Prevalence and prognostic importance of hypomagnesemia and hypocalcemia in horses that have colic surgery

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Objective—To determine the prevalence of hypomagnesemia and hypocalcemia in horses with surgical colic.

Animals—35 horses with surgically managed colic.

Procedure—Serum concentrations of total magnesium (tMg2+) and calcium (tCa2+), as well as ionized magnesium (iMg2+) and calcium (iCa2+) were analyzed before surgery and 1, 3, 5, and 7 days following surgery. A lead-II ECG and pertinent clinical data were also obtained at each time.

Results—Preoperative serum tMg2+ and iMg2+ concentrations were below the reference range in 6 (17%) and 19 (54%) horses, respectively. Serum concentrations of tCa2+ and iCa2+ were less than the reference range in 20 (57%) and 30 (86%) horses before surgery. Horses with strangulating lesions of the gastrointestinal tract had significantly lower preoperative serum concentrations of iMg2+ and iCa2+, as well as a higher heart rate than horses with nonstrangulating lesions. Horses that developed postoperative ileus had significantly lower serum concentrations of iMg2+ after surgery. Serum concentrations of magnesium and calcium (total and ionized) correlated significantly with the PR, QRS, QT, and corrected QT (QTc) intervals. Horses that were euthanatized at the time of surgery (n = 7) had significantly lower preoperative serum concentrations of iMg2+, compared with horses that survived. Neither serum magnesium nor calcium concentrations were predictors of hospitalization time or survival.

Conclusions and Clinical Relevance—Hypomagnesemia and hypocalcemia were common during the perioperative period, particularly in horses with strangulating intestinal lesions and ileus. Serum concentrations of tMg2+ and tCa2+ were less sensitive than iMg2+ and iCa2+ in detecting horses with hypomagnesemia and hypocalcemia. (Am J Vet Res 2001;62:7-12)

Alterations in serum magnesium and calcium concentrations have been investigated in humans and dogs.1-5 In studies of critically ill humans and dogs, >50% were found to be hypomagnesemic, with significantly higher morbidity and mortality rates than in magnesium-repleted patients.1-4 Hypocalcemia has also been described in horses with sepsis or severe trauma.6-8 Sodium and chloride electrolyte abnormalities have been documented in gastrointestinally compromised horses, but little information is published regarding serum magnesium and calcium concentrations.9,10

Magnesium and calcium are 2 of the most common elements in the body.1-5 Magnesium is an important cofactor in many biological functions, including the production and use of ATP, as a coenzyme for the sodium-potassium and calcium ATPase pumps, and for regulation of intracellular potassium balance.1,12,13 Calcium plays an important role in vascular and intestinal smooth muscle contraction, thereby affecting intestinal circulation and motility.1-17 Both cations are found in the extra-cellular fluid as ionized and nonionized forms, but for both, the free ionized fraction is considered to be the biologically active and regulated form.1,13

The measurement of total Mg2+ (tMg2+) and total Ca2+ (tCa2+) concentrations in critically ill humans are poor indicators of the ionized concentrations of these cations.1 Alterations in the acid-base balance and serum protein concentrations, seen commonly in critically ill patients, will cause inaccurate measurement of tMg2+ and tCa2+ concentrations, even when estimations are made on the basis of the patient’s blood pH and serum albumin concentration.7 Measurement of ionized Mg2+ (iMg2+) and ionized Ca2+ (iCa2+) provides the clinician a more accurate determination of the physiologically active magnesium and calcium concentrations in the serum.

Factors that can affect magnesium and calcium concentrations include inadequate intake, IV administration of fluids without magnesium and calcium supplementation, intestinal resection, ileus, endotoxemia, and sepsis.11-17 Therefore, horses with gastrointestinal tract disease that undergo exploratory laparotomy are at risk for developing magnesium and calcium deficiencies. In a study of 147 horses with surgically managed colic, iCa2+ concentration was below the laboratory’s reference range in all horses before and after surgery.1 Horses with strangulating lesions of the intestine had significantly lower iCa2+ concentrations than those with nonstrangulating obstructions.1 Magnesium concentrations, total or ionized, have not been evaluated in horses with colic.

The purpose of the study reported here was to determine the prevalence of hypomagnesemia and
hypocalcemia in horses with colic during the pre- and postoperative period, using serum total and ionized Mg$^{2+}$ and Ca$^{2+}$ concentrations. In addition, we hypothesized that these electrolyte abnormalities would be associated with electrocardiographic abnormalities and affect clinical outcome.

**Materials and Methods**

**Animals**—Adult horses (>1 year of age) that were admitted to the Tufts University School of Veterinary Medicine Large Animal Hospital because of signs of acute or chronic colic and that underwent exploratory celiotomy were enrolled in our study. The Tufts Institutional Animal Care and Use Committee approved the protocol design for the study, and horses entered into the study were done so with the owner's consent. Horses with known systemic diseases in addition to colic were excluded from the study.

