Intraabdominal Carbon Dioxide Insufflation in the Pregnant Ewe

Uterine Blood Flow, Intraamniotic Pressure, and Cardiopulmonary Effects


Background: Laparoscopic surgical procedures are being performed in pregnant women with increasing frequency. Maternal–fetal physiology changes occurring during intraabdominal carbon dioxide insufflation are poorly understood, and maternal–fetal safety is of concern during carbon dioxide pneumoperitoneum. A previous pilot study using end-tidal carbon dioxide-guided ventilation resulted in maternal and fetal acidosis and tachycardia during carbon dioxide pneumoperitoneum. Using serial arterial PaCO2 to guide ventilation, this study was designed to evaluate maternal–fetal cardiopulmonary status, uterine blood flow, and the intraamniotic pressure effects of intraabdominal carbon dioxide insufflation in singleton pregnant ewes between 120 and 135 days of gestation.

Methods: In a prospective randomized cross-over study, nine ewes were to receive either abdominal insufflation with carbon dioxide to an intraabdominal pressure of 15 mmHg (n = 9; insufflation group) or receive no insufflation (n = 9; control group). Anesthesia was induced with thiopental and maintained with end-tidal halothane (1 to 1.5 minimum alveolar concentration/100% oxygen). Mechanical ventilation was guided by serial arterial arterial blood gas analysis to maintain PaCO2 between 35 and 40 mmHg. Data from insufflated animals were collected during insufflation (60 min) and after desufflation (30 min). Control group data were collected and matched to similar time intervals for 90 min. Ewes were allowed to recover, and after a rest period (48 h) they were entered in the cross-over study.

Results: During insufflation there was a significant increase in PaCO2, to end-tidal carbon dioxide gradient and minute ventilation, with concomitant decreases in maternal end-tidal carbon dioxide and PaCO2. Intraamniotic pressure increased significantly during insufflation. No significant changes were observed in maternal hemodynamic variables, fetal variables, or in uterine blood flow during the study. There were no fetal deaths or preterm labor in any of the animals during the experiment.

Conclusions: During the 1-h insufflation, a marked increase in PaCO2, to end-tidal carbon dioxide gradient was observed, suggesting that capnography may be an inadequate guide to the ventilation during carbon dioxide pneumoperitoneum in the pregnant patient. No other significant circulatory changes were observed. (Key words: Anesthesia, obstetrics; maternal; fetal; cardiovascular effects. Carbon dioxide pneumoperitoneum. Laparoscopy. Uterine blood flow.)

LAPAROSCOPIC surgery has become a common therapeutic approach to treat various surgical conditions, particularly cholecystectomy. Conditions such as cholecystitis, ovarian adnexal mass, or appendicitis may require surgical intervention during pregnancy, but abdominal pain during pregnancy can present a diagnostic challenge, and the use of laparoscopy as a diagnostic tool has been reported to reduce the incidence of laparotomies.1

Previous studies have evaluated the cardiopulmonary effects of intraabdominal carbon dioxide (IACO2) insufflation and shown it to be well tolerated in healthy

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nongravid patients. Laparoscopic cholecystectomy, appendectomy, and ovarian cystectomy have been reported during pregnancy. Physiologic changes of pregnancy, predominantly in the respiratory and cardiovascular systems, may contribute to a unique cardiopulmonary response during carbon dioxide pneumoperitoneum in the pregnant patient and should be considered before implementing laparoscopic techniques in these patients.

Studies in animal models have been published focusing on maternal and fetal cardiopulmonary changes during IACO₂ insufflation. Such studies using end-tidal carbon dioxide (ETCO₂)-guided ventilation in gravid models have shown maternal and fetal acidosis and tachycardia during IACO₂ insufflation, and the effects of carbon dioxide pneumoperitoneum on maternal-fetal well being remain a well-founded concern.

