Changes in pH of peritoneal fluid associated with carbon dioxide insufflation during laparoscopic surgery in dogs

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Objective—To evaluate changes in pH of peritoneal fluid associated with CO_2 insufflation during laparoscopy in dogs.

Animals—13 client-owned dogs and 10 purpose-bred teaching dogs.

Procedures—Laparotomy was performed on control dogs; peritoneal fluid pH was measured at time of incision of the abdominal cavity (time 0) and 30 minutes later. Laparoscopic insufflation with CO_2 was performed and routine laparoscopic procedures conducted on the teaching dogs. Insufflation pressure was limited to 12 mm Hg. Intraperitoneal fluid pH was measured by use of pH indicator paper at 4 time points. Arterial blood gas analysis was performed at the same time points.

Results—Peritoneal fluid pH did not change significantly between 0 and 30 minutes in the control dogs. For dogs with CO_2 insufflation, measurements obtained were a mean of 8.5, 24.5, 44.5, and 72.0 minutes after insufflation. The pH of peritoneal fluid decreased significantly between the first (7.825 ± 0.350) and second (7.672 ± 0.366) time point. Blood pH decreased significantly between the first (7.343 ± 0.078), third (7.235 ± 0.042), and fourth (7.225 ± 0.038) time points. The $Paco_2$ increased significantly between the first (39.9 ± 9.8 mm Hg) and fourth (54.6 ± 4.4 mm Hg) time points. Base excess decreased significantly between the first and all subsequent time points.

Conclusions and Clinical Relevance—Pneumoperitoneum attributable to CO_2 insufflation caused a mild and transient decrease in peritoneal fluid pH in dogs. Changes in peritoneal fluid associated with CO_2 insufflation in dogs were similar to those in other animals. (*Am J Vet Res* 2008;69:298–301)

Laparoscopic techniques are being used with increasing frequency for a wide number of diagnostic and surgical procedures in veterinary medicine.[1-5] In human medicine, laparoscopy is considered the standard technique for many surgical procedures.[6-8] However, a major concern associated with laparoscopy for neoplastic disease in humans is port site metastasis,[9-12] which is defined as early recurrent tumorous lesions that develop locally in the abdominal wall within the scar tissue of 1 or more trocar sites that are not associated with diffuse peritoneal carcinomatosis.[13] Port site metastasis has only been reported in veterinary medicine after thoracoscopic surgery in a dog.[5] Factors influencing port site metastasis are unknown[9,12]; however, direct contamination,[14] aerosolization,[15] the chimney effect,[16] the local immune response,[17] and establishment of pneumoperitoneum[18] have been suggested as possible causes.

Studies[11,19] in laboratory animals have revealed that CO_2 insufflation increases the risk of tumor implantation. Other investigations into the effects of CO_2-induced pneumoperitoneum revealed an association with intraperitoneal acidosis in rats,[20,21] mice,[22] and swine.[23] Several investigators have proposed[21,22] that alterations of the peritoneal surface as a result of intraperitoneal acidosis associated with CO_2 insufflation may facilitate port site metastasis.

Laparoscopy is becoming a commonly used method for diagnostic and surgical procedures in dogs. Abdominal neoplasms in dogs are often biopsied by use of laparoscopy, but the risk for development of port site metastasis in these dogs is unknown. To our knowledge, alteration of intraperitoneal pH has not been investigated in dogs. The objective of the study reported here was to investigate the effect of CO_2 insufflation on pH of intraperitoneal fluid in dogs. We hypothesized that CO_2 insufflation during laparoscopy would not induce peritoneal fluid acidosis in dogs.

Materials and Methods

Animals—Thirteen client-owned female dogs undergoing routine ovariohysterectomy via a standard laparotomy technique were used as control dogs. Ten purpose-bred large-breed female dogs (approx body weight of each dog, 25 kg) used for a laparoscopy teaching course were the study population. All dogs were deemed healthy on the basis of results of a physical examination and no known history of disease. Clients provided written consent for use of their dogs in the

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study. The study protocol was approved by the Animal Care and Use Committee at Colorado State University.

