Use of serial measurements of peritoneal fluid lactate concentration to identify strangulating intestinal lesions in referred horses with signs of colic

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Objective—To determine the value of serial measurements of peritoneal fluid lactate concentration (PFL) for detecting strangulating intestinal lesions (SLs) in referred horses with signs of colic.

Design—Retrospective cohort study.

Animals—94 horses with signs of colic.

Procedures—Medical records of horses evaluated between September 2006 and February 2010 because of signs of colic were reviewed. All included horses had ≥2 peritoneal fluid samples collected, including one at admission and another within 1 to 6 hours after admission. Of the 94 horses, 26 were assigned to the SL group on the basis of findings at surgery or necropsy and 68 were assigned to the nonstrangulating intestinal lesion group because their signs of colic resolved with medical management. Peritoneal fluid lactate concentration was measured by use of a handheld lactate monitor. Data were analyzed by use of univariable and multivariable logistic regression analysis.

Results—PFL at admission >4 mmol/L, an increase in PFL over time, and especially an increase in PFL over time in horses with a PFL <4 mmol/L at admission (OR, 62; sensitivity, 95%; specificity, 77%) were significant predictors of horses with an SL.

Conclusions and Clinical Relevance—Serially determined PFL was a strong predictor for differentiating horses with SLs from horses with nonstrangulating intestinal lesions. Given the high OR, sensitivity, and specificity of these tests, serially determined PFL may have potential as a screening test for identifying horses with SLs. Further evaluation of the clinical value of PFL for predicting SLs in a prospective, multicenter study is warranted. (J Am Vet Med Assoc 2012;240:1208–1217)

In oxygen-sufficient states, tissues undergo aerobic metabolism and convert pyruvate to CO₂ and ATP for cellular respiration. In oxygen-deficient states, tissues undergo anaerobic metabolism and convert pyruvate to lactate and 2 molecules of ATP for cellular respiration. Although anaerobic metabolism is generally regarded as the most important reason for high BLs, hyperlactatemia can also result from other mechanisms that create tissue hypoxia, such as pulmonary or circulatory failure and anemia.

Blood lactate concentrations are commonly used as indicators of severe disease in human critical care medicine²⁻⁴ and have been associated with increased morbidity and case fatality proportions and used as a prognostic indicator or a trigger point for treatment.³⁻⁷ High BLs also have been evaluated in critically ill veterinary patients,⁸⁻¹⁰ and numerous studies¹¹⁻²⁰ have demonstrated their value as a prognostic indicator in critically ill neonates and adult horses with signs of colic. A single measurement of lactate concentration has not been universally accepted as a worthwhile prognostic indicator.²¹⁻²⁸ In an effort to address the limitations of a single measurement of BL, human critical care specialists measure BLs sequentially over time.²⁵⁻²⁸ Recently, this approach has been adopted by veterinary critical care specialists,²¹⁻²⁰ sequentially decreasing BLs over time have been associated with improved outcomes in veterinary medicine,²¹ and persistent hyperlactatemia has been associated with failure to survive in foals.²¹⁻²⁰

Lactate concentration is typically greater in blood than in peritoneal fluid in clinically normal horses,¹⁰,²¹⁻²⁹ and intestinal hypoperfusion and ischemia lead to an increase in PFL and BL of horses with colic. However, the increase in lactate concentration does not occur simultaneously in both body compartments, so both
dogs and horses with visceral hypoperfusion and ischemia have PFLs that increase prior to increases found in the systemic circulation. The clinical importance of PFL in the preoperative assessment of horses with signs of colic and intestinal ischemia has been evaluated. Among 20 control horses and 189 horses with signs of colic, mean ± SD PFLs were significantly higher in horses with signs of colic (4.00 ± 4.63 mM/mL) than in control horses (0.6 ± 0.19 mM/mL). Peritoneal fluid lactate concentration was also significantly higher in horses with SLs (8.43 ± 5.52 mM/mL) than in horses with NSLs (2.09 ± 2.09 mM/mL). The authors further documented that a PFL:BL ratio < 1 in contemporaneously collected samples did not offer a sensitive means for determining a horse's need for surgery but was most often found in horses with simple obstructive intestinal lesions. Likewise, a single determination of the BL:PFL ratio has been shown to be an unreliable prognostic tool in horses with colic and to offer no extra information on survival rate in comparison with both separate values.

At times, equine referral facilities have conflicting objectives. It is known that SLs are associated with high case fatality proportions and that horses have a better prognosis if SLs are identified and corrected as early as possible. On the other hand, it also is known that not all horses with signs of colic evaluated at an equine referral hospital require emergency abdominal surgery. In a study of 385 horses with signs of colic admitted on an emergency basis after hours, only 309 horses were managed surgically. The expeditious and accurate differentiation of cases that require abdominal surgery from cases that do not will lead to earlier intervention with resultant improved outcome. The purpose of the study reported here was to determine the value of serial measurements of PFL for detecting SL in referred horses with signs of colic for which the management plan remained uncertain following the diagnostic testing performed at admission. To our knowledge, no equine study is available on the evolution of BL and PFLs for the successful conservative management of a horse with signs of colic. Our hypotheses were that a high PFL at admission and an increase in PFL over time would be strong predictors of an SL among this referral population. Factors that are significantly associated with SLs, such as serially determined PFL, might be used by equine veterinarians to identify such horses so that surgical correction of SLs might be expedited to improve outcomes.

