Lactate as a Diagnostic Test for Septic Peritoneal Effusions in Dogs and Cats

Lactate concentration in peritoneal fluid was evaluated and compared to blood lactate concentration in dogs and cats with septic and nonseptic abdominal effusions. All dogs with septic effusions had a peritoneal fluid lactate concentration >2.5 mmol/L and a peritoneal fluid lactate concentration higher than blood lactate, resulting in a negative blood to fluid lactate difference. In dogs, the diagnostic accuracy of the peritoneal fluid lactate concentration and the blood to fluid lactate difference in differentiating septic peritoneal effusion was 95% and 90%, respectively. Peritoneal fluid lactate concentration and blood to fluid lactate difference were not accurate tests for detecting septic peritoneal effusions in cats. **J Am Anim Hosp Assoc 2004;40:364-371.**

Garrett M. Levin, DVM

Jennifer J. Bonczynski, DVM, Diplomate ACVS

Lori L. Ludwig, VMD, MS, Diplomate ACVS

Linda J. Barton, DVM, Diplomate ACVECC

Andrew S. Loar, DVM, Diplomate ACVIM

From the Departments of Surgery, Medicine, and Pathology, The E. & M. Bobst Hospital, The Animal Medical Center, 510 East 62nd Street, New York, New York 10021.

Doctor Levin's current address is Animal Specialty Group, 4641 Colorado Boulevard, Los Angeles, California 90039.

Introduction

In animals with septic peritonitis, emergency surgery is often recommended based on clinical signs and the presence of intracellular bacteria in abdominal fluid on cytology. Presenting clinical signs of septic peritonitis may include hypotension, abdominal pain, hypovolemia, lethargy, tachycardia, pyrexia, and tachypnea.[1] These clinical signs may be similar to many nonseptic endocrine and metabolic abdominal disorders such as pancreatitis and neoplasia; therefore, septic peritonitis cannot be diagnosed based on clinical signs alone.

Demonstration of intracellular bacteria on fluid cytology is the only rapid diagnostic test currently available to detect septic abdominal effusions. Published reports indicate that fluid cytology is ≤87% accurate in the diagnosis of a septic peritoneal effusion, however.[2-6] Because the results of fluid cytology may be altered by clinical course and antibiotic therapy and are dependent upon technical expertise, other objective tests that can be used in a clinical setting in dogs and cats would be useful. Currently, a definitive diagnosis of a septic peritoneal effusion requires a positive bacterial culture, but culture results are not usually available for several days.

Because of the anaerobic microenvironment and bacterial metabolites present in septic effusions, it was suspected that fluid lactate concentration may be higher in animals with septic peritonitis than in those with nonseptic peritonitis.[3,4,6,7] In humans, lactate concentration in abdominal fluid may be three times higher in patients with a bacterial peritonitis than in those with a nonbacterial peritonitis.[5] Lactate readily diffuses across membranes, and people with severe lactic acidosis may also have high fluid lactate concentrations in abdominal fluid. It has been suggested, therefore, that a blood to fluid lactate gradient may be more accurate in differentiating septic peritonitis from other causes of elevated lactate in abdominal fluid.[5] A recent preliminary study showed promising results

for the use of a blood to fluid lactate difference in small animals with septic peritoneal effusion; however, lack of statistical significance and a small population size prevented definitive conclusions regarding the test's clinical applicability.[2]

The purpose of this study was to assess the ability to differentiate septic peritoneal effusions from nonseptic effusions in dogs and cats by evaluating lactate concentration differences in peritoneal fluid and venous blood. First, it was hypothesized that the lactate concentration of the peritoneal fluid would be higher in septic effusions than in nonseptic effusions. Second, it was hypothesized that the difference between lactate concentration in the peritoneal fluid and lactate concentration in the blood would be greater in septic peritoneal effusions than in nonseptic effusions.