This prospective randomized cross-over study was designed to characterize the effects of IACO₂ insufflation on maternal-fetal cardiopulmonary status, uterine blood flow (UBF), and intraamniotic pressure (IAP) using serial maternal PaO₂ to guide ventilation to maintain maternal normocarbia.

Materials and Methods

Animal Preparation

Nine Dorset-cross ewes with singleton pregnancies of 120 to 135 days’ gestation (full-term at 150 days) were used in this study, which was approved by the Animal Care Protocol Review Committee, University of Saskatchewan, and conducted with agreement from Canadian Council of Animal Care guidelines. The ewes were fasted for 18 h and deprived of water for 8 h before instrumentation and study.

A lumbar epidural injection of 10 ml lidocaine hydrochloride with epinephrine (lidocaine with epinephrine 2%; Langford, Guelph, Ontario, Canada) and 0.07 mg/kg xylocaine hydrochloride (Rompun; Bayvet Division, Chemagro Ltd., Etobicoke, Ontario, Canada) was aseptically administered. Animals were placed in dorsal recumbency with oxygen (inspired oxygen concentration 1.0) via face mask (5 l/min) and received balanced electrolyte solution (5% dextrose and 10 ml·kg⁻¹·h⁻¹ Ringers) intravenously. After a ventral midline laparotomy, the pregnant uterine horn was identified and a 10-cm hysterotomy incision was made to exteriorize the fetal hindlimb. Using local infiltration with 2% lidocaine and a surgical cutdown, the fetal femoral artery was isolated and catheterized with a 21-gauge over-the-needle catheter. Using the Seldinger technique, a 5-French, 6-cm customized silastic infant feeding tube (Bard Canada, Mississauga, Ontario, Canada) was placed over a pediatric J-wire (central vein catheterization set; Arrow International, Reading, PA) and inserted through the femoral artery into the descending aorta. The infant feeding tube was connected to arterial pressure tubing (Abbott Laboratories, North Chicago, IL) and secured with sutures and adhesive (Vetbond; 3M Canada, Toronto, Ontario, Canada). A 12-French Kastlow stomach tube (Baxter Healthcare Corporation, Deerfield, IL) was placed in the amniotic cavity to monitor IAP. The two catheters were exteriorized through one end of the hysterotomy incision. The fetal surgical site and uterine incision were closed with 2-0 absorbable sutures. A calibrated transit time ultrasonic flow probe (model T201; Transonic Systems, Ithaca, NY) was placed around the uterine artery of the pregnant horn just proximal to the arterial bifurcation.

The two intrauterine catheters and the Transonic cable were exteriorized through the ewe’s right flank and the laparotomy site was closed. One hundred twenty milliliters of warm saline solution with 500 mg of sodium ampicillin (Penbritin 500; Ayerst Laboratories, Montreal, Quebec, Canada) were infused into the amniotic cavity through the amniotic catheter to replace amniotic fluid lost during the procedure.

After local infiltration and surgical cutdown, the maternal carotid artery was catheterized using a 16-gauge, 14-cm catheter (Angiocath, Becton-Dickinson, Sandy, UT) and attached to noncompliant pressure tubing. An 8-French pulmonary artery catheter introducer (Cordis Introducer, Daig Corp., Minnetonka, MN) was placed and secured in the jugular vein. Postoperative analgesia consisted of 0.2 mg/kg butorphanol tartrate (Torbugesic; Ayerst Laboratories) intramuscularly, after which ewes were returned to their pen. Antimicrobial therapy consisted of 25,000 IU/kg procaine penicillin (Ethacillin; Rogar/STB, London, Ontario, Canada) given intramuscularly and an intramniotic infusion of 500 mg sodium ampicillin once daily.

Experimental Design

The animals were randomized to receive two treatments: insufflation to an intraabdominal pressure of 15 mmHg and no insufflation (controls). No laparoscopic surgery was done.

Ewes were rested for 48 h between implantation and the time of the study. Once the first study was complete, the ewes rested for a further 7 days and then entered the next study.