**Experimental design**—Signalment, previous colic history, duration of current colic episode, treatments given by the referring veterinarian before referral, and physical examination findings at admission were recorded. Blood was collected by jugular venipuncture at admission and 1, 3, 5, and 7 days following surgery. The blood was centrifuged within 20 minutes of collection, and the serum was frozen at -70°C until analysis. A lead-II ECG was obtained at a paper speed of 25 mm/s at each time to measure heart rate (HR) and PR, QRS, and QT intervals. The QT interval was also corrected for HR (QTc), using the formula QTc = QT/ÖHR. Surgical lesion, surgical procedure(s), postoperative treatments, complications, time for the horse to return to a full diet, days of hospitalization, and survival were recorded. All horses were given potassium penicillin (22,000 U/kg of body weight, IV, q 6 h), gentamicin (8 mg/kg, IV, q 24 h), flunixin meglumine (0.25 to 1.1 mg/kg, IV, q 8 to 12 h), and magnesium-free polyionic fluids (lactated Ringer’s) supplemented with potassium chloride (20 mEq/L). At the request of the attending clinician, 12 horses received calcium borogluconate (500 ml in 10 L of lactated Ringer’s solution IV, once). All horses were offered small amounts of hay within 36 hours after surgery, unless contraindicated.

**Laboratory analyses**—Serum biochemical analyses, including tMg$^{2+}$ and tCa$^{2+}$, were performed, using an automated analyzer.$^7$ Serum samples were frozen and transported for off-site analyses of iCa$^{2+}$ and iMg$^{2+}$ concentrations, using an automated electrolyte analyzer.$^7$ The PCV and total solids were recorded at the time of collection of each blood sample. The serum of 7 healthy horses was analyzed for concentrations of iMg$^{2+}$ and iCa$^{2+}$, and a normal reference range was established, using the mean ± 2 SD.

**Statistical analyses**—The data were analyzed, using commercial statistical software.$^7$ The distribution of data were examined graphically. Data that were not normally distributed were transformed, using logarithmic transformation. Independent t-tests were performed on all continuous variables, and multiple variables were compared, using ANOVA tests. Multivariate linear regression analysis was used to test for confounding factors. Unless otherwise stated, all reported values are mean ± SD. Statistical significance was established as P < 0.05.

**Results**

Thirty-five horses were enrolled in the study over an 8-month period. There were 23 male (66%) and 12 female (34%) horses enrolled in the study. Mean age was 12.4 ± 6.0 years. Breeds represented included Thoroughbred (n = 13), Quarter Horse (9), Morgan (6), Warmblood (6), and American Saddlebred (1).

Of the 35 horses included in the study, 19 had lesions in the large colon, 12 in the small intestine, 2 in the cecum, and 2 in the small colon. Fifteen horses had strangulating lesions of either the small intestine or large colon. Seven horses were euthanatized in surgery...
because of the severity of the lesion. Surgical procedures performed on the horses that recovered from surgery (n = 28) included enterotomy on the antimesenteric border of the left ventral colon at the level of the pelvic flexure and evacuation of impacted feed material (15), repositioning of the large colon with no enterotomy (4), resection with anastomosis of the small intestine (3), manual decompression of the small intestine without resection (3), cecal bypass with a typhlotomy to treat a primary cecal impaction (2), and multiple procedures (1). Thirteen horses (46%) that recovered from surgery developed complications (diarrhea [n = 5], incisional infection [3], ileus [5] and pul-

Figure 2—Concentrations of total calcium (a) and ionized calcium (b) in serum (mg/dl) for each horse before surgery (day 0) and 1, 3, 5, and 7 days following surgery. The dashed lines indicate the upper and lower limits of reference range values.

Figure 3—Mean (± SEM) concentrations of ionized magnesium (a) and ionized calcium (b) in serum in horses with normal intestinal motility (open bars) compared with those with postoperative ileus (closed bars) before surgery (day 0) and 1, 3, 5, and 7 days following surgery. The dashed lines indicate the upper and lower limits of reference range values. * = P < 0.05.
monary edema [1]). One horse had 2 complications following surgery (diarrhea and incisional infection).

Preoperative (day 0) serum iMg2+ concentrations were below the reference range (1.1 to 2.2 mEq/L) in 6 horses (17%), with a gradual return to reference range values following surgery (only 2 horses had values that were still below the reference range on day 7; Fig 1). In contrast, serum iMg2+ concentrations were below the reference range (0.86 to 1.00 mEq/L) in 19 horses before surgery (54%). Only 3 horses had values that were below the reference range for iMg2+ by day 7. Twenty horses (57%) had serum iCa2+ concentrations below the reference range (10.8 to 13.5 mg/dl) before surgery (day 0; Fig 2). In contrast, serum iCa2+ concentrations were below the reference range (6.44 to 6.74 mg/dl) in 30 of the horses (86%) on day 0. Only 3 horses had serum iCa2+ concentrations below the reference range by day 7, whereas 10 horses still had concentrations of iCa2+ below the reference range by day 7.