Materials and Methods

Client-owned dogs and cats that were presented with peritoneal effusion between January 2001 and October 2002 were included in this prospective study as they were diagnosed. Animals were included if at least 1 mL of peritoneal fluid was collected for analysis prior to intravenous (IV) glucose administration and if the source of peritoneal effusion was determined. Animals were excluded if dextrose supplementation was administered prior to sample collection. Animals were excluded if they had confirmed hemoabdomen or concurrent diabetic ketoacidosis. The above inclusion and exclusion criteria provided continuity with a previous report.[2]

Diagnosis of peritoneal effusion was made via abdominocentesis or laparotomy. All samples utilized in this study were collected in the same manner. Abdominal fluid was collected in a 1-mL heparinized syringe.[a] At the same time, 1 mL of venous blood was collected in a 1-mL heparinized syringe. Lactate concentrations (mmol/L) in the peritoneal effusion and peripheral blood were measured with a blood gas analyzer[b] within 15 minutes of collection. Abdominal effusion was placed in an ethylenediamine triacetate (EDTA) sterile blood collection tube[c] for cytological analysis. In addition, a sample of abdominal effusion was submitted for aerobic and anaerobic bacterial culture and sensitivity testing. The blood to fluid lactate concentration difference was calculated by subtracting the concentration of lactate in the peritoneal effusion from the concentration in the peripheral blood. Cytological examinations were performed within 24 hours of collection by one examiner (Loar).

An effusion was considered to be septic if intracellular bacteria were detected on cytology or if bacterial growth occurred on culture. The etiology of the septic peritoneal effusions were established via laparotomy (n=14) or necropsy (n=3). The etiology of the nonseptic effusions were determined via abdominal ultrasonography (n=4), echocardiography (n=4), cytology (n=3), laparotomy (n=8), or necropsy (n=1).

Statistical analysis of blood lactate and abdominal fluid lactate concentrations was performed using a Mann-Whitney test with the level of statistical significance set at $P \leq 0.05$. Sensitivity, specificity, and a diagnostic accuracy were calculated for cases with septic and nonseptic effusions with respect to blood lactate and abdominal fluid lactate concentrations that were determined to have statistical significance.[d]

Results

Nineteen dogs were included in this study. Eight had septic peritoneal effusions, and 11 had nonseptic effusions. Eighteen cats were included in the study, of which nine had septic peritoneal effusions, and nine had nonseptic effusions. Septic peritoneal effusions were caused by intestinal rupture secondary to foreign bodies (three dogs, four cats) and neoplasia (three dogs, two cats), postoperative enterotomy dehiscence (one dog, one cat), splenic abscessation (one dog), and uroabdomen secondary to urinary bladder rupture with concurrent urinary tract infection (two cats). Nonseptic peritoneal effusions were caused by pancreatitis (three dogs, one cat), splenic neoplasia (one dog), hepatic neoplasia (two dogs), adrenal neoplasia (one cat), feline infectious peritonitis (one cat), gastrointestinal foreign bodies (two dogs), gastrointestinal neoplasia (five cats), and right-sided congestive heart failure (three dogs, one cat).

All animals (n=17) with a septic peritoneal effusion were diagnosed by the presence of intracellular bacteria on cytology and a positive bacterial culture. All animals (n=20) with a nonseptic peritoneal effusion were diagnosed based on the absence of intracellular bacteria on cytology and a negative aerobic and anaerobic bacterial culture. In animals with a septic effusion, the most common bacterial isolate was *Escherichia coli* (n=9). Additional isolates included *Enterococcus* spp. (n=4), *Streptococcus* spp. (n=5), *Enterobacter* spp. (n=2), *Klebsiella* spp. (n=3), *Pasteurella* spp. (n=2), *Staphylococcus* spp. (n=2), and *Flavobacterium* spp. (n=1). A mixed-bacterial population was present in 11 of 18 animals with a septic peritoneal effusion [Tables 1-4].

The median blood lactate concentration was significantly (P=0.02) higher in dogs with septic effusions (2.48 mmol/L; range, 1.13 to 6.27 mmol/L) than in dogs with nonseptic effusions (1.05 mmol/L; range, 0.26 to 5.04 mmol/L). At values >2.0 mmol/L, the blood lactate concentration had a 63% sensitivity and 82% specificity for detecting a septic peritoneal effusion. In cats, the median blood lactate concentration was higher with septic effusions (2.49 mmol/L; range, 0.88 to 4.25 mmol/L) than with nonseptic effusions (1.79 mmol/L; range, 0.77 to 6.89 mmol/L); however, this difference was not significant (P=0.10).

