

## Physiological changes of pneumoperitoneum during laparoscopic cholecystectomy

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### الخلاصة

الخلفية العلمية: تزداد في هذه الأيام عمليات الناظور الجراحي بكثرة حتى أصبحت عملية استئصال المرارة بواسطة الناظور هي الأكثر شيوعاً واستخداماً في الداخل الجراحي لإجراء هذه العملية لابتداء من استسقاء غشاء الصفاق (البرتون) بالغاز وغالباً ما يستخدم غاز ثاني أوكسيد الكربون في ذلك ومن المهم جداً معرفة التغيرات الفسيولوجية والمرضية المصاحبة لعملية استسقاء البروتون الناتجة من ضغط الغاز المستخدم وامتصاصه، لاتخاذ الإجراءات الاحترازية اللازمة.

أجريت هذه الدراسة لمعرفة بعض التغيرات الفسيولوجية التي مالمهك أن تطرأ على المرضى الذين تجرى لهم عملية استئصال المرارة بواسطة الناظور، بسبب استسقاء البرتون. المرضى والطرق: تمنت نماذج البحث مئة مريض أجريت لهم عملية استئصال المرارة بالناظور تم اختيارهم بصورة عشوائية (80) و(20) من الذكور كانت أعمارهم تقع بين (19 إلى 60) سنة تم قياس بعض وظائف الرئة وبعض وظائف الكبد شوى اليوريا والكرياتينين في مصل الدم قبل إجراء العملية بساعة وبعدها (24) ساعة وبعدها (24) ساعة. ماقية. اس مس توى  $ETCO_2$  والالبيوتاتيريون، والص وديوم قبل استسقاء البروتون وعند نهاية استسقاء البروتون وانضام مراقبة وقياس ضغط الدم ودقات القلب خلال أوقات مختلفة أثناء العملية.

النتائج: أظهرت النتائج أن ضغط الدم وقلات القلب قد تغيرت تغيراً معنوياً واضحاً خلال أوقات مختلفة أثناء العملية وظائف الرئة انخفضت انخفاضاً واضحاً فحيطاً ارتفاع مس توى بعض انزيمات الكبد ارتفاعاً معنوياً واضحاً بعد (24) ساعة من إجراء العملية بالنسبة لمس توى  $ETCO_2$  والالديستيريون و البوتاسيوم فقد أرتفع مستواها ارتفاعاً معنوياً واضحاً عند نهاية استسقاء البروتون أما قيم اليوريا والكرياتينين والصوديوم في مصل الدم، فلم تظهر النتائج أي تغير معنوي. الاس تنقيح: جاء على هذا نقائلنته ملنجن الممكن أن نستنتج أن لعملية استئصال المرارة بواسطة الناظور الجراحي (البرتون) فسيولوجية واضحة في أثناء العملية وبعدها أن أغلب هذه التأثيرات ناتجة عن استسقاء البرتون بغاز ثاني أوكسيد الكربون وتغير وضعية المريض.

### Abstract

**Background:** Recently, the frequency and indication for laparoscopic surgery have increased, and laparoscopic cholecystectomy has been widely accepted as an alternative to laparotomy. To carry out the laparoscopic procedure, a pressure gas, most commonly  $CO_2$  is used. It is important to know the pathophysiological changes that are caused by an increase in intra-abdominal pressure and by the absorption of  $CO_2$  from an  $CO_2$  pneumoperitoneum.

**Aim this study;** aims to estimate some physiological changes that caused by pneumoperitoneum during laparoscopic cholecystectomy.

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**Patients and methods:** one hundred patients were included in this study randomly selected and consisted of (80 females) and (20 males) their ages were between 19-65 years. Those patients were underwent elective laparoscopic cholecystectomy. we measured some clinical and biochemical parameters (pulmonary function tests, liver function tests, serum urea and creatinine) 24hr before operation as control and 24hr after operation , also we measured end tidal  $\text{CO}_2$ (ET $\text{CO}_2$ ),serum aldosterone, potassium and sodium before insufflation of  $\text{CO}_2$ (as control)and at the end of insufflation ,blood pressure and heart rate recorded at different time throughout the operation.