Horses with strangulating lesions of the gastrointestinal tract had significantly lower preoperative serum concentrations of iMg2+ (0.77 ± 0.13 mEq/L), compared with horses that had nonstrangulating lesions (0.94 ± 0.19 mEq/L; P = 0.002). A similar finding was observed when the mean serum concentrations of iCa2+ on day 1 were compared in horses with strangulating (5.21 ± 0.74 mg/dl) versus nonstrangulating (5.89 ± 0.66 mg/dl; P = 0.009) lesions. Horses that were euthanatized during surgery (n = 7) had a significantly lower mean serum concentration of iMg2+ (0.71 ± 0.10 mEq/L) before surgery, compared with those that recovered from surgery (0.90 ± 0.18 mEq/L; P = 0.002). Five horses developed postoperative ileus (defined by at least 24 hours of enterogastric reflux). Horses with ileus had significantly lower serum concentrations of iMg2+ at day 3 (P = 0.005), day 5 (P = 0.026), and day 7 (P < 0.001) than horses that did not develop ileus (Fig 3). Serum concentrations of iCa2+ were significantly lower in horses with postoperative ileus only on day 3 (6.38 ± 0.08 mg/dl), compared with those without ileus (6.79 ± 0.59 mg/dl; P = 0.004).

One horse had an arrhythmia before surgery (sinus arrhythmia with premature atrial depolarizations), and 2 others developed arrhythmias following surgery (1 had atrial fibrillation and the other the atrial premature depolarizations). There was a significant correlation between serum magnesium concentrations (total and ionized) and the HR, as well as the PR, QRS, QT, and QTc intervals (Table 1). Similar correlations were observed with tCa2+ and iCa2+, although there was no correlation between the QTc and tCa2+ or iCa2+ or between the PR interval and tCa2+. Horses with strangulating lesions of the intestine had significantly shorter PR (P < 0.001), QRS (P = 0.03), and QTc (P = 0.02) intervals, compared with horses without strangulating lesions.

Horses that developed a complication after surgery had a higher preoperative HR (58.7 ± 16.7 beats/min), compared with those without complications (43.4 ± 11.2 beats/min; P = 0.01). The HR in horses with complications remained significantly higher than in those without complications for the first 72 hours after surgery (P < 0.05). There was no significant difference in HR between groups thereafter. Horses with strangulating lesions of the intestine had a significantly higher HR (70.3 ± 25.4 beats/min) before surgery compared with horses with nonstrangulating lesions (44.7 ± 11.8 beats/min; P < 0.002).

Neither total nor ionized Mg2+ or Ca2+ concentrations in serum were predictors of hospitalization time, complications, or survival in our study. Length of time before performing surgery, surgery time, volume of fluids administered IV, PCV, and total solids concentration did not correlate with serum concentrations of iMg2+ and iCa2+. The addition of calcium borogluconate to the fluids did not significantly alter serum concentrations of tCa2+ or iCa2+ in the 7 horses in which it was administered.

### Discussion

In our study, hypomagnesemia and hypocalcemia were common findings during the peri-operative period. These changes are similar to those found in critically ill humans and dogs.1,14,9 Serum concentrations of iMg2+ and iCa2+ were more sensitive than concentrations of tMg2+ and tCa2+ in detecting horses with disturbances of magnesium and calcium status. Only 17% of horses had serum concentrations of tMg2+ below the reference range at the time of admission, whereas 54% were below the reference range for iMg2+ concentration. A similar discrepancy was observed when comparing the serum concentrations of tCa2+ and iCa2+ at the time of admission (57 and 86%, respectively). These differences may be attributed to alterations in the serum protein concentrations, in particular albumin and globulin, and metabolic acidosis. Although pH was not measured in our study, metabolic acidosis would be the most likely acid-base alteration in horses with colic. Metabolic acidosis will decrease the protein binding of magnesium and calcium.