The median lactate concentration in the abdominal fluid was significantly (P<0.01) higher in dogs with septic effusions (7.57 mmol/L; range, 2.69 to 30.00 mmol/L) than in dogs with nonseptic effusions (1.25 mmol/L; range, 0.34 to 5.77 mmol/L). In dogs, a fluid lactate concentration >2.5 mmol/L had a 100% sensitivity and 91% specificity for diagnosing a septic effusion. In cats, the median lactate concentration in the abdominal fluid was significantly (P=0.04) higher with septic effusions (5.18 mmol/L; range, 0.83 to 10.69 mmol/L) than with nonseptic effusions (1.71 mmol/L; range, 0.79 to 8.09 mmol/L). In cats,

a fluid lactate concentration >2.5 mmol/L had a 67% sensitivity and 67% specificity for diagnosing a septic peritoneal effusion.

All dogs (n=8) with septic effusions had a lactate concentration higher in the effusion than in the peripheral blood. Seven of 11 dogs with a nonseptic effusion also had a lactate concentration higher in the abdominal fluid than in the peripheral blood. The median blood to fluid lactate difference was significantly ($P<0.01$) lower in dogs with septic effusions (-3.61 mmol/L; range, -26.90 to -1.10 mmol/L) than in dogs with nonseptic effusions (-0.08 mmol/L; range, -1.58 to 0.70 mmol/L). Similar to a previous report, when the blood to fluid lactate value was < -2.0 mmol/L, there was a 63% sensitivity, a 100% specificity, and an accuracy of 84% for detecting septic effusions in dogs.[2] Using a less stringent blood to fluid lactate value (< -1.5 mmol/L) as a diagnostic criteria, the blood to fluid lactate difference had an 88% sensitivity, a 91% specificity, and an accuracy of 90% for detecting septic effusions. Use of the lower, negative numerical value resulted in a higher diagnostic accuracy than what was previously reported.[2]

Seven of nine cats with septic effusions had a lactate concentration higher in the abdominal fluid than in the peripheral blood. Four of nine cats with nonseptic effusions had a lactate concentration higher in the effusion than in the peripheral blood. In cats, the median blood to fluid lactate difference was significantly ($P=0.02$) lower with septic effusions (-1.49 mmol/L; range, -7.47 to 0.13 mmol/L) than with nonseptic effusions (0.21 mmol/L; range, -5.71 to 3.57 mmol/L). In cats, a blood to fluid lactate difference < -0.5 mmol/L had a 78% sensitivity, a 78% specificity, and an accuracy of 78% for detecting a septic effusion.

There was one canine and one feline outlier in the septic peritoneal fluid populations. If canine case no. 7 (peritoneal effusion lactate concentration of 30.00 mmol/L [Table 1]) is excluded, the median blood to fluid lactate difference (-0.71 mmol/L; range, -6.55 to 0.70 mmol/L) remains statistically significant ($P<0.01$). Furthermore, the sensitivity and specificity remain relatively unchanged at 85% and 91%, respectively, with an accuracy of 89%. If feline case no. 6 (peritoneal effusion lactate concentration of 10.69 mmol/L [Table 3]) is excluded, the median blood to fluid lactate difference (-0.49 mmol/L; range, -6.44 to 3.57 mmol/L) remains statistically significant ($P=0.04$). Furthermore, the sensitivity and specificity remain relatively unchanged at 75% and 78%, respectively, with an accuracy of 77%. Removing the septic effusion cases with the highest lactate concentrations did not affect the statistical analysis; therefore, these animals were not removed from the data pool when conclusions were reached.

