Evaluation of Oxidative Stress in Laparoscopic Cholecystectomy

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Abstract

Purpose. We conducted a prospective study to evaluate the effect of CO₂ pneumoperitoneum and increased intra-abdominal pressure on arterial blood gases, end-tidal CO₂ (ETCO₂), nitric oxide (NO), blood and tissue malondialdehyde (MDA), and total antioxidant (TAOx) levels during laparoscopic cholecystectomy.

Methods. Fifty selected patients with cholelithiasis were randomized to undergo either laparoscopic or open surgery. Blood samples were taken pre-, mid-, and postinsufflation, and 24h postoperatively. To determine the tissue MDA level, tissue samples were taken from the gallbladder just after removal.

Results. The increased levels of ETCO₂ and PCO₂, caused by CO₂ pneumoperitoneum resulted in a minimal decrease in blood pH during the laparoscopic surgery. Although low levels of blood MDA were seen 30min after the start of laparoscopy, due to less oxidative stress response and tissue trauma, increased levels of tissue MDA levels indicated that the gallbladder was more traumatized during laparoscopic dissection and handling. NO levels were slightly lower in the laparoscopic cholecystectomy (LC) group, but there were no significant differences compared with the open cholecystectomy group (OC). TAOx levels were similar in both groups 30min after the start the procedure, but were much lower in the LC group 24h postoperatively.

Conclusions. These findings suggest that the antioxidant defense system is stimulated less with less oxidative stress, providing further evidence to support the opinion that LC is a safe technique.

Key words Cholecystectomy · Laparoscopy · Malondialdehyde · Oxidative stress

Introduction

Intra-abdominal insufflation induces splanchnic vasoconstriction, resulting in decreased inferior caval, renal, and portal venous blood flow. Using Doppler ultrasonography, Schilling et al. found that intra-abdominal arterial blood flow was decreased by increasing intra-abdominal pressure. They also emphasized that even under stable conditions of normal abdominal pressure, there was a reverse relationship between the duration of surgery and the arterial blood flow. Unfortunately, without the appropriate means to examine the microcirculatory changes in the splanchnic area during intra-abdominal insufflation, oxidative stress can be evaluated only by selected indirect methods. CO₂ pneumoperitoneum is associated with a significant increase in arterial CO₂ levels and insignificant changes in arterial O₂ levels. During pneumoperitoneum, the arterial pH decreases, whereas arterial CO₂ tension and end-tidal CO₂ concentration increase. These changes are thought to be due to the absorption of insufflated CO₂ or to ventilation–perfusion mismatching during the procedure. In this prospective randomized study, we examined the effect of intra-abdominal CO₂ insufflation on tissue and blood malondialdehyde (MDA), total antioxidant status (TAOx), arterial blood gases, blood nitric oxide (NO), and end-tidal CO₂ (ETCO₂) in patients who underwent laparoscopic cholecystectomy.

Subjects and Methods

Fifty patients diagnosed with chronic uncomplicated cholelithiasis were randomly divided into two groups of
The patients ranged in age from 28 to 80 years, with a mean age of 48 years, and their disease was classified as ASA status I or II. We selected for randomization, patients who were treated by the same surgical and anesthesiological team, and did not need any associated procedures such as hernia repair or choleodocholithiasis. Patients were excluded when the analysis could not be completed due to technical reasons, or when surgical findings necessitated conversion to open surgery or associated surgical procedures. In the laparoscopic cholecystectomy (LC) group, comprising 23 women and 2 men, a Verress needle was blindly inserted through a small umbilical incision. CO2 pneumoperitoneum was initiated and controlled by an insufflation device (Storz, Tuttlingen, Germany) with maximum intra-abdominal pressure set at 12 mmHg, and LC was performed through four ports. In the open cholecystectomy (OC) group, comprising 22 women and 3 men, laparotomy was performed through a 10-cm subcostal incision (Table 1). Intravenous (i.v.) midazolam 0.5 mm kg⁻¹ was given as premedication 30 min before admission to the operating room. Before the induction of anesthesia, all patients were given 0.5 mg atropine sulfate i.v. Anesthesia was induced by sodium thiopental 6 mg kg⁻¹, and maintained by O₂/N₂O/ISO, with an O₂-fraction of 0.35. Muscle relaxation for tracheal intubation was induced by atracurium 0.5 mg kg⁻¹, and repeated in increments of 0.15 mg kg⁻¹ on clinical demand. End-tidal CO₂ was measured during the operation period and maintained within the normal range, using mechanical ventilation with a 33% to mixture of O₂/N₂O, based on weight, age, previous status, and CO₂ partial pressure oscillations.

To measure the MDA, NO, TAOx, sedimentation, and C-reactive protein (CRP) levels, blood samples were taken before surgery, after 30 min of pneumoperitoneum in the patients undergoing LC, and 30 min after the incision in the patients undergoing OC, which was about 40 min after intubation, then 24 h after surgery. Gallbladder tissue was sampled immediately after being taken from the abdomen. To examine the levels of MDA and TAOx, blood and tissue samples were stored at −20°C.

The tissue MDA levels were measured using thiobarbituric acid (TBA), known as the Uchiyama method, and the blood MDA levels were measured using the method described by Yoshioka and Kawada. Blood NO was measured using a microplate assay, as described by Green and Wagner in 1982, in which the last product of NO known as the soluble nitrite is measured. The blood TAOx was measured using a “Randox Total Antioxidant” kit (Randox Laboratory, Ardmore, UK) which included buffer (1 × 100 ml), chromogen (5 × 10 ml), substrate (2 × 5 ml), and standard (5 × 1 ml). The TAOx level = (Standard concentration/control absorbance-Standard absorbance) × (Control absorbance-Sample absorbance) = mmol/l.

Blood CRP was measured by flow-nephelometry (Amay Protein System, Beckman Instruments, High Wycombe, UK), with a minimum level accepted at 0–0.8 mg/dl. Blood sedimentation was determined by the standard method using a Sediplus-S100 producer. Arterial blood gases were measured using an AVL-995 producer. Statistical analysis was performed using SPSS for Windows 95, version 6.0. The changes in the groups were compared using the paired t-test, unpaired t-test, and Wilcoxon matched-pairs rank test. All results are expressed as mean ± SD. Differences were considered to be significant at P < 0.05. This study was reviewed by the Institutional Board of Ankara Numune Teaching and Research Hospital, and all patients signed a consent form.

**Table 1. Clinical features of the patients who underwent cholecystectomy**

<table>
<thead>
<tr>
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<th>Laparoscopy</th>
<th>Open</th>
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<tbody>
<tr>
<td>Number</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Age (years)</td>
<td>45.8 ± 11 (28–69)</td>
<td>52.9 ± 12.1 (30–80)</td>
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<tr>
<td>Sex (M/F)</td>
<td>2/23</td>
<td>3/22</td>
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<tr>
<td>Operating time (min)</td>
<td>69.2 ± 17.2 (45–105)</td>
<td>66.8 ± 16.8 (45–135)</td>
</tr>
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Mean ± SD