Absorption of carbon dioxide during laparoscopy in children measured using a novel mass spectrometric technique

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Background. Carbon dioxide (CO₂) is absorbed during pneumoperitoneum and may cause adverse haemodynamic effects. The aim of this study was to measure the elimination of exogenous CO₂ during laparoscopy in children.

Methods. Ten children [27.6 (56.5) months; mean (SD)] undergoing laparoscopic and nine [24.5 (17.3) months] undergoing open surgery were studied. Breath samples were collected at the line for end-tidal CO₂ and analysed for 13CO₂/12CO₂ ratio expressed as δPDB (difference from standard), by isotope-ratio mass spectrometry. The proportion of absorbed CO₂ was calculated comparing exhaled 13CO₂/12CO₂ before and during CO₂ pneumoperitoneum.

Results. 13CO₂/12CO₂ in medical CO₂ was −32.7 (2.1) δPDB. 13CO₂/12CO₂ in breath of patients undergoing open procedures was −24.3 (2.4) δPDB at the start of operation and did not change during the operation (P > 0.2). 13CO₂/12CO₂ in breath of patients undergoing laparoscopy was −21.5 (5.4) δPDB at the start of insufflation, and decreased during pneumoperitoneum by 2.5 (1.6) δPDB, indicating absorption of exogenous CO₂. The percentage of expired CO₂ absorbed rose to 15.5 (7.7)% after 30 min of pneumoperitoneum and decreased rapidly after desufflation.

Conclusion. After 10 min of laparoscopy 10–20% of expired CO₂ derives from the exogenous CO₂. CO₂ absorption can be measured using a simple mass spectrometric technique.

Keywords: carbon dioxide, absorption; pneumoperitoneum; procedure, mass spectrometry; surgery, laparoscopy

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Carbon dioxide (CO₂) is commonly used for pneumoperitoneum in adults and children, as it is non-combustible, inexpensive and least likely to cause embolism. Laparoscopy can result in haemodynamic changes and may lead to adverse effects on the cardiovascular system requiring increasing minute ventilation by 20–30% to prevent hypercarbia. Previously, we have demonstrated that small children eliminate relatively more CO₂ (measured as VCO₂ by indirect calorimetry) during laparoscopy and thus require scrupulous anaesthetic management, particularly in the presence of pre-existing pathological conditions. End-tidal CO₂ (EtCO₂) is commonly monitored during laparoscopy in children and minute ventilation is accordingly adjusted in order to avoid hypercapnia. However, some authors suggested that the EtCO₂ is not a reliable measure of arterial CO₂ pressure. Furthermore, EtCO₂ measures total CO₂ elimination and does not allow quantification of the absorption of CO₂ from the peritoneum. Infants and children undergoing laparoscopy are hypermetabolic and the increased elimination of CO₂ during laparoscopy may be metabolic in origin and not arise from the absorption of CO₂ from the pneumoperitoneum; thus changes in VCO₂ measured by indirect calorimetry are not a reliable measure of absorbed CO₂. Development of a method to specifically measure the amount of CO₂ absorbed from the peritoneum during laparoscopy would allow comparison of the amount of CO₂ absorbed from the peritoneum between different surgical or anaesthetic management protocols.

The aim of this study was to determine absorption of exogenous CO₂ in expired breath during laparoscopy in children independently of metabolic CO₂ using a novel isotope-ratio mass spectrometry method. There are two naturally occurring stable isotopes of carbon, ¹²C and ¹³C. Of these, ¹³C makes up about 99%. An ideal way to study CO₂ absorption from pneumoperitoneum would be to insufflate with ¹³CO₂ and measure appearance of ¹³CO₂ in...
CO2 was used to establish a pneumoperitoneum with a pressure of 10–15 mm Hg, according to the surgeon’s preference, and a maximum flow rate of 4 litre min⁻¹. A Hasson cannula was inserted under direct vision just above the umbilicus and unheated (room temperature) air was aspirated into a 10 ml syringe and transferred into 10 ml vacuum test tubes (Labco Limited, High Wycombe, UK) for the analysis. Samples were collected after the patient was intubated and before the start of the operation, during the operation, during pneumoperitoneum, after pneumoperitoneum in patients having open procedure after laparoscopy, and after the end of the operation until the patient was extubated. In addition, samples of air used for ventilation and of medical CO2 used for the pneumoperitoneum were obtained for each operation. \( E_{rCO2} \), and body core temperature were recorded at each sampling point.