Anesthesia—All dogs were anesthetized. A combination of 0.5 mg of acepromazine,[a] 25 mg of morphine,[b] and 0.5 mg of glycopyrrolate[b] was administered SC approximately 30 minutes prior to induction of anesthesia. Anesthesia was induced by IV administration of a combination of 150 mg of ketamine[c] and 7 mg of diazepam,[d] which allowed intubation of the trachea. Isoflurane[e] in oxygen was administered to maintain a surgical plane of anesthesia. Lactated Ringer's solution[f] was administered at an approximate rate of 5 mL/kg/h, IV, during surgery. Standard techniques (eye position, palpebral reflexes, and jaw tone) were used to evaluate anesthetic depth. Dogs were monitored continuously by use of ECG, direct blood pressure measurements, end-tidal capnography, and pulse oximetry. Positive-pressure ventilation was not used in the control dogs but was used in all teaching dogs. Ventilator settings remained unchanged throughout the study period (tidal volume, approx 15 mL/kg; respiratory rate, 12 breaths/min; and inspiration:expiration ratio, approx 1:4). Dogs that became hypotensive (defined as mean arterial pressure < 60 mm Hg) were treated by IV admnistration of a bolus of crystalloid solution. Additional medications or treatments were used when necessary.

Control dogs—Laparotomy was performed on dogs in the control group. The pH was measured by use of a commercially available pH strip[g] (pH scale from 6.0 to 8.1) immediately after the abdominal cavity was incised (time 0) and approximately 30 minutes later before closure of the linea alba. A sterile cotton swab was used to collect abdominal fluid. The swab specimen was then applied to the nonsterile pH paper to measure peritoneal fluid pH. Measurements were determined by a single investigator. Blood gas analysis was not performed for the control group.

Teaching dogs with CO_2 insufflation—Dogs were positioned in lateral or dorsal recumbency, and routine laparoscopic procedures (laparoscopic exploration of the abdominal cavity, collection of liver biopsy specimens, and ovariohysterectomy) were performed. Dogs were excluded when laparoscopic-assisted procedures that required deflation of the abdominal cavity were performed before completion of data acquisition.

A Veress needle[h] was used for insufflation of the abdominal cavity. Insufflation pressure was limited to 12 mm Hg. Time at which insufflation was completed (defined as abdominal distention at a pressure of 12 mm Hg without noticeable flow detection by the insufflating device[i]) was recorded (time 0). Immediately after successful insufflation, routine placement of a laparoscopic cannula was performed as described elsewhere.[24] This cannula was then used to obtain the first measurement of intraperitoneal fluid pH (time point 1). Measurements were repeated 3 additional times (time points 2, 3, and 4, respectively) at approximately 20-minute intervals.

Peritoneal fluid pH was determined by cutting a small piece from a commercially available pH strip[g] such that the piece could be held with laparoscopic forceps. This was then inserted through an abdominal trocar and pressed against the abdominal wall. Care was taken to avoid obtaining a value from areas that contained blood. When severe blood contamination was detected, measurements were repeated. The pH strip was withdrawn from the abdominal cavity, and the pH was determined separately by 4 investigators. Values were determined by comparing the color of the pH strip to the pH scale provided by the manufacturer. All investigators were not aware of the dog or time point that served as the source of each sample. Arterial blood gas analysis was conducted at the same time points as the measurements of peritoneal fluid pH; samples were analyzed by use of a commercially available blood gas analyzer.[j]

Statistical analysis—For the peritoneal fluid pH in the dogs with CO_2 insufflation, the lowest and highest value of each of the 4 measurements for a given time point were excluded from the analysis. The mean of the remaining 2 measurements was calculated. An ANOVA for repeated measurements was used to compare the value for the first pH measurement with values for each subsequent time point. Values of $P < 0.05$ were considered significant. Data were reported as mean ± SD.

Results

Control dogs—For the control group, mean ± SD pH was 8.03 ± 0.13 immediately after the abdominal cavity was incised. Thirty minutes later, mean pH was 8.08 ± 0.08. These values did not differ significantly ($P = 0.298$).