Materials and Methods

Study population—The following cases were included in the study: horses referred to the Equine Medical Center of Ocala with colic that had ≥ 2 abdominocentesis performed, including one at admission and another within 1 to 6 hours after admission. The timing for collection of the second abdominal fluid sample was selected on the basis of the attending clinician’s impression that the patient had deteriorated clinically and was not associated with the passage of a specific amount of time. Horses were excluded from the study if they were < 6 months of age or considered to have diffuse peritonitis or primary kidney or liver disease. Horses were also excluded from the study if they had ≥ 2 of the following conditions: diarrhea (mature that was not supported by straw bedding); leukopenia (WBC count, < 3,000 WBCs/μL); or pyrexia (ie, rectal temperature > 39.2°C [102.6°F]).

Case definitions—An SL was diagnosed when there was gross evidence of the simultaneous occlusion of the intestinal lumen and its blood supply. An NSL (simple intestinal obstruction) was diagnosed when there was gross evidence of intraluminal occlusion without vascular obstruction. Abdominal lesions were classified as being either SLs or NSLs on the basis of findings obtained at either surgery or necropsy. Horses with signs of colic that responded to medical treatment were assumed to have an NSL.

Data collection—Data were collected retrospectively from the medical records of horses admitted with colic between September 2006 and February 2010. All horses had an initial physical examination that included abdominal auscultation and percussion, rectal examination, nasogastric intubation, and abdominal ultrasonography. Information on duration of colic was not reliable or consistently available, so it was not included in analyses. Venous blood was collected aseptically and submitted for hematologic evaluation and serum biochemical analysis. Peritoneal fluid was collected as follows: a 2-cm2 area was clipped of hair immediately caudal to the xiphoid and to the right of the linea alba with the horse standing, the area was scrubbed alternately with chlorhexidine and alcohol solutions, and then a sterile stainless steel teat cannula was inserted through a small stab incision. The second and subsequent peritoneal fluid samples were obtained through the stab incision by use of a sterile teat cannula following scrubbing. Venous blood and peritoneal fluid samples were collected in an evacuated glass tube containing EDTA; peritoneal fluid was obtained by gravity flow from the teat cannula. A 2-cm2 area was clipped of hair over the left jugular vein, the area was scrubbed alternately with chlorhexidine and alcohol solutions, and a silastic catheter was inserted IV and sutured in place. The horse was taken to the stall and administered a 20-L bolus of lactated Ringer’s solution IV within 1 hour.

Clinicopathologic data were determined for all blood and peritoneal fluid samples within 10 minutes after collection. Other values recorded for peritoneal fluid included gross appearance, nucleated cell count, and total protein and lactate concentrations. Hematology values were determined by use of an automated system, and differential diagnoses were determined following a Gram stain of a blood smear and microscopic review by a trained veterinary technician. Serum biochemistry values were determined by use of an automated multiple profile system. All BL and PFL measurements were determined by use of a point-of-care portable lactate monitor. The reliability of this handheld lactate analyzer and the details of its operation have been reported previously. The following variables were recorded for each horse in the study: date of initial evaluation; age; breed (categorized as warmblood, Thoroughbred, Quarter Horse, Paso Fino, Arabian, or other breed); sex (female or gelding or sexually intact male); heart rate (beats/min); findings of rectal examination or abdominal ultrasonography (no abnormalities detected, cecal distension, small intestinal distension, colonic impaction, colonic displacement, colonic distension, or other); signs of pain (absent, mild, moderate, or severe or the horse was dull or lethargic);
were included in multivariable logistic regression analysis. Variables significantly associated as categorical variables on the basis of findings of exploratory data analysis. Some continuous variables were recoded for a given variable) also was reported. Some continuous variables were recoded as categorical variables on the basis of findings of exploratory data analysis. Variables significantly associated with SLs by use of univariable logistic regression analysis were included in multivariable logistic regression analysis; both forward and purposeful regression modeling was performed that included all variables associated with being in the SL group with a value of P ≤ 0.20. The specificity and sensitivity for various test measurements were determined from 2 × 2 contingency tables, with sensitivity defined as the proportion of horses with SL that tested positive and specificity defined as the proportion of horses with NSL that tested negative. For all analyses, values of P ≤ 0.05 were considered significant; analyses were performed by use of statistical software.\(^1\)

**Results**

Among 804 horses admitted to the Equine Medical Center of Ocala during the study period, 94 (11.7%) met the inclusion criteria. Of the 94 horses, 26 (28%) had an SL (SL group). These horses included 10 horses with small intestinal volvulus, 8 with large colon volvulus, 5 with SLs associated with pedunculated lipomas, and 3 with mesenteric rents. The remaining 68 horses had NSLs (NSL group) and included 15 horses with ileal impactions, 18 with large colon impaction, 12 with large colon displacement other than renoesplenic entrapment, 11 with spasmodic or gas colic, 5 with renoesplenic entrapment, 2 with intraintestinal foreign bodies, and 5 with duodenitis or proximal jejunitis.