**Sample collection and analysis**

Breath samples were collected at 5 min intervals using a 10 ml syringe connected to a 3-way valve at the sampling line for measurement of \( E_{rCO2} \). The air was aspirated into a 10 ml syringe and transferred into 10 ml vacuum test tubes (Labco Limited, High Wycombe, UK) for the analysis. Samples were collected after the patient was intubated and before the start of the operation, during the operation, during pneumoperitoneum, after pneumoperitoneum in patients having open procedure after laparoscopy, and after the end of the operation until the patient was extubated. In addition, samples of air used for ventilation and of medical CO2 used for the pneumoperitoneum were obtained for each operation. \( E_{rCO2} \), and body core temperature were recorded at each sampling point.

**Sample analysis**

Breath CO2 was analysed for \(^{13}\)CO2/^{12}\)CO2 enrichment by gas chromatography on a CP-Poraplot-Q column (Varian Inc., Oxford, UK) followed by isotope-ratio mass spectrometry on a Thermo Finnigan Delta-XP (Thermo Finnigan, Bremen, Germany). Sample \(^{13}\)CO2/^{12}\)CO2 enrichment was standardized against a CO2 cylinder (5.0 grade, BOC Special Gases, Guildford, Surrey, UK), which had been calibrated against the international standard PDB (Iso-Analytical, Sandbach, Cheshire, UK). Using the \(^{13}\)CO2/^{12}\)CO2 of the medical CO2 used for insufflation to represent 100% of exhaled CO2 originating from pneumoperitoneum and baseline breath \(^{13}\)CO2/^{12}\)CO2 to represent 0%, the percentage of exhaled CO2 originating from the pneumoperitoneum at time \( x \) was calculated as:

\[
100 \times \frac{(\text{breath } ^{13}\text{C} \text{ at time } x) - (\text{breath } ^{13}\text{C} \text{ at time zero})}{(\text{breath } ^{13}\text{C} \text{ of medical CO2} - (\text{breath } ^{13}\text{C} \text{ at time zero})).
\]

**Statistical analysis**

Data are given as mean (SD) or median (range) and were compared by paired and unpaired t-tests, and by linear regression analysis, using Prism 4 software (GraphPad Software Inc., San Diego, USA). Results with a \( P \)-value of <0.05 were considered significant, and results were corrected for multiple comparisons by Bonferroni’s correction where appropriate.

**Results**

Age at operation was comparable between the two groups, median 8 months (range, 1 month–15 yr) for the laparoscopic group and 24 months (3 months–4.5 yr) for the open group (\( P=0.7 \)). Weight at operation was 11.1 (8.6) kg and 11.8 (4.0) kg in the laparoscopic and open groups, respectively (\( P=0.7 \)). The surgical procedures performed in each group are listed in Table 1. Core temperature did not show any significant variation and remained within a normal range during the surgical procedure in all patients.
Table 1 Surgical procedures performed in each group. PEG, percutaneous endoscopic gastrostomy; PSARP, posterior sagittal anorectoplasty