Discussion

Prompt recognition of a septic peritoneal effusion is essential in order to initiate appropriate medical and surgical therapy. Because 24 to 72 hours are required for bacterial culture results, a septic effusion must usually be diagnosed on the basis of clinical findings and cytological examination of abdominal fluid. Cytology of abdominal fluid has been reported as ≤87% accurate; however, in the study reported here, cytology was 100% diagnostic.[1,2,8,9] The higher accuracy documented in the present study may have occurred from all examinations being performed by the same experienced cytopathologist. In a normal clinical setting, many variables may affect cytological results, such as clinical experience of the cytopathologist, presence of localized infections, staining techniques used, and prior antibiotic therapy; therefore, an alternative method to diagnose septic peritoneal effusions in dogs and cats would be very useful.

The concentration of lactate in septic peritoneal effusions may become elevated from an anaerobic microenvironment, production of lactate by neutrophilic glycolysis, and from the presence of bacterial metabolites.[3,4,6] For these reasons, lactate concentration in abdominal fluid may be higher in animals with septic effusions than in those with nonseptic effusions. Results of the study reported here showed that lactate concentration in abdominal fluid from dogs with septic effusions was increased (>2.5 mmol/L).

One dog (case no. 9) with a nonseptic effusion also had an elevated lactate concentration in the abdominal fluid [Table 2]. This animal was diagnosed with pancreatitis, had a history of spinal lymphoma, and upon presentation may have had a lactic acidosis possibly associated with pancreatitis, shock, or neoplasia. The systemic lactic acidosis may have contributed to the high lactate concentration in the abdominal fluid. In addition, degenerative neutrophils comprised 90% of the cells present in the abdominal effusion of this dog, and the neutrophils may have been responsible for increased lactate production.[3,4,6]

Based upon a prior report, animals with septic peritoneal effusions may have elevated blood lactate concentrations.[2] Although blood lactate concentrations were significantly higher in the animals with septic effusions studied in this report, the diagnostic value chosen had a low sensitivity and specificity. Even though three of eight dogs (case nos. 1,2,5) with septic effusions had blood lactate concentrations <2.0 mmol/L [Table 1], it is interesting that all three dogs had a lactate concentration in their effusion >2.5 mmol/L and a blood to fluid lactate difference < -1.5 mmol/L. These dogs were correctly diagnosed with a septic peritoneal effusion when the abdominal fluid lactate concentration and blood to fluid lactate difference values were assessed. These animals were appropriately treated with IV fluid therapy prior to blood sampling, thereby lowering their blood lactate concentration. These results support the use of lactate concentrations in effusion and the blood to fluid lactate difference for diagnosing septic effusions rather than the use of blood lactate concentrations alone.

Two dogs (case nos. 9,16) with nonseptic effusions had a lactate concentration in the blood >2.0 mmol/L [Table 2]. One of these dogs (case no. 9) was previously diagnosed with severe pancreatitis and a history of spinal lymphoma. The other dog (case no. 16) was diagnosed with cardiac disease, and its slight increase in blood lactate concentration may have been associated with cardiogenic shock, hypoxemia, or myocardial dysfunction.

Table 1

Data on Eight Dogs With Septic Effusions

Case No.	Peripheral Blood Lactate (mmol/L)	Peritoneal Effusion Lactate (mmol/L)	Blood to Fluid Lactate Difference	Etiology of Effusion	Fluid Type Based on Cytology	Bacteria Cultured From Effusion
1	1.87	4.15	-2.28	Intestinal perforation; lymphosarcoma	Pyogranulomatous inflammation	*Staphylococcus* spp.
2	1.81	8.36	-6.55	Intestinal perforation; undifferentiated sarcoma	Suppurative, septic exudate	*Gram-positive cocci*
3	2.72	3.82	-1.10	Intestinal perforation; foreign body	Suppurative, septic exudate	*Escherichia coli* *Streptococcus* spp.
4	3.04	7.99	-4.95	Intestinal perforation; lymphosarcoma	Suppurative, septic exudate	*Klebsiella* spp. *Enterococcus* spp. *Escherichia coli*
5	1.13	2.69	-1.56	Intestinal perforation; foreign body	Suppurative, septic exudate	*Escherichia coli* *Enterococcus* spp.
6	6.27	7.97	-1.70	Postoperative intestinal dehiscence	Suppurative, septic exudate	*Escherichia coli* *Klebsiella* spp.
7	3.10	30.00	-26.90	Intestinal perforation; foreign body	Suppurative, septic exudate	*Escherichia coli* *Enterobacter* spp.
8	2.23	7.17	-4.94	Splenic abscess	Suppurative, septic exudate	*Streptococcus* spp. *Flavobacterium* spp.