**Signalment**—Horses in the SL group were significantly (P = 0.004) older than horses in the NSL group (Table 1). There was no significant difference in the distribution of

<table>
<thead>
<tr>
<th>Variable</th>
<th>SL group</th>
<th>NSL group</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>11.7 ± 6.9</td>
<td>7.4 ± 5.5</td>
<td>1.1</td>
<td>1.0–1.2</td>
<td>0.004</td>
</tr>
<tr>
<td>PFL at admission (mmol/L)</td>
<td>3.3 ± 2.7</td>
<td>2.2 ± 2.2</td>
<td>1.2</td>
<td>1.0–1.5</td>
<td>0.049</td>
</tr>
<tr>
<td>Log (_{10}) PF WBC count 1 to 6 h after admission (cells/μL)</td>
<td>3.7 ± 0.7</td>
<td>3.3 ± 0.6</td>
<td>2.2</td>
<td>1.1–4.4</td>
<td>0.027</td>
</tr>
<tr>
<td>PF TP 1 to 6 h after admission (g/dL)</td>
<td>3.6 ± 1.2</td>
<td>2.8 ± 1.0</td>
<td>1.7</td>
<td>1.1–2.6</td>
<td>0.010</td>
</tr>
<tr>
<td>PFL 1 to 6 h after admission (mmol/L)</td>
<td>4.7 ± 2.7</td>
<td>1.9 ± 2.3</td>
<td>1.5</td>
<td>1.2–1.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PFL 1 to 6 h after admission – PFL at admission (mmol/L)</td>
<td>1.4 ± 3.5</td>
<td>−0.3 ± 1.7</td>
<td>1.4</td>
<td>1.1–1.8</td>
<td>0.087</td>
</tr>
<tr>
<td>Categorical variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10 y</td>
<td>10 (38)</td>
<td>43 (63)*</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>≥ 10 y</td>
<td>16 (62)*</td>
<td>25 (37)</td>
<td>2.8</td>
<td>1.1–7.0</td>
<td>0.036</td>
</tr>
<tr>
<td>PFL at admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 4 mmol/L</td>
<td>19 (73)</td>
<td>62 (91)*</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>≥ 4 mmol/L</td>
<td>7 (27)*</td>
<td>6 (9)</td>
<td>3.8</td>
<td>1.1–12.7</td>
<td>0.032</td>
</tr>
<tr>
<td>PFL:BL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 1</td>
<td>15 (58)</td>
<td>55 (81)*</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>&gt; 1</td>
<td>11 (42)*</td>
<td>13 (19)</td>
<td>3.1</td>
<td>1.1–9.0</td>
<td>0.027</td>
</tr>
<tr>
<td>PF WBC 1 to 6 h after admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 5,000 cells/μL</td>
<td>14 (54)</td>
<td>58 (85)*</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>≥ 5,000 cells/μL</td>
<td>12 (46)*</td>
<td>10 (15)</td>
<td>2.2</td>
<td>1.3–3.7</td>
<td>0.003</td>
</tr>
<tr>
<td>PF TP 1 to 6 h after admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 3.5 g/dL</td>
<td>11 (42)</td>
<td>54 (79)*</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>≥ 3.5 g/dL</td>
<td>10 (38)*</td>
<td>14 (21)</td>
<td>2.3</td>
<td>1.4–3.7</td>
<td>0.001</td>
</tr>
<tr>
<td>PFL 1 to 6 h after admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 4 mmol/L</td>
<td>12 (46)</td>
<td>61 (90)*</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>≥ 4 mmol/L</td>
<td>14 (54)*</td>
<td>7 (10)</td>
<td>3.2</td>
<td>1.8–5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Change in PF WBC count from admission to 1 to 6 h after admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No increase</td>
<td>7 (27)</td>
<td>35 (51)*</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Increase</td>
<td>19 (73)*</td>
<td>33 (49)</td>
<td>2.9</td>
<td>1.1–7.7</td>
<td>0.029</td>
</tr>
<tr>
<td>Change in PFL from admission to 1 to 6 h after admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No increase</td>
<td>7 (27)</td>
<td>35 (51)*</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Increase</td>
<td>19 (73)*</td>
<td>33 (49)</td>
<td>10.8</td>
<td>3.7–31.4</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Continuous variables are reported as mean ± SD. Categorical variables are reported as No. (%) of horses.

* Sensitivity for SL. † Specificity for SL.

NA = Not applicable. PF = Peritoneal fluid. TP = Total protein concentration.
breed of horses between the SL and NSL groups. Among the SL group, the breeds represented were Thoroughbred (n = 8 horses), warmblood (5), Arabian (3), Quarter Horse (3), Paso Fino (2), and other breeds (3). Among the NSL group, breeds represented included Thoroughbred (n = 25), Quarter Horse (13), warmblood (11), Arabian (6), Paso Fino (2), and other breeds (11). Although the proportion of Arabsians was greater among horses in the SL group (5/26 [19%]) than in the NSL group (6/68 [9%]), the odds of being Arabian were not significantly (P = 0.173) different between groups. The distribution of sexes was similar among the SL and NSL groups; in the SL group, there were 5 (19%) geldings, 6 (23%) sexually intact males, and 15 (58%) female, and in the NSL group, there were 18 (26%) geldings, 12 (18%) sexually intact males, and 38 (56%) females. Relative to male horses (geldings or sexually intact males), the odds of being female were not significantly (P = 0.803) greater for the SL group. Horses in the SL group were less likely to survive to discharge than were horses in the NSL group; the proportion of survivors among the SL group (10/26 [38%]) was significantly (P < 0.001) less than that of the NSL group (62/68 [91%]). The odds of survival were 16-fold greater (95% CI, 5.2 to 52.2; P < 0.001) for the SL group relative to the NSL group.

Physical examination findings—Heart rate was considered as a categorical variable for 2 reasons. First, the effects of heart rate did not appear to be linear in the logistic scale and the distribution of heart rates for the SL group was skewed toward higher values (mean, 60 beats/min; median, 51 beats/min). Thus, heart rate data were considered as a categorical variable (<60 beats/min or ≥60 beats/min). Although the proportion of horses with heart rates >60 beats/min in the SL group (14/26 [54%]) was greater than that in the NSL group (31/68 [46%]), this difference was not significant (P = 0.171). The median heart rate in the NSL group was 46 beats/min, similar to that of the SL group (51 beats/min).