<table>
<thead>
<tr>
<th>Laparoscopic group (n=10)</th>
<th>Open group (n=9)</th>
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<tbody>
<tr>
<td>Nissen fundoplication 4</td>
<td>Nissen fundoplication 2</td>
</tr>
<tr>
<td>Pancreatic biopsy and PEG 2</td>
<td>PSARP 2</td>
</tr>
<tr>
<td>Right inguinal herniotomy 2</td>
<td>Bilateral orchidopexy 1</td>
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<tr>
<td>Ladd's procedure 1</td>
<td>Partial splenectomy 1</td>
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<tr>
<td>De-roofing of liver cyst 1</td>
<td>Right inguinal herniotomy 1</td>
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<tr>
<td>Right inguinal herniotomy 1</td>
<td>Closure of ileostomy 1</td>
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<tr>
<td>Right hemicolectomy 1</td>
<td>Right hemicolectomy 1</td>
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$^{13}$CO$_2$/^{12}$CO$_2$ in medical CO$_2$ was $-32.7$ $(2.1)$ δPDB. $^{13}$CO$_2$/^{12}$CO$_2$ in exhaled breath of patients undergoing open procedures was $-24.3$ $(2.4)$ δPDB at the start of operation and did not change significantly during the operation ($P>0.2$) (Fig. 1A). $^{13}$CO$_2$/^{12}$CO$_2$ in exhaled breath of patients undergoing laparoscopy was $-21.5$ $(5.4)$ δPDB at the start of insufflation, similar to baseline $^{13}$CO$_2$/^{12}$CO$_2$ of patients undergoing open surgery ($P=NS$). $^{13}$CO$_2$/^{12}$CO$_2$ progressively decreased during pneumoperitoneum, reducing by $2.5$ $(1.6)$ to $-24.1$ $(4.1)$ δPDB ($P=0.0015$ vs baseline by paired $t$-test with Bonferroni correction) at the end of pneumoperitoneum in each patient [35.0 (19.9) min, range 10–75 min], indicating absorption of exogenous CO$_2$ (Fig. 1B). The percentage of expired CO$_2$ absorbed rose to 16.4 $(8.6)$% after 30 min of pneumoperitoneum ($P=0.012$), and then decreased rapidly after discontinuing the CO$_2$ insufflation (desufflation) (Fig. 2). As five patients received open procedure after laparoscopy, we were able to obtain additional CO$_2$ samples before extubation, thus establishing that $^{13}$CO$_2$/^{12}$CO$_2$ returns to baseline 30 min after the end of pneumoperitoneum (Figs 1B and 2). After the end of pneumoperitoneum, $^{13}$CO$_2$/^{12}$CO$_2$ returned towards baseline, but required approximately 30 min to return to baseline values (Fig. 1B).

No patients in either group experienced cardiovascular or respiratory compromise during or after surgery and all had an uncomplicated postoperative recovery.

**Discussion**

Laparoscopy introduces new variables into anaesthetic management: effects of elevated intraabdominal pressure, effects of intraperitoneal gas insufflation and alterations caused by differences in patient positioning. As CO$_2$ is highly soluble, it is easily absorbed through the peritoneum. Experimental models in animals have documented CO$_2$ absorption during pneumoperitoneum, causing acidemia, hypercarbia and depressed haemodynamic function.$^{10–12}$ Absorption of CO$_2$ through the peritoneal surface is also documented in adults, resulting in an increase in $E_{CO_2}$.$^{13–17}$ Although this can lead to a decrease in blood pH,$^{18}$ in otherwise healthy patients undergoing laparoscopic surgery, this CO$_2$ load does not produce a clinically significant respiratory or metabolic challenge$^{19,20}$ and is usually adequately dealt with by an increase in minute ventilation. Several studies in adults have examined the time course of CO$_2$ elimination by indirect calorimetry, and although some authors have suggested that the rate of CO$_2$ elimination reaches a plateau within 15–40 min of pneumoperitoneum,$^{14,16,17,21}$ others have documented increases up to 2 h.$^{22}$ These discrepancies could be related to differences in insufflation pressure, alterations in absorption of CO$_2$ from injured and non-injured peritoneum,$^{15,23}$ or to hypercapnia and CO$_2$ retention in the body. However, in studies using indirect calorimetry$^9$ or respiratory mass spectrometry$^{15,16}$ to measure total CO$_2$ elimination as the difference between inspired and expired CO$_2$ (VCO$_2$), it is difficult to distinguish between metabolically produced CO$_2$ and CO$_2$...
absorbed through the peritoneum. As substrate utilization and metabolic CO₂ production may well change during surgery, the time to achieve plateau VCO₂ may vary in different studies depending on metabolic changes, and the estimation of absorbed CO₂ is not accurate as it depends on the assumption that metabolic CO₂ production is unchanged during the laparoscopic procedure.