Before incision, blood samples were obtained and pH was normal (7.35 to 7.45 mmol/L) in all laboratories. Mean arterial blood pressure and end-tidal halothane concentration were recorded in all studies. End-tidal halothane concentration was maintained at 1.5% to 2% (Vetcon; Hill, Ontario, Canada). Intravenous fentanyl (Fenticon, TX) was administered as needed.

In both insufflation and no-insufflation studies, the ECO₂ Romex (Edwards Cardiac Output System) (Drager AW 4000, PA) was used to obtain data. The ECO₂ Romex was used to adjust the tidal ventilation rate, end-tidal CO₂ concentration, and end-tidal arterial blood gas analysis. The ECO₂ Romex was used to monitor end-tidal arterial blood pressure and end-tidal arterial pH. The end-tidal arterial blood pressure and end-tidal arterial pH were recorded with the ECO₂ Romex system. The end-tidal arterial blood gas analysis was monitored with the ECO₂ Romex system.

The end-tidal arterial blood pressure and end-tidal arterial pH were monitored with the ECO₂ Romex system. The end-tidal arterial blood pressure and end-tidal arterial pH were monitored with the ECO₂ Romex system. The end-tidal arterial blood pressure and end-tidal arterial pH were monitored with the ECO₂ Romex system.

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the ewes recovered from anesthesia, rested for 48 h, and then entered the cross-over study.

Before inducing anesthesia, fetal and maternal arterial blood samples were drawn. If fetal acidemia (pH < 7.2) was present, the study was postponed until the fetal pH was normal. After anesthesia was induced with 10 to 15 mg/kg sodium thiopental (Pentothal, Abbott Laboratories, Montreal, Quebec, Canada), the trachea was intubated and the animal maintained at a constant end-tidal halothane (MTC Pharmaceuticals, Cambridge, Ontario, Canada) administered at 1 to 1.5 minimum alveolar concentration (MAC; 1 MAC was taken as 0.78%12) and 100% oxygen. Continuous skeletal muscle relaxation was provided with 0.01 mg/kg intravenous vecuronium bromide (Norcuron; Organon Canada Ltd., West Hill, Ontario, Canada) and monitored using a peripheral nerve stimulator (Digi Stim III, Neurotechnology, Houston, TX) placed over the peroneal nerve.

In both insufflation and control groups, changes in mechanical ventilation were made to maintain \( \text{PaCO}_2 \) between 35 and 40 mmHg. A volume-cycled ventilator (Drager AV Ventilator, North American Drager, Telford, PA) was used to control and maintain ventilation by adjusting tidal volume up to 20 ml/kg and then respiratory rate, guided by intraoperative maternal arterial blood gas analysis. Minute ventilation was obtained from ventilator settings of tidal volume and respiratory rate. Circuit airway peak pressure was measured from the Bourdon gauge of the breathing circuit. Maternal \( \text{ETCO}_2 \), end-tidal halothane, and respiratory rate were recorded with a gas analyzer (Ohmeda 5250 respiratory gas monitor; Ohmeda, Louisville, KY).

A 7-French triple-lumen pulmonary artery catheter (Edwards Swan-Ganz catheter; Baxter Corp., Toronto, Ontario, Canada) was advanced through the catheter introducer and positioned in the pulmonary artery to measure cardiac output, pulmonary arterial wedge pressure, mean pulmonary arterial pressure, and central venous pressure. Correct placement was confirmed by observing characteristic pressure waveform. Maternal mean arterial pressure (MAP), pulmonary artery wedge pressure, mean pulmonary artery pressure, central venous pressure, IAP, heart rate (HR), and fetal MAP and HR were recorded with a multichannel computer system (Hewlett-Packard M1092A, Sorronia, Italy). Cardiac output was determined using the thermodilution technique, using 10 ml room temperature 5% dextrose and a cardiac output computer (Gould Hemodynamic Profile Computer SP1445; Gould, Cardiovascular Products Division, Oxnard, CA). Three measurements were averaged and recorded. Blood samples were drawn from the fetus and the maternal carotid and pulmonary arteries to measure blood gases (Copenhagen Radiometer Acid-Base Laboratory 330, Copenhagen, Denmark).