Findings on abdominal palpation per rectum or on percutaneous abdominal ultrasonography performed at admission (Table 2) indicated that horses in the SL group were more likely than those in the NSL group to have either small intestinal distension or cecal distension detected by either method. Although the odds of having small intestinal distension detected at admission were greater for horses in the SL group (OR, 1.6; 95% CI, 0.9 to 2.7), the difference was not significant (P = 0.086). Small intestinal distension was detected in 8 of 26 (31%) horses in the SL group and 11 of 68 (16%) horses in the NSL group.

Signs of pain—Signs of pain were categorized as absent, mild, moderate, or severe, or the horse was assessed as dull or lethargic. For purposes of analysis, signs of pain were considered as either moderate to severe or not moderate to severe. The odds of observing moderate to severe signs of pain were greater for the SL group relative to the NSL group (OR, 1.5; 95% CI, 1.0 to 2.5), but this difference was not significant (P = 0.079). Eleven of 26 (42%) horses in the SL group and 16 of 68 (24%) horses in the NSL group had moderate to severe signs of pain observed at admission.

Clinicopathologic data at admission—The WBC count in blood at admission did not differ significantly (P = 0.295) between the SL group (mean ± SD, 9.9 ± 3.7 × 10³ cells/µL) and the NSL group (mean, 9.1 ± 2.9 × 10³ cells/µL). The values of PCV determined at admission did not differ significantly (P = 0.510) between the SL group (mean, 38 ± 7.7%) and the NSL group (mean, 39 ± 7.3%). The blood total protein concentration at admission did not differ significantly (P = 0.614) between the SL group (mean, 6.9 ± 0.74 g/dL) and the NSL group (mean, 6.8 ± 0.80 g/dL). Although not significant (P = 0.068), the BL at admission of horses in the SL group (mean, 3.3 ± 2.17 mmol/L) was higher than that for those in the NSL group (mean, 2.6 ± 1.43 mmol/L). By use of various cutpoints suggested by exploratory data analysis to create dichotomous variables, BL was not significantly associated with the SL group (data not shown).

The distribution of peritoneal fluid WBC count at admission was skewed toward higher values for the SL (median, 1,700 WBCs/µL; mean, 6,235 WBCs/µL) and NSL (median, 1,150 WBCs/µL; mean, 9,228 WBCs/µL) groups. Consequently, data were transformed by use of the logarithm function for purposes of analysis. There was no significant (P = 0.656) association of peritoneal fluid WBC count with being in the SL group. Although the mean peritoneal fluid total protein concentration at admission was higher in the SL group (mean, 3.0 ± 1.2 g/dL) than in the NSL group (mean, 2.7 ± 1.1 g/dL), there was no significant (P = 0.274) association of peritoneal fluid total protein concentration with being in the SL group.

Higher PFL at admission was significantly associated with being in the SL group, whether considered as a continuous variable or as a categorical variable (<4 or ≥4 mmol/L; Table 1). The specificity and sensitivity of a PFL at admission of >4 mmol/L for an SL was 91% and 27%, respectively.

Table 2—Findings on abdominal palpation per rectum or percutaneous abdominal ultrasonography of the same horses as in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No abnormality</th>
<th>Cecal distension</th>
<th>Small intestinal distension</th>
<th>Colonic impaction</th>
<th>Colonic displacement</th>
<th>Colonic distension</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>SL</td>
<td>9</td>
<td>17</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>26</td>
</tr>
<tr>
<td>NSL</td>
<td>10</td>
<td>26</td>
<td>8</td>
<td>10</td>
<td>9</td>
<td>19</td>
<td>4</td>
<td>68</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>43</td>
<td>16</td>
<td>13</td>
<td>12</td>
<td>19</td>
<td>4</td>
<td>94</td>
</tr>
</tbody>
</table>

Data are No. of horses.
The association of SLs with the PFL:BL ratio at admission was examined. Because exploratory data analysis revealed that the distribution of this ratio did not appear Gaussian, the data were transformed by use of the logarithm, function. Although values of the logarithm, of PFL:BL ratio at admission were higher for the SL group (mean, −0.03 ± 0.26) than for the NSL group (mean, −0.13 ± 0.27), this difference was not significant (P = 0.147). However, when the ratio was considered as a categorical variable (≤ 1 or > 1), horses in the SL group had significantly (P = 0.027) higher odds of having a ratio > 1 (Table 1).

Peritoneal fluid data collected 1 to 6 hours after admission—All horses included in the study also had a second peritoneal fluid sample collected. The distribution of WBC counts in these second peritoneal fluid samples was skewed toward higher values for the SL (median, 4,400 WBCs/µL; mean, 12,631 WBCs/µL) and NSL (median, 1,700 WBCs/µL; mean, 13,288 WBCs/µL) groups. Consequently, data were transformed by use of the logarithm, function for purposes of analysis. The log-transformed peritoneal fluid WBC counts were significantly higher in the SL group than in the NSL group (Table 1). Peritoneal fluid WBC count also was considered as a dichotomous variable with a cutoff of 5,000 WBCs/µL. The odds of having the second peritoneal fluid WBC count ≥ 5,000 WBCs/µL were significantly (P = 0.003) greater for the SL group than for the NSL group. The specificity and sensitivity of a peritoneal fluid WBC count ≥ 5,000 WBCs/µL at 1 to 6 hours after admission for an SL was 85% and 46%, respectively. The total protein concentrations in the second peritoneal fluid sample collected were significantly higher in the SL group than in the NSL group. The total protein concentration was also considered as a categorical variable. Although the increase in peritoneal fluid total protein concentration for an SL was 51% and 73%, respectively.