Table 2

Data on 11 Dogs With Nonseptic Effusions

Case No.	Peripheral Blood Lactate (mmol/L)	Peritoneal Effusion Lactate (mmol/L)	Blood to Fluid Lactate Difference	Etiology of Effusion	Fluid Type Based on Cytology	Bacterial Culture Results
9	5.04	5.77	-0.73	Pancreatitis	Pyogranulomatous inflammation	Negative
10	1.05	1.07	-0.02	Pancreatitis	Modified transudate	Negative
11	0.90	2.48	-1.58	Splenic leiomyosarcoma	Modified transudate	Negative
12	1.25	1.25	0.00	Hepatic adenocarcinoma	Modified transudate	Negative
13	0.89	0.88	0.01	Cardiac disease	Modified transudate	Negative
14	0.68	0.56	0.12	Pancreatitis	Modified transudate	Negative
15	1.60	2.28	-0.68	Cardiac disease	Modified transudate	Negative
16	2.82	2.12	0.70	Cardiac disease	Modified transudate	Negative
17	1.68	2.07	-0.39	Intestinal foreign body	Modified transudate	Negative
18	0.26	0.34	-0.08	Intestinal foreign body	Modified transudate	Negative
19	0.54	0.64	-0.10	Hepatic adenocarcinoma	Modified transudate	Negative

Table 3

Data on Nine Cats With Septic Effusions

Case No.	Peripheral Blood Lactate (mmol/L)	Peritoneal Effusion Lactate (mmol/L)	Blood to Fluid Lactate Difference	Etiology of Effusion	Fluid Type Based on Cytology	Bacteria Cultured From Effusion
1	3.15	10.62	-7.47	Postoperative intestinal dehiscence	Suppurative, septic exudate	*Enterococcus* spp. *Streptococcus* spp.
2	2.49	6.33	-3.84	Intestinal perforation; linear foreign body	Suppurative, septic exudate	*Escherichia coli* *Streptococcus* spp.
3	3.23	6.21	-2.98	Intestinal perforation; lymphosarcoma	Suppurative, septic exudate	*Escherichia coli* *Klebsiella* spp.
4	1.63	3.07	-1.44	Intestinal perforation; linear foreign body	Suppurative, septic exudate	*Enterobacter* spp. *Enterococcus* spp. *Clostridium* spp.
5	2.40	2.27	0.13	Intestinal perforation; lymphosarcoma	Suppurative, septic exudate	*Staphylococcus* spp.
6	4.25	10.69	-6.44	Intestinal perforation; foreign body	Suppurative, septic exudate	*Pasteurella* spp.
7	1.75	2.47	-0.72	Uroabdomen; urinary bladder rupture	Modified transudate	*Streptococcus* spp. *Pasteurella* spp.
8	0.88	0.83	0.05	Intestinal perforation; foreign body	Suppurative, septic exudate	*Escherichia coli*
9	3.69	5.18	-1.49	Uroabdomen; urinary bladder rupture	Suppurative, septic exudate	*Escherichia coli*