Teaching dogs with CO_2 insufflation—The only complication detected for these dogs was hypotension

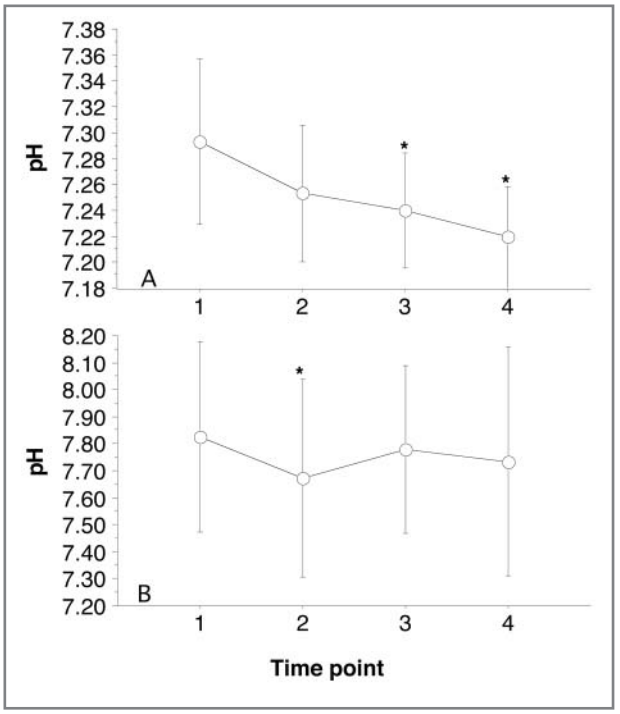

Figure 1—Mean ± SD blood pH (A) and peritoneal fluid pH (B) for 9 dogs that had CO_2 insufflation of the abdominal cavity for laparoscopic teaching procedures. Time points 1 to 4 represent (mean ± SD) 8.5 ± 3 minutes, 24.5 ± 5 minutes, 44.5 ± 7.0 minutes, and 72.0 ± 14 minutes after insufflation, respectively. *Value differs significantly ($P < 0.05$) from the value for time point 1.

Table 1—Mean ± SD values for blood gas analysis for 9 dogs that had CO_2 insufflation of the abdominal cavity for laparoscopic teaching procedures.

Time point*	No. of dogs	$Paco_2$ (mm Hg)	Bicarbonate (mEq/L)	Base excess (mEq/L)
1	9	39.9 ± 9.8	20.80 ± 2.25	–4.48 ± 2.00
2	7	47.7 ± 9.0	20.80 ± 1.92	–6.37 ± 1.84†
3	6	46.9 ± 13.2	21.97 ± 1.00	–6.37 ± 1.61‡
4	8	54.6 ± 4.4§	22.29 ± 0.94	–6.02 ± 1.33‖

*Represents a mean ± SD of 8.5 ± 3 minutes, 24.5 ± 5 minutes, 44.5 ± 7 minutes, and 72.0 ± 14 minutes after insufflation for time points 1 to 4, respectively. †,‡,§,‖Within a column, value differs significantly (†$P = 0.008$, ‡$P < 0.05$, §$P = 0.001$, and ‖$P = 0.009$) from the value for time point 1.

during anesthesia in 4 dogs. Each of the 4 dogs received 1 or 2 fluid boluses of 100 mL of lactated Ringer's solution to treat hypotension. Two of the 4 dogs did not respond adequately to administration of the fluid boluses and therefore were administered 1 or 2 doses of ephedrine[k] (2.5 mg, IV), and 1 of these 2 dogs was subsequently treated by administration of dobutamine[l] as a continuous rate infusion (2 µg/kg/min, IV).

One dog was excluded because a laparoscopic-assisted procedure that required deflation of the abdominal cavity was performed prior to completion of data acquisition. Consequently, data were available for 9 dogs.

Measurements of peritoneal fluid pH were obtained at a mean ± SD of 8.5 ± 3 minutes, 24.5 ± 5 minutes, 44.5 ± 7 minutes, and 72.0 ± 14 minutes after insufflation for the first to fourth time points, respectively. Because of difficulty in obtaining blood samples close to the time at which pH of peritoneal fluid was measured, blood gas values were obtained for all 9 dogs at the first time point but only for 7, 6, and 8 dogs at the second, third, and fourth time points, respectively.

Peritoneal fluid pH decreased significantly ($P = 0.020$) between the first and second time points (**Figure 1**). Blood pH decreased significantly between the first time point and the third ($P = 0.035$) and fourth ($P = 0.020$) time points. The $Paco_2$ increased significantly ($P = 0.002$) between the first and fourth time points (**Table 1**). Base excess decreased significantly between the first time point and all subsequent time points. Bicarbonate concentrations did not differ significantly among any of the time points.