Table 3—Multivariable model of factors significantly associated with SLs in the same horses as in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFL at admission of ≥ 4 mmol/L</td>
<td>60.0</td>
<td>5.6–638.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Increase in PFL from admission to 1 to 6 h after admission</td>
<td>61.7</td>
<td>7.3–697.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PFL at admission × increase in PFL</td>
<td>&gt; 0.0</td>
<td>&gt; 0.0–0.3</td>
<td>0.008</td>
</tr>
<tr>
<td>Best-fitting model obtained by use of forward stepwise logistic regression with categorical term for age purposely included in the model</td>
<td>Age ≥ 10 y</td>
<td>3.1</td>
<td>0.9–10.8</td>
</tr>
<tr>
<td>PFL at admission &gt; 4 mmol/L</td>
<td>74.2</td>
<td>6.5–843.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Increase in PFL from admission to 1 to 6 h after admission</td>
<td>63.0</td>
<td>7.6–518.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PFL at admission × increase in PFL</td>
<td>&gt; 0.0</td>
<td>&gt; 0.0–0.2</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Differences in peritoneal fluid values between admission and within 1 to 6 hours after admission—Although the peritoneal fluid WBC count had a larger increase (ie, higher positive difference between samples obtained within 1 to 6 hours after admission and at admission) among horses in the SL group (mean, 6,396 ± 14,471 WBCs/µL) than in the NSL group (mean, 4,060 ± 30,654 WBCs/µL), this difference was not significant (P = 0.712). However, when considered as a categorical variable (0 or > 0 WBCs/µL), the odds of having an increase in peritoneal fluid WBC count was significantly (P = 0.039) greater for the SL group than for the NSL group (Table 1). The specificity and sensitivity of an increase in peritoneal fluid WBC count for an SL was 51% and 73%, respectively.

Although the increase in peritoneal fluid total protein concentrations was higher for the SL group (mean, 0.5 ± 1.2 g/dL) than for the NSL group (mean, 0.1 ± 0.7 g/dL), the difference was not significant (P = 0.056). Increase in total protein concentration in peritoneal fluid also was considered as a categorical variable. Although the odds of SL group horses having an increase in peritoneal fluid total protein concentration were increased relative to NSL group horses (OR, 2.1; 95% CI. 0.8 to 5.4), this finding was not significant (P = 0.108).

Values of the difference in PFL were significantly (P = 0.007) greater among horses in the SL group than in the NSL group (Table 1). When considered as a categorical variable, the odds of PFL increasing between admission and 1 to 6 hours after admission were significantly (P < 0.001) higher for the SL group relative to the NSL group. The specificity and sensitivity of an increase in PFL over time for an SL was 51% and 73%, respectively.

Multivariable logistic regression—Variables significantly associated with being in the SL group on the basis of univariable logistic regression were included by use of a forward stepwise scheme. This included all variables associated with being in the SL group (P ≤ 0.20). The best-fitting model included the following variables: PFL at admission (≤ 4 or > 4 mmol/L), an increase in PFL (PFL 1 to 6 hours after admission − PFL at admission; > 0 mmol/L), and the interaction of these 2 terms (Table 3). After accounting for these variables, no other factors were significantly associated with the SL group. Although the P value for age (< 10 or ≥ 10 years of age) was not significant, a second model was
purposely fit that included this term. Age did not appear to be an important confounding variable, and all trivariate and bivariate interaction terms including age were not significant.

The significant interaction term in the final multivariable model indicated that the positive association of an increase in PFL with presence of an SL depended on the value of PFL at admission (Table 4). When the PFL at admission was < 4 mmol/L, an increase in PFL was significantly (P < 0.001) associated with a 61.7-fold greater odds of having an SL (95% CI, 7.6 to 518.7). Among horses with a PFL at admission of < 4 mmol/L, the sensitivity for detecting members of the SL group from an increase in PFL was 95% and the specificity was 77%. When PFL at admission was ≥ 4 mmol/L, an increase in PFL was not significantly associated with having an SL. Among horses with a PFL at admission of > 4 mmol/L, the sensitivity for detecting members of the SL group was 29% and specificity was 67%.

Discussion

In clinically normal horses, it has been reported that PFL ranges from 0.22 to 1.47 mmol/L.9–11,21,29 and that BL is always higher than PFL.10 Among 20 control horses and 189 horses with signs of colic in a previous study,29 mean ± SD PFLs were significantly (P < 0.001) higher in horses with signs of colic (4.00 ± 4.65 mmol/L) than in controls (0.6 ± 0.19 mmol/L). Of 126 horses with signs of colic in that study,29 39 (31%) were classified as having an SL and 87 (69%) were classified as having an NSL; the mean ± SD PFL was significantly (P < 0.05) higher in horses with ESs (3.45 ± 5.52 mmol/L) than in horses with ESs (2.09 ± 2.09 mmol/L). Of the 94 horses with signs of colic in the present study, 26 (28%) were classified as having ESs and 68 (72%) were classified as having NSLs. The mean PFL at admission was significantly (P = 0.0499) higher in horses with ESs (3.3 ± 2.7 mmol/L) than in horses with ESs (2.2 ± 2.2 mmol/L), and the mean PFL 1 to 6 hours after admission was significantly (P < 0.001) higher in horses with ESs (4.7 ± 2.7 mmol/L) than in horses with ESs (1.9 ± 2.3 mmol/L).