The intraamniotic, fetal, and maternal lines were connected to a pressure transducer computer (Hewlett Packard M1092A) and the Transonic flow cable was connected to a computerized monitor (model T201; Transonic Systems).

Carbon dioxide pneumoperitoneum to a pressure of 15 mmHg was achieved by insufflating carbon dioxide through a Verres needle placed in the supraumbilical area using a standard procedure. An automatic laparoscopic insufflator (SOLOS Endoscopy, Atlanta, GA) was used to monitor the intraperitoneal pressure during insufflation. Baseline measurements were taken 30 min after anesthesia was induced. Data were collected at regular intervals during the 60-min insufflation period and during the first 30 min after desufflation.

Corrected fetal MAP was calculated by subtracting the IAP from the measured fetal MAP. Maternal and fetal heart rate (m-HR, f-HR), maternal MAP, and UBF were measured every 5 min. Central venous pressure, mean pulmonary arterial pressure, pulmonary artery wedge pressure, cardiac output, \( \text{ETCO}_2 \), and maternal and fetal serum lactate, m-ABG, and f-ABG measurements were taken every 15 min. Respiratory rate, tidal volume, airway peak pressure, fresh gas flow, and IAP were measured every 20 min. All pressures and cardiac output
measurements were taken at the end-expiration phase of the respiratory cycle. Percentage of venous admixture, minute ventilation, cardiac index, systemic vascular resistance (dyne·s·cm⁻²), pulmonary vascular resistance (dyne·s·cm⁻²), and to ETCO₂ (PaCO₂ - ETCO₂) gradient were calculated using standard formulas. All ewes and fetuses were killed at the end of the study by an overdose of sodium thiopental.

**Statistical Evaluation**

One-way analysis of variance for repeated measures was used for statistical evaluation of the results. A probability value less than 0.05 was considered significant. Differences over time in variables that were significant according to the analysis of variance were examined using the Student’s *t* test for paired observations.

**Results**

The animal population did not differ significantly from each other in their mean weight (58 ± 8 kg) or stage of pregnancy (125 ± 6 days) at the time of surgical instrumentation. One ewe was allowed to rest for an additional 24 h after instrumentation because the fetal arterial pH was 7.2. This animal recovered without complications and completed the cross-over study. All of the variables investigated were normally distributed.

**Maternal Variables**

Increases in the PaCO₂ - ETCO₂ gradient to a mean maximal value of 16 mmHg (*P = 0.04*) occurred during insufflation, with values returning to baseline with desufflation. In the control group, the gradient remained constant at approximately 6 mmHg (fig. 1). Decreases in ETCO₂ were statistically significant (*P = 0.0006*) during insufflation (table 1). To maintain maternal normocarbia, an increase in minute ventilation (*P = 0.001*) was required during insufflation up to 300 ml·kg⁻¹·min⁻¹ (fig. 2). Maternal PaO₂ decreased significantly (*P = 0.02*) during insufflation, with a mean minimal value of 137 ± 35 mmHg. Values returned toward baseline with desufflation (fig. 3.)

Breathing circuit peak pressure increased significantly during insufflation to a mean maximal value of 25 ± 28 cm water (*P < 0.001*), returning toward baseline with desufflation.

A constant IACO₂ pressure of 15 mmHg was maintained during insufflation. Statistically significant increases (*P = 0.02*) in IAP, on average 9 mmHg greater than baseline values, were recorded (fig. 4).

**Fetal Variables**

Fetal PaO₂, PaCO₂, and pH in both groups increased significantly, with values returning to baseline with desufflation (fig. 5). Maternal arterial blood gas and blood pressure were normal in both groups (fig. 6). No significant differences were noted between groups with respect to fetal acid-base status and no premature deaths occurred in this study.