Table 4

Data on Nine Cats With Nonseptic Effusions

Case No.	Peripheral Blood Lactate (mmol/L)	Peritoneal Effusion Lactate (mmol/L)	Blood to Fluid Lactate Difference	Etiology of Effusion	Fluid Type Based on Cytology	Bacterial Culture Results
10	1.37	1.16	0.21	Cardiac disease	Modified transudate	Negative
11	6.89	3.32	3.57	Intestinal lymphosarcoma	Modified transudate	Negative
12	1.79	2.99	-1.20	Intestinal carcinoma	Pyogranulomatous inflammation	Negative
13	2.38	8.09	-5.71	Pancreatitis	Modified transudate	Negative
14	1.09	0.79	0.30	Intestinal lymphosarcoma	Modified transudate	Negative
15	1.16	0.84	0.32	Intestinal lymphosarcoma	Modified transudate	Negative
16	1.80	1.90	-0.10	Adrenal pheochromocytoma	Modified transudate	Negative
17	2.10	1.71	0.39	Feline infectious peritonitis	Modified transudate	Negative
18	0.77	1.26	-0.49	Intestinal adenocarcinoma	Modified transudate	Negative

Similar to a previous report, the animals with septic peritoneal effusions in the study reported here had a higher peritoneal fluid lactate concentration than blood lactate concentration.[2] The blood to fluid lactate difference in this study was calculated by subtracting fluid lactate concentration from the blood lactate concentration, resulting in a large negative number. One dog (case no. 3) with a septic effusion had a blood to fluid lactate difference of -1.10 mmol/L [Table 1]. This dog was diagnosed with an intestinal perforation secondary to an intestinal foreign body. Although the peritoneal fluid lactate concentration was higher than the blood lactate concentration in this animal, it did not satisfy the diagnostic criteria of a value < -1.5 mmol/L. The peritoneal fluid lactate concentration, however, exceeded the diagnostic criteria of a lactate value >2.5 mmol/L. The failure of the blood to fluid lactate difference to identify a septic effusion in this case may have resulted from the small study population. Future studies using a larger population of cases may allow selection of a more accurate diagnostic criteria.

One dog (case no. 11) with a nonseptic effusion had a blood to fluid lactate difference < -1.5 mmol/L [Table 2]. This dog was diagnosed with a splenic leiomyosarcoma. People with abdominal neoplasia have been shown to have a high lactate concentration in their abdominal effusion.[7] This dog had no clinical signs of a septic abdomen but was entered into the study because of the presence of peritoneal effusion.

Although the peritoneal fluid lactate concentration and blood to fluid lactate difference were statistically significant, they did not accurately diagnose septic peritoneal effusions in cats. Based on results of this study, there were no clear explanations for the poor diagnostic capabilities of these assays in cats. Possible explanations include the unique glucose metabolism of cats and increased blood lactate concentrations following catecholamine release. Cats are deficient in glucokinase, an enzyme in the liver responsible for phosphorylation of glucose to form glucose 6-phosphate.[11] Glucose 6-phosphate is either polymerized into glycogen or catabolized; therefore, sick and anorexic cats have poor glycogen-generating capacity and tend to have lower glucose concentrations in peripheral blood when compared to sick dogs.[11] In addition, glycogen is broken down by the action of catecholamines on α-adrenergic receptors in the liver.[11] The release of catecholamines in a cat in a state of shock also decreases glycogen storage.[11] Cats may, therefore, have a tendency toward more anaerobic metabolism that subsequently increases the lactate concentration in peripheral blood.[11] More anaerobic metabolism would decrease the difference between the lactate concentrations in peritoneal fluid and peripheral blood in cats, regardless of disease.

Conclusion

Based on the results of this study, the peritoneal fluid lactate concentration, blood to fluid lactate difference, and fluid cytopathology were accurate diagnostic tests for detecting septic effusions in dogs. All dogs with septic peritoneal effusions had a lactate concentration >2.5 mmol/L in peritoneal fluid and a fluid lactate concentration greater than the blood lactate concentration. Despite a statistical significance, the fluid lactate concentration and the blood to fluid lactate difference were not reliable detectors of septic peritoneal effusions in cats.

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[a] Marquest Arterial Blood Sampler; Marquest Medical Products, Inc., Englewood, CO 80112
[b] Rapidlab 860; Bayer Corporation, Tarrytown, NY 10591
[c] Monoject EDTA (K_3) Blood Collection Tube; Sherwood Medical Company, St. Louis, MO 63139
[d] StatView Software; SAS Institute, Inc., Cary, NC 27513

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