Laparoscopic cholecystectomy: haemodynamic and neuroendocrine responses after pneumoperitoneum and changes in position†

E. O’LEARY, K. HUBBARD, W. TORMEY AND A. J. CUNNINGHAM

Summary

We have assessed the potential for myocardial ischaemia during laparoscopic cholecystectomy in 16 otherwise healthy patients. Continuous ambulatory ECG monitoring was commenced 12 h before operation and continued for 24 h after operation. The neuroendocrine stress response was assessed by measuring plasma concentrations of adrenaline and noradrenaline, human growth hormone, cortisol, renin and aldosterone, and prolactin, at specified times during surgery. Acute ST segment changes in the ECG occurred in only two patients. These episodes were independent of creation of pneumoperitoneum and changes in position. Acute intraoperative increases in MAP were noted during insufflation of carbon dioxide and reverse Trendelenburg positioning (P < 0.05). A four-fold increase in plasma concentrations of renin and aldosterone was noted after pneumoperitoneum and reverse Trendelenburg positioning (P > 0.05). There was a linear correlation between changes in plasma renin and aldosterone concentrations and MAP (r = 0.97 and r = 0.85, respectively). Prolactin concentrations increased four-fold after induction of anaesthesia. Cortisol, HGH, adrenaline and noradrenaline concentrations increased after deflation of the pneumoperitoneum. The time profile–concentration changes of increased MAP and renin–aldosterone suggests a cause–effect relationship. Increased intra-abdominal pressure and reverse Trendelenburg positioning may reduce cardiac output and renal blood flow. The early increase in prolactin concentration was probably secondary to the effect of the opioid fentanyl.

(Br. J. Anaesth. 1996; 76: 640–644)

Key words


Laparoscopic cholecystectomy has four potential causes of major physiological changes in the anaesthetized patient: initial Trendelenburg position, creation of the pneumoperitoneum, potential for systemic absorption of carbon dioxide and reverse Trendelenburg position [1].

The extent of the cardiovascular changes associated with the creation of pneumoperitoneum depends on the intra-abdominal pressure attained, volume of carbon dioxide absorbed, patient’s intravascular volume, ventilatory technique, surgical conditions and anaesthetic agents used [2, 3]. The haemodynamic effects include an increase in mean arterial pressure (MAP), decrease in cardiac output (CO) and increase in systemic vascular resistance (SVR).

Induction of pneumoperitoneum and changes in position appear to be associated with a biphasic haemodynamic response, with an early reduction followed by partial recovery of cardiac index [4]. Joris and colleagues [5] used flow-directed pulmonary artery catheters to assess the haemodynamic effects of peritoneal carbon dioxide insufflation to an intra-abdominal pressure (IAP) of 14 mm Hg in healthy non-obese patients with no cardiac disease. Cardiac index was reduced to 50 % of its preoperative value 5 min after the beginning of insufflation. The relative roles of the factors which contribute to changes in CO are difficult to separate, but may include mechanical factors and neurohumoral responses [5, 6]. Increased venous resistance and compression of the abdominal aorta may contribute to the increase in cardiac afterload. Potential mediators of increased SVR include catecholamines, prostaglandins, the renin–angiotensin system and vasopressin [5, 7, 8]. During pneumoperitoneum, plasma concentrations of dopamine, vasopressin, adrenaline, noradrenaline, renin and cortisol increase significantly. Of particular interest is the time course of the increase in vasopressin and noradrenaline. The plasma time course profile parallels that of changes in CI, MAP and SVR, suggesting a possible cause and effect relationship.

In this study, we quantified some of the neuroendocrine stress responses during and after pneumoperitoneum and also the incidence of intraoperative ST segment changes in the ECG.

Patients and methods

After obtaining local Ethics Committee approval, we studied 16 consecutive patients, free of cardiac
disease, undergoing elective laparoscopic cholecystectomy. Preoperative assessment included history and physical examination, specifically documenting the presence of ischaemic heart disease, for example previous myocardial infarction (MI), angina, left ventricular failure (LVF) or hypertension. Preoperative investigations included full blood count, urea and electrolyte concentrations, chest x-ray and resting 12-lead electrocardiograph (ECG).

Exclusion criteria included patients with documented ischaemic heart disease (history of angina, previous MI, hypertension) or signs of left ventricular failure. Patients who refused to participate and those in whom ECG interpretation was difficult, that is pre-existing left bundle branch or left ventricular hypertrophy with strain, and patients with hypokalaemia or those receiving digoxin therapy were also excluded from the study.

