, 1.5% sevoflurane and 0.15–0.25 µg kg⁻¹ remifentanyl infusion were used. When necessary, additional rocuronium doses of 10 mg were used to sustain muscle relaxation. During the anaesthesia, mechanical ventilation was performed using the Datex-Ohmeda S/5 Avance anaesthesia machine. In the beginning, the respiration volume was set at 8 mL kg⁻¹, respiration frequency at 10 respirations/min and inspiration:expiration setting at 1:2. When necessary, respiration volume and frequency adjustments were performed to sustain end-tidal CO₂ levels between 35 and 45. The duration of the operation was measured by recording the starting time of the operation and the time of the last stitch. After inflating with CO₂, intra-abdominal pressure was measured with the Storz Thermoflator and recorded with 5-min intervals. The gas that was used for inflating the abdomen was emptied in the position that the patient's operation was performed. At the end of the intervention, the effect of the muscle relaxant was reversed with 0.04 mg kg⁻¹ neostigmine and 0.02 mg kg⁻¹ atropine.

At the 6th postoperative hour, vein blood samples were taken again and LDH, CK, CK-MB, ALT, AST, ALP, MY and d-D values were measured, and EKG of the patients was performed.

Statistical analysis

Statistical analyses were performed by STATISTICA AXA 7.1 (Tulsa, USA) program. Data are given as an average (±standard deviation). It was calculated that to demonstrate a 15% difference between preoperative and postoperative values, 39 patients had to be included in the study with 0.05 type 1 margin of error and 80% statistical power, and 40 patients were included in the study, taking a possible exclusion from the study into account.

After evaluation by one-sample Kolmogorov–Smirnov test, whether or not the data conformed to the normal distribution, Wilcoxon test was used for the comparison of the intra-group data. $p < 0.05$ was considered to be statistically significant.

Results

Forty female patients were included in the study. None of the patients was excluded. Age, weight, BMI, operation time and mean intra-abdominal pressure (IAP) are shown in Table 1.

A statistically significant difference between preoperative and postoperative ALT (16.8 ± 9.4 ; 17.8 ± 9.3 ; $p = 0.579$),

AST (19.4 ± 7 ; 20.9 ± 7.6 ; $p=0.361$) and ALP (65.2 ± 16.2 ; 63.3 ± 16.9 ; $p=0.609$) values was not found. However, a statistically significant increase was observed in postoperative LDH (385.1 ± 117.3 ; 460.6 ± 156.3 ; $p=0.003$), CK (113.8 ± 138.5 ; 247.9 ± 283.5 ; $p=0.0001$), CK-MB (22.8 ± 13.3 ; 28.7 ± 16 ; $p=0.011$), MY (28.1 ± 12.9 ; 138.8 ± 129 ; $p=0.0001$) and d-D (509.5 ± 815 ; 1026 ± 1054 ; $p=0.0001$) values compared with that in preoperative values (Table 2).

A statistically significant pathological change was not detected when preoperative and postoperative EKGs were compared. ST-elevation or non-ST-elevation acute coronary syndrome was not detected in any of the patients during their time in the hospital.

Discussion

It is known that when pneumoperitoneum is performed during laparoscopic interventions, CO₂ used for establishing pneumoperitoneum and the Trendelenburg position have effects on patients' haemodynamic functions (2, 6, 7). In our study, we aimed to investigate whether these haemodynamic changes have effects on cardiac and pulmonary markers as well.

It is determined in our study that, in the postoperative period, LDH, CK, CK-MB, MY and d-D values significantly increased but that ALT, AST and ALP values showed no significant change. Even though LDH, CK, CK-MB, MY and d-D values increased in the postoperative period, EKG change did not accompany these findings.

Our findings that show no statistically significant change for preoperative and postoperative ALT, AST and ALP values is generally consistent with the literature, although a few different results are achieved in the prior literature. Etoh et al. (11) claimed that temporary liver function disorder, due to decrease in portal blood flow, can be observed during pneumoperitoneum with CO₂. In a series of 355 patients, Ahmad et al. (12) demonstrated that after laparoscopic cholecystectomies, serum ALT and AST values increased but ALP values did not change. Pressure applied to liver during cholecystectomies, retraction of the gallbladder and the presence of micro stones in biliary tracts can also cause an increase in liver enzymes (13). Eryılmaz et al. (14) reported that an intra-abdominal pressure ≥ 14 mmHg increases the ALT and AST values in the first postoperative hour in laparoscopic cholecystectomies. Yoon et al. (15) demonstrated that in laparoscopic gastrectomies, postoperative ALT, AST and ALP values did not significantly change compared to preoperative values. Because, differing from our study, the studies cited here were conducted in laparoscopic cholecystectomies and gastrectomies, increases in the ALT and AST values can be expected, depending on the property of the intervention and the area of surgery. In a study about laparoscopic gynaecological interventions, Beyaz et al. (16) found out that ALT and AST values measured at the 1st and 24th postoperative hour did