**Results:** there is a statistically significant changes in haemodynamic responses (systolic, diastolic and heart rate) after pneumoperitoneum and changes in position; Pulmonary function tests (VC, FVC, FEV1, FEV1/FVC) show highly significant decrease ( $p < 0.01$ ) ,highly significant increase ( $p < 0.01$ ) in serum level of ALT and AST enzymes 24hrs post-operative . There was highly significant increase ( $p < 0.01$ ) in ET $\text{CO}_2$ , serum aldosterone and serum potassium level . Serum sodium, urea and creatinine show no significant changes.

**Conclusion:** we concluded that laparoscopic cholecystectomy causes notable physiological alteration intraoperatively and postoperatively, caused mainly by pneumoperitoneum and change in position.

**Key words:**pneumoperitoneum, laparoscopic cholecystectomy,physiological changes.

## Introduction

Laparoscopic surgery is a surgical technique in which operations in the abdomen are performed through small incisions in the abdominal or pelvic cavities. It is a form of "minimally invasive surgery" <sup>(1)</sup>. Since 1987, when the first laparoscopic cholecystectomy was performed, laparoscopic procedure have been the standard care of many routine diagnostic and therapeutic procedure for conditions such as appendicitis, gallstones, hernia, gastro-esophageal reflux, etc. <sup>(2)</sup>. Today, more than 90% of cholecystectomies are performed laproscopically, and has been accepted as the gold standard in the treatment of benign gallbladder disease. <sup>(3)</sup>.Laparoscopy requires the creation and maintenance of pneumoperitoneum which is the key step in the procedure in order to visualize the operative field within the abdominal and pelvic cavities <sup>(4)</sup>. Pneumoperitoneum is a complex and dynamic environment with significant potential alterations on a patient's mechanical, physiologic, and immunologic state. The various effects of pneumoperitoneum have been studied extensively by researchers in many fields <sup>(5)</sup>.  $\text{CO}_2$  is usually used for insufflation due to its low cost, non-flammability, chemical stability, and high diffusion capacity with subsequent rapid absorption and excretion,  $\text{CO}_2$  is also highly soluble and, therefore, poses a lower risk of gas embolism <sup>(6)</sup>.The  $\text{CO}_2$

pneumoperitoneum causes an increase in intra-abdominal pressure with a consecutive elevation of the diaphragm which can result in hyperventilation. The compression of the vena cava causes the cardiac output volume to be reduced and the central venous pressure to be increased, resulting in increased vascular resistance in the arterial circulation <sup>(7)</sup>.

In addition, an increase in intra-abdominal pressure above the normal physiological portal circulation pressure (7-10 mmHg) results in splanchnic ischemia. During laparoscopy, there is a marked reduction in blood flow to the hepatic, renal, and intestinal circulatory systems, when the laparoscopic procedure is completed, abdominal deflation is performed this reduces the intra-abdominal pressure and increases splanchnic perfusion. During reperfusion, free oxygen radicals, which are the most important mediators of oxidative tissue damage and consequential organ dysfunction, are generated as a result of ischemia-reperfusion induced by the inflation and deflation of the peritoneum. <sup>(8)</sup>In general, the most likely causes of oxidative stress as a consequence of CO<sub>2</sub> pneumoperitoneum are ischemia-reperfusion injury due to changes in the abdominal pressure, inflammation associated with tissue trauma, and diaphragmatic dysfunction <sup>(9)</sup>. These problems are well tolerated in most patients. Nevertheless, older patients and those with conditions such as emphysema and chronic obstructive pulmonary disease and cardiovascular disease are at an increasing risk of perioperative complications. These effects can be minimized with appropriate dedicated anesthetics management <sup>(10)</sup>.

### **Aim of the study**

This study aims to estimate some physiological changes associated with pneumoperitoneum during laparoscopic cholecystectomy. So this study is designed to determine the systolic, diastolic blood pressure and HR during pneumoperitoneum, the end tidal CO<sub>2</sub> during operation, some pulmonary function tests (VC, FVC, FEV<sub>1</sub>, and FEV<sub>1</sub>/FVC), some renal function tests (serum urea, serum creatinine), some liver function tests (ALT, AST, GGT, ALK. Phosphatase, T.S. B), serum aldosterone hormone, potassium and sodium ions.