**Discussion**

Fetal death rates exceeding 50% have been reported in workers after undergoing complicated endoscopic surgery. The use of carbon dioxide insufflation during pregnancy remains controversial, and maternal and fetal variables were monitored.
than baseline pressure, resulted during insufflation, whereas values remained constant in the control group (fig. 4).

No significant differences were found between insufflation and control groups with respect to MAP, HR, central venous pressure, pulmonary artery wedge pressure, mean mean pulmonary artery pressure, cardiac index, systemic vascular resistance, pulmonary vascular resistance, UBF, or venous admixture.

Fetal Variables

Fetal \( PaO_2 \) remained within physiologically normal limits in both groups (table 2). Corrected fetal MAP to account for IAP changes was not different between groups (fig. 5). No significant differences in HR were noted between study groups, nor were there changes in acid-base status (table 2). There were no fetal deaths and no preterm labor was detected in any of the animals in this study.

Discussion

Fetal death, spontaneous abortion, and preterm labor have been reported in pregnant patients shortly after undergoing laparoscopic surgery. However, uncomplicated completion of pregnancy after laparoscopic surgery has also been reported.

The use of laparoscopic surgical procedures during pregnancy remains controversial. Potential risks include maternal and fetal acid-base disturbances and uteroplacenental perfusion alterations secondary to carbon dioxide pneumoperitoneum. Physiologic implications of pregnancy must be considered in addition to the known effects of IACO\(_2\) insufflation before considering the use of laparoscopic techniques in pregnant women.

Previous studies in pregnant animal models have shown maternal and fetal acidosis and tachycardia using ETCO\(_2\)-guided ventilation. In our previous pilot study, maternal acidosis confounded the interpreta-

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tion of the fetal acidosis. In the present study, PaCO₂
guided ventilation was used to maintain maternal normocaemia and define the effects of carbon dioxide pneumoperitoneum on fetal acid-base status and maternal cardiopulmonary parameters, UBF, and IAP changes.

Precise control of ventilation during the insufflation and early desufflation periods is required to avoid maternal hypercarbia and hypocarbria, respectively. During desufflation, ventilatory parameters must be regulated because hyperventilation can result in decreased UBF, and hypocarbria may increase maternal hemoglobin oxygen affinity with potential detrimental effects on fetal oxygenation.16,17

During carbon dioxide pneumoperitoneum, increased intraabdominal pressure can result in decreased diaphragmatic excursion, reduced pulmonary compliance, and increased deadspace ventilation.8 In addition, absorption of carbon dioxide from the peritoneal cavity19,20 can result in increased PaCO₂ unless appropriate ventilatory adjustments are made to eliminate the excess carbon dioxide and overcome the increased deadspace ventilation.21 The marked increase in the PaCO₂-ETCO₂ gradient observed in our study reflects the inadequacy of ETCO₂ to estimate PaCO₂ accurately.

Decreases in maternal oxygenation probably was a reflection of decreased functional residual capacity and increased ventilation/perfusion ratio mismatch. Despite the decrease in maternal oxygenation, the fetal PaO₂ remained within normal limits. The absence of fetal acidosis in this model would suggest that fetal acidosis reported in other studies20 has been due to the concurrent maternal respiratory acidosis resulting from ineffective ventilation.

As in other gravid animal studies,10,22,23 § no significant changes occurred in maternal hemodynamics during a 1-h insufflation period to an intraabdominal pressure of 15 mmHg in dorsal recumbency. Galan and associates6 reported increases in pulmonary artery wedge pressure, central venous pressure, and mean pulmonary artery pressure at 20 mmHg but not at 10 mmHg insufflation pressure using the gravid baboon model.