Continuous ambulatory electrocardiographic (CAECG) monitoring was commenced the evening before surgery and continued for 30 h after operation. Ambulatory ECG monitoring was performed using a Reynolds Medical Tracker model using leads II and V5. A Reynolds Medical Path-finder, Mark111, 24-h Holter monitoring system, incorporating Reynolds Medical version 2.2 software and hardware system, was used for analysis of ST segment changes. The Holter tape was run through the system for the full 24 h (or the duration of the tape). The software produces a trend or graph of ST changes against time for the duration of the recording. A reference ST level is determined and all ST changes are calibrated to this (the reference ST level is usually calibrated using patients’ resting ST level). Changes are not considered significant unless greater than ±1 mm from the reference. All ST changes were printed with an accompanying ECG strip. The software system is heavily dependent on human intervention. For the purpose of standardizing intraoperative management and indications for treatment, tachycardia was considered as 20 % above the mean preoperative heart rate or 90 beat min⁻¹. Acute changes in heart rate and arterial pressure had to be ≥4 min duration. Myocardial ischaemia was defined as >0.1 mV or more positive or negative horizontal ST segment shift, which extended at least 80 ms beyond the J point of the QRS and was at least 1 min duration. Heart rate, arterial pressure and ST segment analysis were measured for a minimum of 12 h before operation, during operation and for 24 h after operation.

A standard general anaesthetic technique was used for all patients. Patients were premedicated with diazepam 10 mg orally, 1 h before surgery. Anaesthesia was induced with fentanyl 1–2 µg kg⁻¹ and thiopentone 3–4 mg kg⁻¹. Vecuronium 0.1 mg kg⁻¹ was administered to facilitate tracheal intubation. Anaesthesia was maintained with 0.5–1 % end-tidal isoflurane and 50 % nitrous oxide in oxygen. Intraoperative monitoring included continuous ECG, systemic arterial pressure using an automated cuff, pulse oximetry, inspired oxygen fraction and peak airway pressure. Intermittent positive pressure ventilation was used with an Ohmeda volume cycle ventilator maintaining the end-tidal carbon dioxide partial pressure at 4–5.3 kPa. Intraoperative i.v. fluids were administered at 3 ml kg⁻¹ h⁻¹.

The surgical technique involved intraperitoneal insufflation of carbon dioxide via a Verres needle inserted into a small umbilical incision in the 15–20° Trendelenburg position. An electronic variable-flow insufflator terminated flow when the intra-abdominal pressure reached 15 mm Hg. A cannula was inserted in place of the needle to provide and maintain insufflation adequate for surgery. A video laparoscope was inserted through the cannula and the operative field was seen. The patient’s position was changed to steep reverse Trendelenburg, with lateral tilt, to facilitate retraction of the gall bladder fundus.

Neuroendocrine stress responses were assessed by measuring resting plasma concentrations of adrenaline and noradrenaline, renin and aldosterone, prolactin, growth hormone and cortisol in 20-ml blood samples obtained via a catheter inserted in the antecubital fossa. Samples were obtained on the evening before surgery (T1), before induction (T2), after induction (T3), 5 min before insufflation of carbon dioxide (T4), 5 min after insufflation of carbon dioxide (T5), 5 min after tilting in the reverse Trendelenburg position (T6) and after exsufflation in the recovery room (T7). Plasma adrenaline and noradrenaline concentrations were measured by high pressure liquid chromatography with electrochemical detection [5]. The sensitivity of both assays was 10 pg ml⁻¹ and intra-assay and inter-assay coefficients of variation were 5 % and 8 %, respectively, for both. Human growth hormone, cortisol and aldosterone concentrations were measured by direct radioimmunoassay with a sensitivity of 0.5 ng litre⁻¹, 30 nmol litre⁻¹ and 6.0 pg ml⁻¹, respectively. The intra-assay and inter-assay coefficients of variation were 6.3 % and 13.1 %, 11.2 % and 13.5 %, and 4.12 % and 3.82 %, respectively. Plasma renin activity was measured as the amount of angiotensin produced in ng ml⁻¹ h⁻¹. The sensitivity of this assay was 0.039 ng ml⁻¹ and the intra-assay and inter-assay coefficients were 5.82 % and 4.82 %, respectively. Prolactin was measured by immunofluorometric assay with a sensitivity of 9 mIU litre⁻¹ and the intra-assay and inter-assay coefficients of variation were 4.3 % and 6.5 %, respectively.