### **Patients and method**

This prospective study was carried out in Al-Diwanyia General Teaching Hospital lasted from November (2011) to May (2012), one hundred patients were included in this study randomly selected and consisted of 80 females and 20 males. Those patients were diagnosed by specialist doctors to have uncomplicated, symptomatic gallstones, who underwent elective laparoscopic cholecystectomy. Patients with respiratory, hepatic, cardiovascular (ischemic heart disease and hypertension), diabetes or renal disease, heavy smoking and morbid obesity (body mass index > 40) were excluded from this study. All

patients were operated on a standardized regime of general anesthesia, after an overnight fast, anesthesia was induced with fentanyl (2 µg/kg) and thiopentone (2-5 mg/kg), and was maintained with isoflurane (1%) in a mixture of nitrous oxide (30-50%) and oxygen (70-50%). Monitoring of surgical progress included ECG, and noninvasive assessment of blood pressure, heart rate and endtidalCO<sub>2</sub> (EtCO<sub>2</sub>).Respiration was maintained using a mechanical ventilator commencing at a rate of 12 breaths/min and featuring a tidal volume of 10mL/kg. cholecystectomy was performed using a typical four-trocar technique. Carbon dioxide was used for peritoneal insufflation by closed and Husson method with the intraabdominal pressure maintained at 12 mmHg and all subjects were kept at 15° head-up throughout the operation, during operative period, all patients received intravenous 5% glucose or glucose saline solution for fluid replacement and antibiotic prophylaxis (ceftriaxon).

**Statistical analysis**

All values were expressed as means ± SD. The data were analyzed by using of computer SPSS program. P values of less than or equal to 0.05 was considered to indicate statistical significance .Student's paired t - test was used to examine the differences between different groups and repeated-measures analysis of variance on ranks was used to compare measurements of each variable at the different time points.

**Results:**

**Table (1) patient's data**

| variable           | male         | female      |
|--------------------|--------------|-------------|
| number             | 20           | 80          |
| Age /years         | 40.05±8.98   | 39.44±11.34 |
| Weight /Kg         | 81.22±11.57  | 78.74±11.22 |
| Operative time/min | 52.894±11.46 | 51.01±10.39 |

Values are mean ± SD , means without any \* are insignificant at (p > 0.05)

There was a significant changes in heart rate,systolic and diastolic blood pressure throughout the operation for both female and male patients;as HR ,systolic and diastolic blood pressure significantly increase(p<0.01) after insufflation of carbon dioxide then these values show significant decrease(p<0.01) regarding systolic and diastolic blood pressure and(p<0.05)for HR at 20 min of insufflation and reverse Trendelenburge positioning and hypotension continue throughout the operation until the end of insufflation and change in position as in figures( 1),(2)and(3).

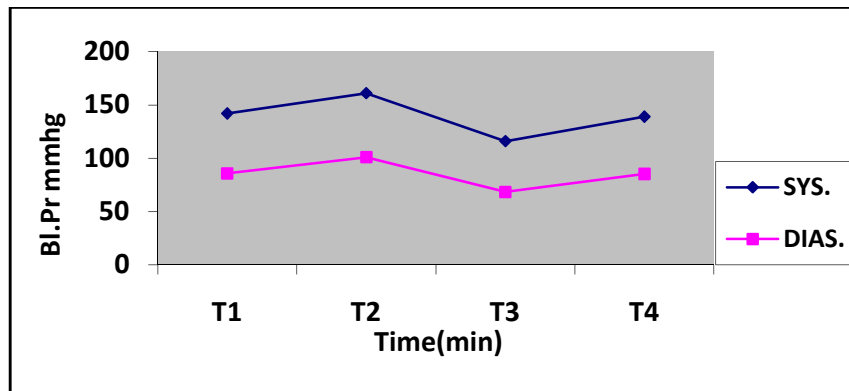


figure (1) :Changes in systolic and diastolic blood pressure (mean  $\pm$  SD) for female patients during operation( laparoscopic cholecystectomy) at different times (T1 before operation in operating theater,T2 after creation of pneumoperitoneum ,T3 20 minutes after pneumoperitoneum and change in position and T4 at the end of insufflation.