In nongravid patients, wide variations in hemodynamic responses to insufflation have been observed. Most studies report an increase in systemic vascular resistance, MAP, and right atrial pressure and a decrease

### Table 2. Fetal Blood Gas Data and Serum Lactate Levels (SD) during Control (C) and Insufflation (I)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>PaO₂ (mm-Hg)</th>
<th>PaCO₂ (mm-Hg)</th>
<th>pH</th>
<th>O₂ Sat</th>
<th>ABE</th>
<th>Lactate (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>33 ± 1</td>
<td>31 ± 1</td>
<td>7.34 ± 0.05</td>
<td>93 ± 1</td>
<td>-0.5</td>
<td>2.5 ± 0.6</td>
</tr>
<tr>
<td>15</td>
<td>29 ± 1</td>
<td>34 ± 1</td>
<td>7.32 ± 0.07</td>
<td>92 ± 1</td>
<td>-0.3</td>
<td>2.8 ± 0.3</td>
</tr>
<tr>
<td>30</td>
<td>29 ± 1</td>
<td>34 ± 1</td>
<td>7.30 ± 0.07</td>
<td>91 ± 1</td>
<td>-0.1</td>
<td>2.8 ± 0.4</td>
</tr>
<tr>
<td>60</td>
<td>29 ± 1</td>
<td>34 ± 1</td>
<td>7.30 ± 0.07</td>
<td>92 ± 1</td>
<td>-0.1</td>
<td>2.8 ± 0.4</td>
</tr>
<tr>
<td>90</td>
<td>29 ± 1</td>
<td>34 ± 1</td>
<td>7.29 ± 0.07</td>
<td>93 ± 1</td>
<td>-0.1</td>
<td>2.8 ± 0.4</td>
</tr>
</tbody>
</table>

INTRAABDOMINAL CO\textsubscript{2} INSUFFLATION IN THE PREGNANT EWE

Fig. 5. Corrected fetal mean arterial pressure in control and infusion groups.

in cardiac index. Venous return is reduced when infusion pressures approach those used in our study. Other studies did not report a significant change in cardiac output, although there was an increase in MAP, central venous pressure, and HR.

Increased intrathoracic pressure also may develop in pregnant patients during insufflation because of decreased chest compliance as the diaphragm is pushed into the thorax. Although it is an inaccurate reflection of true intrathoracic pressure, circuit pressure was increased significantly in this study during insufflation.

We noted no changes in UBF. In a previous study, carbon dioxide pneumoperitoneum at an intraabdominal pressure of 20 mmHg resulted in pressure-dependent decreased perfusion of the maternal placenta. However, no changes were seen in maternal arterial pressure, fetal cardiopulmonary, or acid-base status.

We observed a significant increase in Pa\textsubscript{CO\textsubscript{2}}-ETCO\textsubscript{2} gradient during insufflation. A considerable underestimation of Pa\textsubscript{CO\textsubscript{2}} can occur if ETCO\textsubscript{2} is used to monitor the adequacy of ventilation of pregnant patients undergoing lACO\textsubscript{2} insufflation. There were no changes in fetal MAP, HR, acid-base status, or serum lactate.

Additional studies investigating delayed fetal effects of lACO\textsubscript{2} insufflation, cardiopulmonary effects of patient positioning, and laparoscopic surgery should be done to identify pathophysiologic changes in pregnant women.

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Background: Pain relief during surgical procedures has generally been achieved with the use of opioids. However, there is concern that these agents may be systolic, diastolic, and mean arterial pressure.

Their role in the current era of laparoscopic surgery has been re-evaluated using different methods.

Methods: Morphine, clonidine, and halothane in non-laparoscopic conditions that had no specific response control. The study was blinded. Morphine in the laparoscopic condition was fixed-dose and compared to clonidine in a double-blind study. Morphine was given at a level of 1.5 mg, and the clonidine was given in two doses of 25 and 50 μg.

Results: The effect of morphine had a lower ratio of clonidine to morphine and was compared to clonidine at a fixed-dose and ratio. The effect of morphine was found to be lower than that of clonidine. The effect of clonidine was found to be lower than that of morphine.

Conclusions: This study provides evidence for the use of clonidine as a potential alternative to morphine.

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