Table 1. Demographic data (Mean $\pm$ SD)

Age (year)	39.4 $\pm$ 11.6
Weight (kg)	79.3 $\pm$ 11.5
BMI (kg m ⁻²)	30.4 $\pm$ 4.9
Duration of operation (min)	82.6 $\pm$ 74
IAP (mmHg)	12.5 $\pm$ 0.8

SD: standard deviation; BMI: body mass index; IAP: intra-abdominal pressure

Table 2. Biochemical markers (Mean $\pm$ SD)

	Preoperative	Postoperative	p value
ALT (IU L ⁻¹)	16.8 $\pm$ 9.4	17.8 $\pm$ 9.3	0.579
AST (IU L ⁻¹)	19.4 $\pm$ 7	20.9 $\pm$ 7.6	0.361
ALP (IU L ⁻¹)	65.2 $\pm$ 16.2	63.3 $\pm$ 16.9	0.609
LDH (IU L ⁻¹)	385.1 $\pm$ 117.3	460.6 $\pm$ 156.3	0.003
CK (IU L ⁻¹)	113.8 $\pm$ 138.5	247.9 $\pm$ 283.8	0.0001
CK-MB (ng mL ⁻¹)	22.8 $\pm$ 13.3	28.7 $\pm$ 16	0.011
Myoglobin (ng mL ⁻¹)	28.1 $\pm$ 12.9	138.8 $\pm$ 129	0.0001
d-Dimer (mg L ⁻¹)	509.5 $\pm$ 815	1026 $\pm$ 1054	0.0001

Values are presented as mean $\pm$ standard deviation. Wilcoxon test was used for comparison. ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; LDH: lactate dehydrogenase; CK: creatine kinase; CK-MB: creatine kinase-MB

not significantly differ from the preoperative values. Jeong et al. (17) compared preoperative and postoperative ALT and AST values in laparoscopic gastrectomy and colectomy surgeries and determined that there was no statistically significant increase in postoperative ALT and AST values in colon surgeries, whereas there was a significant increase in ALT and AST values following gastric surgeries, and thought that this may be caused by direct liver manipulation or aberrant hepatic artery ligation. Because it is very difficult for either of these assumptions to occur in laparoscopic gynaecological interventions, having obtained similar results to laparoscopic colon interventions in our study reinforces this thesis.

Similar to our study, Güven et al. (18) detected an increase in LDH after laparoscopic cholecystectomies and attributed this to high intra-abdominal pressure affecting mesentery blood flow. Because mesenteric blood flow can also be affected in gynaecological laparoscopic interventions performed in the Trendelenburg position, this is an acceptable hypothesis for us as well.

It is known that creatine kinase, CK-MB and myoglobin are also secreted from damaged cardiomyocytes (19, 20). CK and myoglobin increase observed in our study can be dependent on, as have also been shown in other studies before, operation time, muscle incision or position (21). Youssef et al. (22) reported that creatine kinase and myoglobin increase after major interventions in children, and Laurence (23) and Cohen et al. (24) reported that they increase after various surgical and orthopaedic interventions. Öztürk et al. (24),

however, demonstrated that in the blood samples taken at the 6th postoperative hour from patients that underwent thyroid surgery, CK-MB and myoglobin values did not significantly increase. Because the ischemic findings were not present in our patients in EKGs taken at the postoperative period and that our patients did not develop any cardiac complications, we maintained that the postoperative CK, CK-MB and myoglobin value increases detected in our study are due to the laparoscopic surgical intervention performed in the Trendelenburg position.

Nomura et al. (26) detected significant increases in d-D values after laparoscopic urologic surgeries. Kart et al. (27), in an experimental study they conducted on rats, found out that ovarian torsion increases d-D levels. Because many processes such as tissue damage, surgical operation and even intramuscular injection can activate coagulation and increase d-D levels, narrow specificity of the postoperative d-D test must be taken into consideration (27, 28). We are of the opinion that the statistically significant postoperative d-D level increase seen in our study is due to surgical intervention and coagulation that is activated during the intervention.

Because patients are generally hospitalized for 24 h after laparoscopic surgeries, postoperative blood analyses was limited to the first day. We were unable to determine whether the values returned to normal or whether they increased even more because we were unable to perform analyses in the following days. Because all gynaecological laparoscopic operations in our hospital are performed following the increase of intra-abdominal pressure, we were unable to compare with gynaecological operations performed without the increase of intra-abdominal pressure.

Conclusion

In laparoscopic interventions performed in the Trendelenburg position, serum ALT, AST and ALP values do not significantly change in the 6th postoperative hour compared to preoperative values, whereas LDH, CK, CK-MB, myoglobin and d-D values significantly increase.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Bagcilar Training and Research Hospital (28.06.2011-2011/26).

Informed Consent: Verbal informed consent was obtained from patients who participated in this study.

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