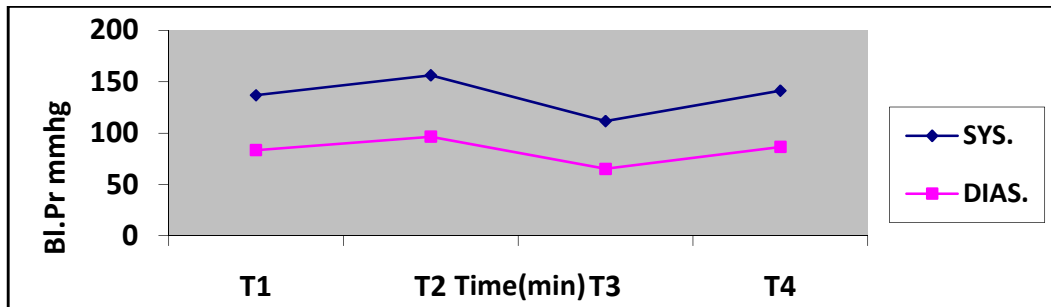
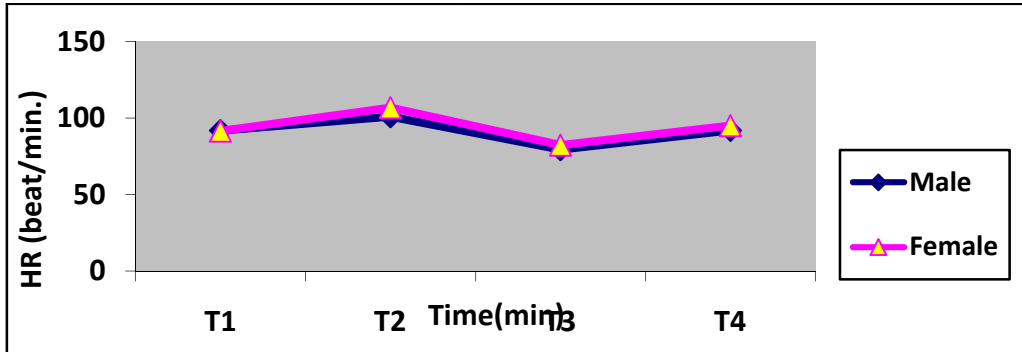
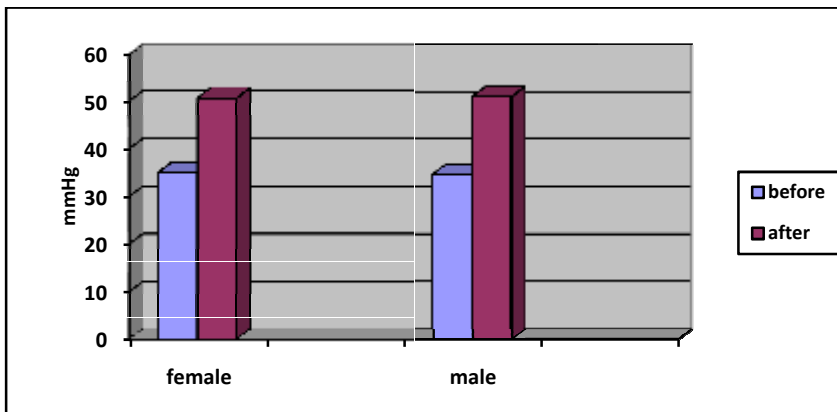


Figure (2) : Changes in systolic and diastolic blood pressure( mean  $\pm$  SD) for male patients during operation( laparoscopic cholecystectomy) at different times (T1: before operation in operating theater,T2: after creation of pneumoperitoneum,T3: 20 minutes after pneumoperitoneum and change in position and T4: at the end of insufflation.