Under aerobic conditions, a single molecule of glucose is converted to pyruvate and 2 molecules of ATP, and following diffusion of pyruvate into the mitochondria, it is converted to CO2 and H2O, with a theoretic yield of 36 molecules of ATP via the Krebs cycle.33,34 During anaerobic conditions, glucose is converted to pyruvate but cannot be processed in the mitochondria because the final event of the electron transport chain in the Krebs cycle is oxygen dependent.33,34 Therefore, in oxygen-deficient conditions, pyruvate is converted to lactate and the total energy yield is reduced to 2 molecules of ATP. In most critically ill patients, hypoperfusion and hypoxia are responsible for the increases in lactate concentrations identified in blood and peritoneal fluid. In the present study, referred horses with signs of colic were reviewed to determine the value of serial measurements of PFL in identifying horses with SLs. The best-fitting multivariable logistic regression model included the following variables as significantly associated with SLs: PFL at admission (< 4 or ≥ 4 mmol/L), an increase in PFL (ie, PFL 1 to 6 hours after admission – PFL at admission of > 0 mmol/L), and the interaction of these 2 terms (when PFL at admission was < 4 mmol/L, an increase in PFL was associated with a 61.7-fold greater odds of having an SL).

In a study20 of serial measurements of BL in adult horses treated on an emergency basis, it was demonstrated that BL at admission (< 4.1 mmol/L) and an increase in BL over time had the strongest associations with non-survival for horses with strangulating disease of the large intestine and colitis. Conflicting information was found in another study,21 in which a statistical relationship between the presence of ischemic intestine and lactate concentrations could not be demonstrated for BL but was demonstrated for PFL. The results of the present study are consistent with the report by Delesalle et al,21 although the BL of horses in the SL group (mean, 3.3 mmol/L) was higher than that in the NSL group (mean, 2.6 mmol/L), the difference was not significant (P = 0.0673). In a study34 that used 8 pigs, segments of the small intestine were isolated by a vascular pedicle containing 1 artery and 1 vein so that intestinal ischemia could be created by occluding the mesenteric vasculature. It was demonstrated that PFL started to increase within 1 hour after occlusion, but systemic BL did not increase for the entire experiment (250 minutes).35 When looking at PFL and survival rate in the study reported here, horses in the SL group (10/26 [38%]) were significantly (P < 0.001; OR, 16) less likely to survive to discharge than were horses in the NSL group (62/68 [91%]). A previous study34 found that PFL is superior in its ability to predict the need for surgery or intestinal resection, probability of ileus development during hospitalization, and probability of death. It has been suggested that PFL, rather than BL, is more suitable and sensitive for early recognition of intestinal ischemia and concomitant prediction of outcome.21,35

Peritoneal fluid lactate concentration and BL have been compared previously as the PFL:BL ratio. In healthy horses, this ratio is always < 1 because BL is always higher than PFL in clinically normal horses at rest.10,21,26 Among horses with signs of colic in 1 study,26 this ratio was < 1.0 in 52 of 54 (96%) horses with simple obstructions. When this ratio has been used as an indication of the need for surgery, there was decreased need for surgical treatment of horses with a PFL:BL ratio < 1.0.36 The ability of the PFL:BL ratio to identify horses with SLs was evaluated.

Table 4—The positive interaction term from the final multivariable model for SLs in the same horses as in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>≤ 0</th>
<th>&gt; 0</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horses with PFL &lt; 4 mmol/L at admission (n = 81)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SL</td>
<td>1 (5)</td>
<td>18 (95)*</td>
<td>19 (23)</td>
</tr>
<tr>
<td>NSL</td>
<td>48 (77)</td>
<td>14 (23)</td>
<td>62 (77)</td>
</tr>
<tr>
<td>Total</td>
<td>49 (60)</td>
<td>32 (40)</td>
<td>81 (100)</td>
</tr>
<tr>
<td>Horses with PFL ≥ 4 mmol/L at admission (n = 13)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SL</td>
<td>5 (71)</td>
<td>2 (29)*</td>
<td>7 (54)</td>
</tr>
<tr>
<td>NSL</td>
<td>4 (67)</td>
<td>2 (33)</td>
<td>6 (46)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (69)</td>
<td>4 (31)</td>
<td>13 (100)</td>
</tr>
</tbody>
</table>

Data are No. (%) of horses. See Table 1 for remainder of key.
in the study reported here. When the ratio was > 1, the odds of horses having an SL (42%) was significantly (P = 0.0266; OR, 3.1) greater than for horses having an NSL (19%); however, this variable was not retained in the final multivariable model. In other studies, in which this ratio was evaluated as a predictor of survival rate in horses with signs of colic, all horses with a value < 1 survived. In another study, 47 of 54 (87%) horses with a PFL:BL ratio < 1.0 survived. In another report, it was suggested that the PFL:BL ratio had limited value because the ratio offered little additional information than when PFL and BL were evaluated individually.