Perioperative cardiac morbidity was defined as including the presence of myocardial ischaemia, unstable angina, arrhythmias, congestive heart failure or death. History, physical examination, daily 12-lead ECG and cardiac specific enzymes were performed before operation and after surgery for 2 days. Criteria for diagnosing an MI included serial ECG and cardiac enzymes. Criteria for diagnosing left ventricular failure included chest pain, a gallop rhythm or basal crepitations. Daily ECG were performed noting the presence of new Q waves >0.04 s and >1 mm deep, or new left bundle branch block (LBBB). Measurement of serial cardiac enzymes was performed and a creatine kinase MB fraction (CK-MB) greater than 8 %, using an immunoinhibition method, was considered indicative of myocardial damage.

Data are expressed as mean (SD). Data were analysed by one-way analysis of variance for repeated
measures (ANOVA) followed by Scheffé’s post hoc tests. For inter-group comparisons, $P < 0.05$ was considered significant.

**Results**

We studied 16 (12 females) ASA I–II patients, mean age 40 (range 24–72) yr. Mean duration of surgery was 94 (SD 30) min (table 1).

Ambulatory ECG recordings revealed that patient No. 4 had an episode of acute ST segment changes before insufflation of carbon dioxide. This was associated with hypotension (MAP 45 mm Hg) and bradycardia (heart rate of 38 beat min$^{-1}$), which responded to i.v. fluids and atropine. Patient No. 8 had an episode of ST segment changes which began during exsufflation of carbon dioxide and continued for 69 min. Serial ECG, cardiac enzymes and physical examination for 2 days after operation revealed no evidence of cardiac morbidity in either patient. No abnormalities were detected in the recordings of the other 14 patients.

There were no significant changes in heart rate throughout the study. There was a significant increase in MAP after insufflation of carbon dioxide and reverse Trendelenburg positioning ($P = 0.01$ and 0.0003 respectively) (fig. 1).

Plasma concentrations of noradrenaline increased after exsufflation of carbon dioxide. However, this increase was not statistically significant ($P = 0.48$). Plasma concentrations of adrenaline increased after reverse Trendelenburg and exsufflation of carbon dioxide. Again, these increases were not statistically significant (fig. 2).

Plasma concentrations of renin increased four-fold during changes in position but this was not significant ($P = 0.31$). This increase continued after exsufflation of carbon dioxide and reached statistical significance ($P = 0.005$). Similarly, plasma concentrations of aldosterone increased four-fold after reverse Trendelenburg positioning but was not significant. The increase continued during exsufflation and achieved statistical significance ($P = 0.0001$) (fig. 3).

There was a linear increase in plasma prolactin concentrations after induction of anaesthesia. This became significant before insufflation of carbon dioxide.

---

**Table 1** Patient data (mean (SD or range) or number)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>16</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>40(24–72)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>4/12</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>94 (30)</td>
</tr>
</tbody>
</table>

---

**Figure 1** Mean (SD) changes in heart rate (HR) ($) and mean arterial pressure (MAP) ($) 5 min before (T2) and 5 min after (T3) induction, 5 min before (T4) and 5 min after (T5) insufflation of carbon dioxide, 5 min after reverse Trendelenburg positioning (T6) and after exsufflation of carbon dioxide (T7). T1 = Baseline. Significant difference (*) $P < 0.05$ in MAP from T4 to T5, T6 and T7.

**Figure 2** Mean (SD) changes in plasma concentrations of adrenaline ($) and noradrenaline ($\bullet$). Times T1–T7 as in figure 1.

**Figure 3** Mean (SD) changes in plasma concentrations of renin ($) (normal range 0.5–4.2 ng ml$^{-1}$ h$^{-1}$) and aldosterone ($) (normal range 30–1000 pg ml$^{-1}$). Times T1–T7 as in figure 1. Significant difference (*$P < 0.05$) in: plasma renin from T1, T2 and T3 to T7; plasma aldosterone from T1, T2, T3, T4, T5 and T6 to T7.
dioxide ($P = 0.003$) and remained increased for the rest of the study. Human growth hormone remained relatively stable after induction of anaesthesia and showed a significant increase after exsufflation of carbon dioxide ($P = 0.01$) (fig. 4).