**Figure (3) :**Changes in heart rate ( mean  $\pm$  SD) for female and male patients during operation( laparoscopic cholecystectomy) in different times (T1 before operation in operating theater,T2 after creation of pneumoperitoneum ,T3 20 minutes after pneumoperitoneum and change in position and T4 at the end of insufflation).

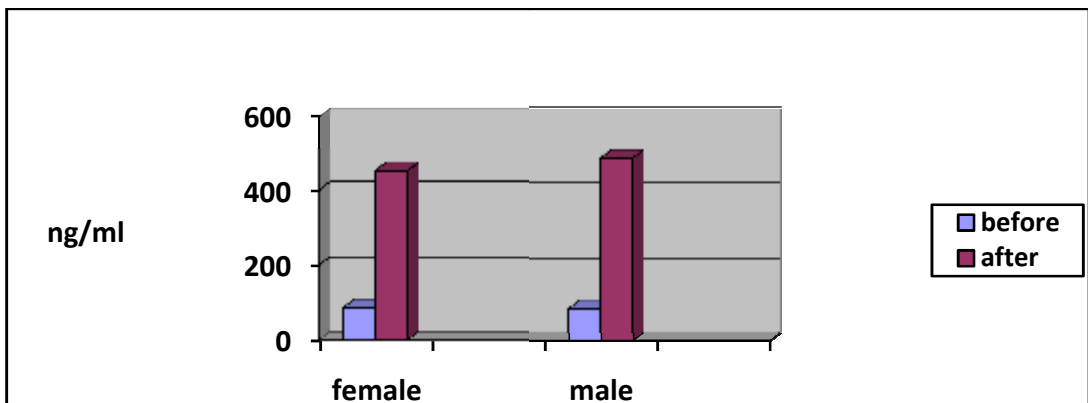


**Figure (4.5):** Changes in end tidal CO2 (mean  $\pm$  SD) for female and male patients before insufflation of CO2 and at the end of insufflation.

**Table (2): Changes in pulmonary functions (VC,FVC, FEV1, FEV1/FVC) for female and male patients 24 hr before operation and 24hr after operation.**

| Sex    | VC L   |          | FVC L  |         | FEV1 L |         | FEV1/FVC % |          |
|--------|--------|----------|--------|---------|--------|---------|------------|----------|
|        | before | after    | before | after   | before | after   | before     | after    |
| Female | 3.146  | 2.290    | 3.050  | 2.339±  | 2.417  | 1.533±  | 74.608±    | 60.685±  |
|        | ±      | ±        | ±      | 1.050** | ±      | 0.908** | 4.791      | 12.698** |
| Male   | 4.043  | 3.189    | 4.121  | 3.160±  | 3.178  | 2.255±  | 75.983±    | 66.638±  |
|        | ±      | ±        | ±      | 0.845** | ±      | 0.779** | 4.012      | 9.872**  |
|        | 0.986L | 1.045L** | 1.011  |         | 0.866  |         |            |          |
|        | 0.945  | 0.884**  | 0.956  |         | 0.846  |         |            |          |

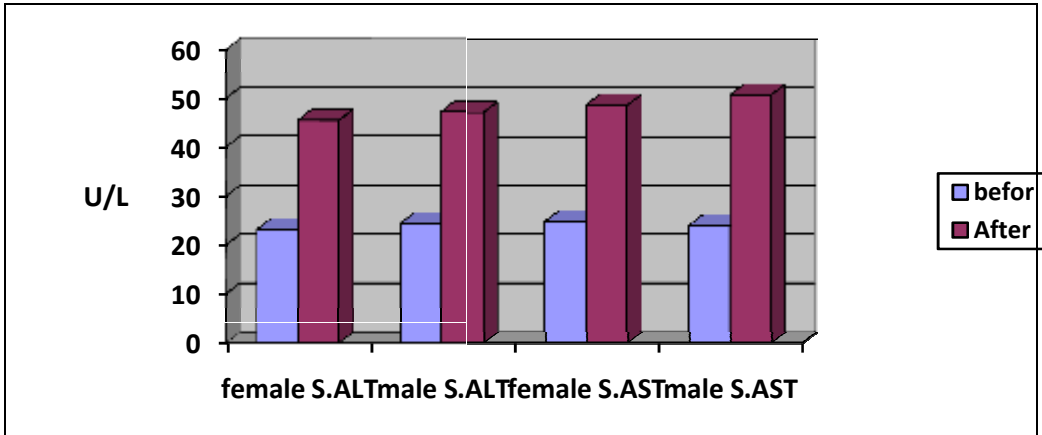
- Values are mean ± SD, \*\* (p < 0.01)