Few studies have investigated the pathophysiological effects of laparoscopy in children and results have been extrapolated from studies conducted in adults. Similarly to adults, CO₂ absorption does not appear to be a problem in patients with normal cardiovascular function and healthy children undergoing short laparoscopic procedures have minimal adverse effects. However, an increase in minute ventilation is usually required to prevent hypercarbia. In previous studies, we have shown, using indirect calorimetry, that children increase VCO₂ during laparoscopy and that younger children eliminate relatively more CO₂ compared with older children. However, we have also shown that children undergoing laparoscopic procedures are hypermetabolic and would therefore be expected to have an increase in metabolic CO₂ production, and an increase in CO₂ absorption from the peritoneum. In order to accurately determine the timecourse of CO₂ absorption in children undergoing laparoscopic procedures, we aimed to develop an unambiguous method to quantify the absorption of exogenous CO₂, and to use this method to accurately determine the time course of CO₂ absorption during laparoscopy in children.

The high precision of isotope-ratio mass spectrometry enabled us to utilize the small differences in natural carbon abundance in different sources (i.e. CO₂ metabolically produced from the patient and CO₂ used for pneumoperitoneum). Using this technique, we have estimated that 10–20% of CO₂ eliminated during laparoscopy in children is derived from absorption through the peritoneum. The variability observed in our study may be related to different insufflation pressures. Minute ventilation was adjusted by the anaesthetist throughout the pneumoperitoneum to maintain \( E_{\text{CO}_2} \) between 4 and 6 kPa and none of the patients in the laparoscopic group required desufflation of the pneumoperitoneum and conversion to an open procedure. CO₂ absorption reached a plateau after 20–25 min of pneumoperitoneum, a finding comparable with several of the adult studies based on VCO₂ measurement. At plateau, 10–20% of exhaled CO₂ originated from the pneumoperitoneum, comparable with the 18% estimated by Kazama and colleagues in adults, but somewhat lower than the 30% estimated by Mullett and colleagues. Differences between all these studies may be related to different intraabdominal pressures. This amount of CO₂ could potentially cause significant acidosis if not corrected by increased minute ventilation, suggesting that although arterial blood gas analysis is not routinely performed because of its invasive nature, it may be a useful precaution in children with suspected significant arterial CO₂–\( E_{\text{CO}_2} \) gradients or with pulmonary or cardiovascular compromise. In addition, as absorbed CO₂ reached a plateau after about 20 min, any changes in \( E_{\text{CO}_2} \) subsequent to this are likely to be attributable to other reasons such as metabolic or haemodynamic alterations, or s.c. CO₂ emphysema. As several patients in our series required additional open procedures after the end of pneumoperitoneum, we were able to determine that absorbed CO₂ continued to be eliminated for up to 30 min after desufflation, very similar to the results of Katama and colleagues in adults. Although none of our patients experienced respiratory problems after extubation, the persistent elimination of the absorbed CO₂ after desufflation should be taken into account to prevent possible complication in children with pulmonary disease during recovery from anaesthesia.

In conclusion, CO₂ absorption from pneumoperitoneum can be measured using a new, simple method which does not require administration of labelled compounds. Using this method, we have demonstrated that in children after 10–20 min of laparoscopy, 10–20% of expired CO₂ is derived from the absorption of exogenous CO₂, and that exogenous CO₂ continues to be eliminated for up to 30 min after desufflation. Further studies using this technique may clarify the exact pathophysiological changes occurring during laparoscopy in children and adults.

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