Discussion

Pneumoperitoneum attributable to insufflation with CO_2 causes transient intraperitoneal acidosis in dogs. The findings for the study reported here are similar to those in other animals.[20-23] However, in our study, a decrease in intraperitoneal pH was only detected during the initial period of CO_2-induced pneumoperitoneum. This finding is consistent with results of a clinical study[25] in humans undergoing laparoscopic surgery.

Changes in blood pH in our study population were comparable to those in a study[26] in dogs in which investigators evaluated the cardiopulmonary effects of CO_2 insufflation. No significant changes in $Paco_2$ were detected in that study because it had been designed to maintain a constant end-tidal CO_2 throughout the procedure. In contrast, our study was designed to allow changes at a fixed ventilator setting that would be commonly used in practice. In the study reported here, intraperitoneal pH decreased significantly only within the first 20 minutes after insufflation and then stabilized. Those changes were likely caused by peritoneal fluid acidosis and carbonic acid production, rather than systemic hypercarbia and acidemia, because the blood pH, $Paco_2$, and base excess decreased over the entire study period.

Significant differences between sample time points for blood pH and $Paco_2$ were detected toward the end of the study period. In contrast, significant changes for peritoneal fluid pH were not evident at the conclusion of the study period. If the changes in peritoneal fluid pH were secondary to systemic changes, it would be expected that they would follow the same pattern of systemic alterations (ie, they should have changed toward the end of the study period). In a study[25] in human patients, this finding was even more dramatic because peritoneal acidosis was only detected 10 minutes after insufflation, and there was a shift from the initial peritoneal acidosis toward alkalosis after 30 minutes of insufflation. The difference between results for that study[25] and our results is more likely attributable to the application of positive-pressure ventilation. In other studies,[27-29] investigators have reported that intra-abdominal insufflation with CO_2 is associated with systemic hypercarbia and acidemia. These changes are attributable to systemic absorption of CO_2.[30] In the study reported here, changes in base excess were mild and were detected during the entire study period, which would make it unlikely that they were related to the peritoneal fluid changes.

Changes in pH of peritoneal fluid in the study reported here are consistent with results of other studies[20,23] in which investigators found a decrease in intraperitoneal pH. These changes likely resulted from the direct effects of CO_2 insufflation; however, they may also have been caused by impaired tissue perfusion secondary to abdominal insufflation.[31] Regardless of the cause of intraperitoneal acidosis, concerns exist in human medicine with regard to the potential correlation with port site metastasis.

Several procedures to prevent changes in intraperitoneal pH have been investigated. Heating, humidification, and use of bicarbonate had a positive effect on peritoneal acidosis in 1 study[23]; however, that result was not statistically significant. Intraperitoneal lavage, gasless laparoscopy, and use of helium instead of CO_2 have also been used with mixed results.[20,25,32-35]

A shortcoming of the study reported here was the lack of an exactly similar control group. In our control

group, the technique used to measure intraperitoneal pH was not exactly the same as for the laparoscopic group; thus, we did not proceed with statistical comparison between the groups. It would have been beneficial to include a control group insufflated with an inert gas such as helium. However, special insufflators are needed for the administration of helium, and these insufflators were not available to the authors.

Analysis of the results of the study reported here established that pneumoperitoneum attributable to CO_2 insufflation can lead to peritoneal fluid acidosis, at least at the onset of the insufflation period. Peritoneal fluid changes associated with CO_2 insufflation in dogs are similar to those in humans and other animals. These changes may facilitate tumor implantation during laparoscopic surgery in cancer patients. Because dogs appear to have a response to CO_2 insufflation that is similar to the response for human patients, dogs may be useful in studies conducted to investigate strategies to decrease the risk of port site metastasis.

a. Vedco Inc, St Joseph, Mo.
b. Baxter Healthcare Corp, Deerfield, Ill.
c. VetaKet, Phoenix Scientific Inc, St Joseph, Mo.
d. Hospira Inc, Lake Forest, Ill.
e. Abbott Laboratories, North Chicago, Ill.
f. Hospira Inc, Lake Forest, Ill.
g. pH-indicator type CS, Whatman International Ltd, Maidstone, England.
h. Auto Suture, United States Surgical Corp, Norwalk, Conn.
i. Storz Endoflator 26012, Karl Storz Endovision, Charlton, Mass.
j. IRMA Trupoint blood gas analysis system, ITC, Edison, NJ.
k. Parenta Pharmaceuticals Inc, West Columbia, SC.
l. Bedford Laboratories, Bedford, Ohio.

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