**Figure (5): Changes in serum aldosterone hormone (mean ± SD) for female and male patients before insufflation of CO<sub>2</sub> and at the end of insufflation.****Table (3): Changes in serum of urea and creatinine for female and male patients 24 hr before operation and 24hr after operation.**

| Sex    | S .urea mg/dl |              | S. creatinine mg/dl |             |
|--------|---------------|--------------|---------------------|-------------|
|        | before        | after        | before              | after       |
| Female | 31.514±7.773  | 29.585±6.753 | 0.740±0.126         | 0.712±0.127 |
| Male   | 31.894±7.922  | 28.473±6.266 | 0.738±0.097         | 0.683±0.092 |

Values are mean ± SD , Means without any \* are insignificant at (p > 0.05)

The values of liver enzymes ALT and AST for females and males cholelithiasis patients are significantly increased (p<0.01) 24hr after operation in comparison with control values (24hr before operation) .While the values of serum GGT, ALP and T. S.B (total serum bilirubin) show no significant changes (p>0.05)



**Figure (6):** Changes in serum of ALT and AST (mean ± SD) for females and males patients 24 hr before operation and 24hr after operation

**Table (4):** Changes in serum of GGT, ALP and T.S.B for females and males patients 24 hr before operation and 24hr after operation.

| Sex    | S.GGT U/l |          | S.ALP U/L |          | TSB mg/dL |         |
|--------|-----------|----------|-----------|----------|-----------|---------|
|        | before    | after    | before    | after    | before    | after   |
| Female | 29.077    | 24.833   | 85.671    | 88.644   | 0.857     | 0.967   |
|        | ± 17.410  | ± 8.4451 | ± 28.543  | ± 30.870 | ± 0.366   | ± 0.533 |
| Male   | 22.918    | 20.653   | 82.473    | 81.210   | 0.891     | 0.850   |
|        | ± 10.447  | ± 6.249  | ± 21.344  | ± 19.608 | ± 0.205   | ± 0.161 |

**Table (5):** Changes in the serum potassium and sodium for females and males patients before insufflation of CO2 and at the end of insufflation.

| Sex    | Serum potassium mmol/L |                 | Serum sodium mmol/L |               |
|--------|------------------------|-----------------|---------------------|---------------|
|        | Before                 | After           | Before              | After         |
| Female | 3.661 ± 0.374          | 4.223 ± 0.381** | 135.794±1.673       | 135.666±1.284 |
| Male   | 3.720 ± 0.376          | 4.239 ± 0.461** | 136.00±2.00         | 135.071±1.328 |

-Values are mean ± SD .

- \*\* (p < 0.01), Means without any \* are insignificant at (p > 0.05)



## Discussion

In the present study, female patients predominated (80%) in contrast to male patients (20%). This may be due to the fact that incidence of cholelithiasis is more common in females as compared to males<sup>(11)</sup>.

The mean age in laparoscopic cholecystectomy for females and males patients was,  $39\pm 11$ ;  $40\pm 8$  years respectively. Slightly higher mean age in other studies and this is due to excluded criteria in our study, usually women can develop gallstones at a young age due to increased risk during pregnancies and effects of estrogen<sup>(12)</sup>.

mean weight in this study for female and male patients was  $78\pm 11$ ;  $81\pm 11$  kg respectively. Slightly higher mean weight in this study than other studies. This result goes with fact that obesity is a major risk factor for gallstones, especially in women<sup>(13)</sup>.