Horses with colic can be categorized into 3 groups: those that need surgery, those that do not need surgery, and those for which, without further observation and monitoring of key clinical signs, the need for surgery is uncertain. In the study reported here, 94 horses underwent ≥ 2 abdominal fluid evaluations because the necessity of surgery could not be determined. Of the key clinical signs used to evaluate such horses, persistent signs of pain and the ability of analgesics to eliminate signs of pain are the variables that have the most influence on a surgeon’s decision to perform a celiotomy. It has been demonstrated that the severity of signs of abdominal pain is related to the severity of the conditions causing colic, and the ability of analgesics to eliminate abdominal pain has been used to determine the need for surgery. In that report, it was proposed that signs of pain alone are not a reliable indicator of the need for surgery in individual horses because 10 of 22 (45%) horses that had constant signs of pain after treatment with analgesia did not require surgery. The results of the present study also demonstrate that the presence of moderate to severe signs of pain was not significantly (P < 0.001; OR, 62) associated with the presence of an SL. When horses at admission had a PFL > 4 mmol/L (13/94 horses), an increase in PFL was not significantly associated with having an SL (Table 4). It is not clear why this occurred. The utility of an increase in lactate concentrations and a decrease in glucose concentration was evaluated at 30-minute intervals in 2 studies that isolated the small intestine on a vascular pedicle containing a single artery and vein. With the initiation of vascular occlusion recorded as time zero, lactate concentrations increased and glucose concentrations decreased until hour 2, after which further increases in lactate and decreases in glucose concentrations were not identified as new steady-state concentrations were reached. It is likely that because the supply of glucose to the pedicle was exhausted, so too was the ability to produce lactate. In the present study, 5 of 7 horses with SLs had a PFL > 4 mmol/L at initial evaluation but the PFL did not increase over time. It is plausible that the supply of glucose and hence the ability to produce lactate was also exhausted in these patients. Recognizing that horses with a PFL > 4 mmol/L have disease that has progressed beyond what is found in horses with a PFL < 4 mmol/L, it has been previously speculated that the timing at which abdominocentesis is performed during the colic episode is important.

Changes in PFL were evaluated every 1 to 2 hours in several horses in the present study for up to 6 evaluations during the first 24 hours (data not shown). In these same horses, evaluation of PFL was continued until the signs of colic resolved, an exploratory celiotomy was performed, or the horse was euthanized on the basis of financial constraints or a poor prognosis. The value of serial evaluations of PFL is supported by several reports. Fetal scalp BL during labor and delivery has been found to be a useful indicator of fetal distress due to lack of oxygen. Fetal scalp BL testing has been shown to be as predictive as fetal scalp pH testing, with the added benefits of requiring less blood, fewer scalp incisions, less time, and a lower sampling failure rate, compared with the pH testing.

In a recent study, 12 pigs had their entire small intestine divided into 3 segments, with each segment isolated by a vascular pedicle containing 1 artery and 1 vein. Three study groups of 10 control segments, 10 segments with arterial ischemia, and 9 segments with venous ischemia were provided for lactate and glucose concentration evaluation every 30 minutes via microdialysis. Ischemia caused a significant (P = 0.001) increase in lactate and decrease in glucose concentrations that was different with respect to surgery or necropsy, their lesions were classified as NSLs. It is plausible that a hemorrhagic strangulating obstruction was a possible explanation for increasing PFL identified in these 8 horses. True-negative results were identified in 48 of 62 (77%) horses and false-negative results were identified in 14 of 62 (23%) horses, which included these 8 horses (Table 4). Thus, the specificity for the test would have been higher if the study definition for SL included horses with a hemorrhagic strangulating obstruction.

The final multivariable model in the present study identified a positive interaction term. The positive association of an increase in PFL with presence of an SL depended on the initial PFL being < 4 mmol/L and was significantly (P < 0.001; OR, 62) associated with the presence of an SL. When horses at admission had a PFL > 4 mmol/L (13/94 horses), an increase in PFL was not significantly associated with having an SL (Table 4). It is not clear why this occurred. The utility of an increase in lactate concentrations and a decrease in glucose concentration was evaluated at 30-minute intervals in 2 studies that isolated the small intestine on a vascular pedicle containing a single artery and vein. With the initiation of vascular occlusion recorded as time zero, lactate concentrations increased and glucose concentrations decreased until hour 2, after which further increases in lactate and decreases in glucose concentrations were not identified as new steady-state concentrations were reached. It is likely that because the supply of glucose to the pedicle was exhausted, so too was the ability to produce lactate. In the present study, 5 of 7 horses with SLs had a PFL > 4 mmol/L at initial evaluation but the PFL did not increase over time. It is plausible that the supply of glucose and hence the ability to produce lactate was also exhausted in these patients. Recognizing that horses with a PFL > 4 mmol/L have disease that has progressed beyond what is found in horses with a PFL < 4 mmol/L, it has been previously speculated that the timing at which abdominocentesis is performed during the colic episode is important.

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to all groups at 1 hour, and the effect was even more pronounced 1.5 hours after the initiation of ischemia.45

Ileal impaction is a leading cause of NSLs in horses. These impactions are more commonly diagnosed in the southeastern United States and in horses fed coastal Bermuda grass hay, a fact that can be useful when generating a list of differential diagnoses.46 Differentiating an ileal impaction from an SL or anterior enteritis can be difficult and problematic, recognizing that an SL should be treated with an emergency celiotomy and an ileal impaction is initially treated medically with analgesics and IV fluids. It has been suggested that surgical treatment for ileal impactions should be pursued when horses are unresponsive to pain-reducing medications or that changes in the peritoneal fluid WBC count and total protein concentration suggest that the intestines are compromised.48 In the present study, signs of pain and serial changes in peritoneal fluid WBC count were not included in the best-fitting model following multivariable logistic regression. On the basis of the results of the present study, serial evaluation of PFL could be used to differentiate ileal impactions that remain as NSLs versus those that become hemorrhagic strangulating obstructions.49,50 When a rectal examination provides a definitive diagnosis of ileal impaction, serial evaluation of PFL would provide additional data to indicate whether these cases are likely to resolve with medical treatment.