Plasma concentrations of cortisol increased threefold after exsufflation of carbon dioxide ($P = 0.0002$) (fig. 5).

There was a linear correlation between changes in MAP and plasma concentrations of renin and aldosterone ($r = 0.97$ and 0.85, respectively) after pneumoperitoneum and reverse Trendelenburg positioning.

**Discussion**

The sequential effects of anaesthesia, positioning (20° reverse Trendelenburg), and mechanical and neuroendocrine effects of pneumoperitoneum and absorbed carbon dioxide combine to produce a characteristic haemodynamic response [4]. A biphasic pattern of initial reduction in cardiac index with subsequent recovery after pneumoperitoneum has been described [4]. In this study, we demonstrated that peritoneal insufflation of carbon dioxide to an intra-abdominal pressure of 14 mm Hg induced characteristic increases in MAP but no acute ECG ST segment changes in a series of healthy, non-obese patients, free from cardiac disease, undergoing elective laparoscopic cholecystecomy.

In patients with mild heart disease or those with clinically severe systemic disease (ASA III–IV), the pattern of changes in cardiac index, MAP and SVR is qualitatively similar to that observed in series of healthy patients [9–11]. The most striking features are the considerable initial reductions in cardiac index occurring simultaneously with large increases in MAP and SVR, followed by recovery of cardiac index, as described in healthy patients. This study suggests that acute haemodynamic changes during pneumoperitoneum and changes in position in healthy patients do not provoke ECG ST segments changes characteristic of myocardial ischaemia. Such changes were observed in only two patients, in one case associated with an episode of hypotension and bradycardia after induction of anaesthesia and in the other during peritoneal exsufflation.

Continuous ambulatory electrocardiographic (CAECG) monitoring has been developed as a non-invasive method of detecting perioperative myocardial ischaemia [12]. A variety of independent measures of ischaemia, including abnormalities of myocardial perfusion, regional left ventricular dysfunction, and pulmonary and left ventricular changes have been correlated with transient ST segment changes [13]. Little information is available, however, on the diagnostic accuracy of CAECG monitoring in patients with no known history of coronary heart disease, especially in those patients with a relatively low pre-test probability of the disease [12]. Studies in normal subjects without coronary artery disease (CAD) have demonstrated a very low incidence of such ECG changes. Current consensus does not support the use of continuous ST segment monitoring as a screening tool for detecting CAD [12]. In our series of 16 patients, free from cardiac disease, only one patient developed acute ST segment changes during deflation of the pneumoperitoneum. There were no postoperative sequelae, as detected by clinical assessment, serial ECG and cardiac enzymes.

The effects of abdominal distension with carbon dioxide are complex and may combine direct mechanical compressive effects, neurohumoral responses and changes induced by the absorbed carbon dioxide. Possible mediators of the initial and delayed changes in CI, MAP and SVR observed in this and other studies include catecholamines, prostaglandins, the renin–angiotensin system and vasopressin [5]. Joris and Lamy [8] documented significant vasopressin release after pneumoperitoneum that paralleled the time course of the increase in SVR. In this study, plasma concentrations of adrenaline, renin–aldosterone and prolactin increased considerably after
pneumoperitoneum and change in position. Of particular importance was the time course of the increase in renin–aldosterone. The plasma concentration–time course profile of renin–aldosterone paralleled that of changes in MAP, suggesting a possible cause–effect relationship. Increased abdominal pressure associated with pneumoperitoneum may reduce venous return, compress the abdominal capacitance vessels, reduce cardiac output and renal blood flow. These factors may combine to activate the renin–aldosterone system. Even though prolactin increases in response to stress, the time course of its changes suggests an interaction with the opioid fentanyl [14]. The peak HGH and cortisol responses reflect the postoperative stress response and parallel the ischaemic experience in patient No. 8.

Considerable systemic absorption of carbon dioxide occurs during prolonged insufflation [15]. Hypercapnia may contribute to the delayed recovery of cardiac index and may attenuate the adverse haemodynamic effects of intra-abdominal pressure. Hypercapnia may also contribute to the documented changes in MAP and plasma concentrations of adrenaline observed in this and other studies [16, 17]. Deflation of the induced pneumoperitoneum is associated with acute increases in plasma concentrations of noradrenaline and cortisol. These may be secondary to a combination of factors, including the drugs used in reversal, the patient’s return to consciousness or as a result of the patient experiencing pain.

References