The mean operative time in laparoscopic cholecystectomy for females and males patients in this study is shorter than other studies this because we exclude certain patients (because of exclusion criteria).

**Systolic, diastolic blood pressure and heart rate:** There was a significant changes in heart rate, systolic and diastolic blood pressure throughout the operation for both female and male patients. The most common cause of an increase in heart rate and blood pressure during laparoscopy is believed to be hypercarbia due to absorption of carbon dioxide from peritoneal cavity. This induces release of catecholamines which causes tachycardia and increase MAP. An increase in intra-abdominal pressure (IAP) with decrease in venous return may also cause a compensatory increase in heart rate<sup>(14)</sup>. Bradycardia has also been reported which may be due to vaguely mediated reflex initiated by stretching of peritoneum or by inadequate ventilation and hypoxia, also high increase in IAP can lead to emptying of abdominal capacitance vessels with a fall in central venous reserve and decrease in the cardiac output and BP<sup>(15)</sup>.

**End tidal CO<sub>2</sub>:** The values of end tidal CO<sub>2</sub> for females and males cholelithiasis patients show significant increase ( $p < 0.01$ ) at the end of insufflation in comparison with before insufflation values. the most important factor for the increase in EtCO<sub>2</sub> seen during laparoscopic cholecystectomy is absorption of CO<sub>2</sub> from peritoneum. Apart from this, respiratory changes because of raised IAP and decreased diaphragmatic movements and ventilation perfusion mismatch with increased dead space lead to decreased CO<sub>2</sub> elimination from the lungs. This increases arterial alveolar CO<sub>2</sub> gradient in circulation<sup>(14)</sup>.

**Pulmonary functions tests:** The values of pulmonary functions (VC, FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC) for both females and males patients show significant decrease ( $p < 0.01$ ) 24hr after laparoscopic cholecystectomy in comparison with control values (24 hr before operation) Therefore, laparoscopic

cholecystectomy also results in postoperative spirometric changes and they considered the diaphragm dysfunction is the major causative factor related to ventilatory defects after laparoscopic procedures. As well as the dysfunction is independent of postoperative pain, lasts approximately one week, and is mediated by an afferent reflex mechanism of phrenic nerve inhibition. Another important factor in the genesis of ventilatory defects is postoperative pain, which also contributes to pulmonary function deterioration after upper abdominal surgical procedures<sup>(16)</sup>. Osman *et.al.*,<sup>(17)</sup> also in agree with this study and they pointed to general anaesthesia which has an important role in pulmonary complications, as there is deterioration in gas change, this deterioration starts as a result of changes in lung volume, shunts, ventilation-perfusion, lung and chest wall mechanics. This effect of general anesthetics is short and respiratory functions return to the baseline within 24 hours. While they reported that all respiratory function test values become normal on postoperative 4-10th day.

**Serum aldosterone hormone:** The values of serum aldosterone hormone for females and males cholelithiasis patients show significant increase ( $p < 0.01$ ) changes at the end of insufflation in comparison with before insufflation values. a possible cause of this result is response to stress. In addition increased abdominal pressure associated with pneumoperitoneum may reduce venous return, compress the abdominal capacitance vessels and reduce cardiac output and renal blood flow. These factors may combine to activate the rennin-aldosterone system<sup>(18)</sup>. One should also consider that systemic hormonal stress responses might also be a result of decreases in cardiac output and stroke volume. Serum urea and creatinine: The values of serum urea and creatinine for females and males cholelithiasis patients show no significant changes ( $p > 0.05$ ) 24hr after operation in comparison with 24hr before operation values. This result is in agreement with other studies Chang *et. al.* and Kwak *et al.*<sup>(19),(20)</sup> they demonstrated that, postoperative blood urea nitrogen and creatinine concentrations did not significantly differ. In spite of the development of oliguria in the setting of the increased intra-abdominal pressure of pneumoperitoneum and the implications of this acute but reversible renal dysfunction.