In a multicenter, open-label, randomized controlled trial on 348 ICU patients, the objective for patients in the treatment group was to decrease lactate concentration by 20% every 2 hours for the initial 8 hours of ICU stay.51 In the control group, attending clinicians had no knowledge of lactate concentrations other than the value at admission. When adjusted for predefined risk factors, lactate-guided treatment significantly (P = 0.006) reduced hospital mortality rate in the treatment group, sequential organ failure assessment scores were lower, inotropes and mechanical ventilation were stopped earlier, and discharge from the ICU occurred earlier.52

An important limitation of the present study was that only a small fraction of horses with colic referred to our facility underwent 2 peritoneal fluid analyses. Because of this potential selection bias, it is unclear whether the specificity and, less likely, the sensitivity of the serial evaluation of PFL would have been different had all horses admitted to the clinic for colic and hospitalized for at least 6 hours been included. Moreover, the extent to which the findings of the present study can be generalized to other clinics or to geographic locations where ileal impactions are rare is unknown. Also, the duration of colic prior to initial evaluation was not known and was not included in analyses. Another limitation of the present study was that the timing for collection of the second peritoneal fluid was variable and occurred between 1 and 6 hours after admission. More consistent sampling or protocols for sampling might have resulted in different results.

Another limitation of the present study was that many of the factors examined were strongly correlated or coassociated. For example, PFL and BL were significantly correlated. Collinearity of variables could have impacted our multivariable modeling. To the authors’ knowledge, there is no satisfactory way to deal with this problem. In the present study, each of the variables selected in the final multivariable model was replaced by variables with which it was significantly correlated (data not shown); none of these iterations resulted in a model that increased the magnitude or significance of observed associations (indeed, the magnitude and significance were uniformly reduced for the substituted coassociated variables). For example, PFL was a stronger (ie, had a greater estimated OR) and more significant (ie, had a lower P value) predictor of being in the SL group and thus collinearity with serum lactate concentration was not an issue.

Public auction companies for Thoroughbreds require disclosure of the fact that any horse that has undergone abdominal surgery in the last 2 calendar years preceding the day of sale and disclosure of the fact that any horse that has had a resection of an abdominal organ (partial or complete) regardless of the day of surgery. Owners that sell Thoroughbreds at public auction are under financial pressure to avoid abdominal surgery because the resale value for these horses is substantially reduced. Anecdotally, equine surgeons that provide services to Thoroughbreds sold at these public auctions are frequently pressured to delay celiotomy until the necessity for surgery is absolute. Thus, a highly sensitive test or testing algorithm for the need for abdominal surgery is much needed.53 Although no such test exists, the ideal screening test would detect every case of ischemia (100% sensitivity) and do so without false-positive results (100% specificity). Monitoring for intestinal ischemia is a challenge because lesions are obstructed from view and neglected intestinal ischemia can become fatal because of its location, a situation that is not the case with bone or muscle ischemia.54 With these considerations in mind, it may be preferential to have a screening test for intestinal ischemia with a high sensitivity and an acceptable specificity.55 The results of...
the study reported here suggest that PFL determined at admission and an increase in PFL, especially among horses without a markedly high PFL at admission, move us closer to this single distinguishing test suggesting when the requirement for surgery is absolute; however, a multicenter, prospective study needs to be conducted to more completely identify the utility of PFL in determining the need for emergency surgery in horses with signs of colic evaluated at referral facilities.

References

43. Birke-Sorensen H, Andersen NT. Metabolic markers obtained


From this month’s AJVR

Effect of ketamine hydrochloride on the analgesic effects of tramadol hydrochloride in horses with signs of chronic laminitis-associated pain

Alonso G. P. Guedes et al

Objective—To investigate the effects of ketamine hydrochloride on the analgesic effects of tramadol hydrochloride in horses with signs of pain associated with naturally occurring chronic laminitis.

Animals—15 client-owned adult horses with chronic laminitis.

Procedures—Each horse received tramadol alone or tramadol and ketamine in a randomized, crossover study (≥ 2 months between treatments). Tramadol (5 mg/kg) was administered orally every 12 hours for 1 week. When appropriate, ketamine (0.6 mg/kg/h) was administered IV for 6 hours on each of the first 3 days of tramadol administration. Noninvasive systemic blood pressure values, heart and respiratory rates, intestinal sounds, forelimb load and off-loading frequency (determined via force plate system), and plasma tumor necrosis factor-α and thromboxane B₂ concentrations were assessed before (baseline), during (7 days), and after (3 days) each treatment.

Results—Compared with baseline data, arterial blood pressure decreased significantly both during and after tramadol-ketamine treatment but not during treatment with tramadol alone. Forelimb off-loading frequency significantly decreased during the first 3 days of treatment with tramadol only, returning to baseline frequency thereafter. The addition of ketamine to tramadol treatment reduced off-loading frequency both during and after treatment. Forelimb load did not change with tramadol alone but increased with tramadol-ketamine treatment. Plasma concentrations of tumor necrosis factor-α and thromboxane B₂ were significantly reduced with tramadol-ketamine treatment but not with tramadol alone.

Conclusions and Clinical Relevance—In horses with chronic laminitis, tramadol administration induced limited analgesia, but this effect was significantly enhanced by administration of subanesthetic doses of ketamine. (Am J Vet Res 2012;73:610–619)

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