**Liver enzymes:** The values of liver enzymes ALT and AST for females and males cholelithiasis patients are significantly increased ( $p < 0.01$ ) 24hr after operation in comparison with control values (24hr before operation). While the values of serum GGT, ALP and T. S.B (total serum bilirubin) show no significant changes ( $p > 0.05$ ) 24 hr after operation in comparison with control values (24 hr before operation) elevation of hepatic transaminases showed no apparent clinical implication in most patients who underwent laparoscopic surgery, these changes might be attributed to hepatocellular dysfunction secondary to one or combination of CO<sub>2</sub> pneumoperitoneum, diathermy,

extruding liver, branch of the hepatic artery injured and general anesthesia, and the CO<sub>2</sub> pneumoperitoneum might be one of the main reasons for the change of serum liver enzymes. Also It is mainly attributed to the high intraabdominal pressure of carbon dioxide pneumoperitoneum, which may compromise the hepatic blood flow causing alterations in the microcirculation<sup>(21), (22)</sup>. In present study the time of operation is shorter so the patients subjected to a less effect of drugs and general anesthesia so changes in liver enzymes might be due to pneumoperitoneum.

**Serum potassium:** The values of serum potassium for females and males cholelithiasis patients show significant increase ( $p < 0.01$ ) changes at the end of insufflation in comparison with before insufflation values. The increase in potassium level was not relevant clinically and there was no an ECG change or arrhythmia in any patient. Demirogluk *et. al.*,<sup>(23)</sup> they claimed that hyperkalemia can occurs secondary to the movement of intracellular potassium into the serum as a result of acidosis caused by CO<sub>2</sub> absorption from the peritoneal cavity. On the other hand, abdominal wall ischemia that is secondary to the increase in intra-abdominal pressure and local intracellular acidosis that is created by peritoneal CO<sub>2</sub> insufflation can cause the increase in serum potassium level. As well as Hasankhani *et. al.*,<sup>(24)</sup> and Gutiérrez *et. al.*,<sup>(25)</sup> also noticed increasing in potassium level during laproscopic surgery and pointed to another possible cause of hyperkalemia is hypothermia which is usually caused by a prolonged time of CO<sub>2</sub> insufflation during the laparoscopic surgery. In addition, the anesthetics, sedatives, and muscle relaxants are other factors able to potentiate the effect of CO<sub>2</sub> insufflation on hypothermia causing a significant increase in the serum-potassium levels.

**Serum sodium:** The values of serum sodium for females and males cholelithiasis patients show on significant changes ( $p > 0.05$ ) at the end of insufflation in comparison with before insufflation values (table 4.6). This result is in agreement with study of Dencic *et. al.*,<sup>(26)</sup> and Kwak *et. al.*,<sup>(20)</sup> as they observed that; there was no substantial statistical difference between serum Na<sup>+</sup> values during laproscopic cholecystectomy. the explanation of this result; as there is no significant blood loss during laproscopic surgery and there is no evaporation and water loss as the internal abdominal organs not exposed to external environment by large abdominal incision. In addition there is special process in renal tubules of the kidney called glomerulotubular balance this make the percentage of the solute reabsorbed constant, and it is particularly prominent for Na<sup>+</sup><sup>(27)</sup>. and in spite of increase aldosterone hormone level and also this is because of fact that aldosterone hormone need 30 min before their effects on Na<sup>+</sup> reabsorption become manifested, because of time required for the steroid to alter protein synthesis via their action on DNA<sup>(27)</sup>.

## Conclusions

From the present study we can conclude the following:

1-laparoscopy for cholecystectomy in head-up position results in significant hemodynamic changes in healthy patients, particularly at the induction of pneumoperitoneum and change in position.

2-Laparoscopic cholecystectomy produces significant increases in stress hormone level (aldosterone), and elevations in stress hormones suggest that laparoscopic cholecystectomy is not physiologically minimally invasive.

3-Pneumoperitoneum during laparoscopic surgery did not adversely alter postoperative renal function and renal function remained stable.

4-Alterations in hepatic function occur after laparoscopic cholecystectomy and appear to be clinically insignificant.

5- In spite of small abdominal incision laparoscopic cholecystectomy results in postoperative spirometric changes.

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