### Table 1—Correlation between concentrations of total and ionized magnesium and calcium with heart rate, PR, QRS, and QT intervals, and the QT corrected for heart rate (QTc)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Heart Rate</th>
<th>PR</th>
<th>QRS</th>
<th>QT</th>
<th>QTc</th>
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<tbody>
<tr>
<td>Total magnesium</td>
<td>r = -0.47</td>
<td>r = 0.27</td>
<td>r = 0.26</td>
<td>r = 0.22</td>
<td>r = -0.25</td>
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<tr>
<td>(mEq/L)</td>
<td>P &lt; 0.001</td>
<td>P = 0.002</td>
<td>P = 0.002</td>
<td>P = 0.01</td>
<td>P = 0.004</td>
</tr>
<tr>
<td>Ionized magnesium</td>
<td>r = -0.54</td>
<td>r = 0.38</td>
<td>r = 0.36</td>
<td>r = 0.17</td>
<td>r = -0.35</td>
</tr>
<tr>
<td>(mEq/L)</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P = 0.04</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>Total calcium</td>
<td>r = -0.52</td>
<td>r = 0.14</td>
<td>r = 0.26</td>
<td>r = -0.05</td>
<td>r = -0.54</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>P &lt; 0.001</td>
<td>P = 0.13</td>
<td>P = 0.003</td>
<td>P = 0.61</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>Ionized calcium</td>
<td>r = -0.46</td>
<td>r = 0.25</td>
<td>r = 0.25</td>
<td>r = -0.07</td>
<td>r = -0.51</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>P &lt; 0.001</td>
<td>P = 0.004</td>
<td>P = 0.003</td>
<td>P = 0.41</td>
<td>P = 0.00</td>
</tr>
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</table>

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ly successful. Measurement of the ionized form, which is less affected by pH and protein concentrations, is a more accurate indicator of the concentrations of these cations in the systemic circulation.

Serum concentrations of ionized magnesium were significantly lower in horses with ileus in the postoperative period (days 3 to 7), compared with horses with clinically normal intestinal motility. Similar findings were observed for serum concentrations of iCa2+ after surgery (day 3) in horses with ileus. Multiple factors, including anorexia, diarrhea, prolonged IV administration of magnesium- and calcium-free fluids, endotoxemia, intestinal resection, and ileus have been associated with low magnesium and calcium concentrations in humans and dogs. These same factors are common to horses after surgery for colic, predisposing them to low serum concentrations of magnesium and calcium. Conditions such as adynamic ileus and gastric reflux can further exacerbate the depletion of the cations by prolonged inappetence and requiring prolonged fluid therapy, which may not be adequately supplemented with magnesium or calcium. In addition, hypomagnesemia and hypocalcemia may contribute to ileus because of their critical role in smooth muscle contraction.

Other complications encountered following surgery in our study (diarrhea, incisional infection, and pulmonary edema) did not appear to be significantly related to serum concentrations of magnesium and calcium. If horses euthanatized at surgery (n = 7) were grouped with surviving horses developing complications, iMg2+ (P = 0.016) and iMg2+ (P = 0.027) concentrations would be significantly lower before surgery in horses that developed complications than in those that did not. Because of the significant difference in preoperative serum iMg2+ and iCa2+ concentrations between horses with strangulating lesions of the intestine and those without, we examined whether low concentrations of these cations could potentially serve as predictors for such lesions. The predictive value of preoperative serum iMg2+ and iCa2+ concentrations for identifying horses with or without strangulating lesions of the intestine, however, had an accuracy of only 46 to 69%. Therefore, neither iMg2+ nor iCa2+ concentrations in serum were useful for predicting strangulating lesions before surgery in our study.

The differences in the serum concentrations of magnesium and calcium observed in horses that had strangulating lesions of the intestine or were euthanatized (all of which had strangulating lesions) and those without strangulating lesions could potentially serve as predictors for such lesions. The predictive value of preoperative serum iMg2+ and iCa2+ concentrations for identifying horses with or without strangulating lesions of the intestine, however, had an accuracy of only 46 to 69%. Therefore, neither iMg2+ nor iCa2+ concentrations in serum were useful for predicting strangulating lesions before surgery in our study.

The horses with strangulating lesions of the intestine and those that developed complications after surgery had a significantly higher HR than those that did not have a strangulating lesion or postoperative complication. Endotoxemia, incisional infection, and signs of pain secondary to gastrointestinal tract ileus can elevate the HR. Horses with strangulating lesions also had significantly shorter PR, QRS, and QTc intervals than those without strangulating lesions. Although there were significant correlations between serum concentrations of magnesium and HR, PR, QRS, QT, and QTc intervals, it was difficult to assess their importance in our study, because there were only a few horses with arrhythmias (n = 3). Magnesium supplementation has been successfully used to treat humans and dogs with ventricular tachycardia (torsade de pointes) and associated prolonged QT intervals and those with myocardial ischemia. The electrocardiographic changes observed in humans and dogs with hypomagnesemia and hypocalcemia include prolongation of the PR and QT intervals and a widening of the QRS complex, in addition to various arrhythmias. In our study, there was a positive correlation between serum concentrations of magnesium and the PR, QRS, and QT intervals. To assess whether this correlation was real or an artifact resulting from the higher preoperative HR when magnesium concentrations were low, the QT interval was corrected for the HR. The QTc was negatively correlated with iMg2+ and iMg2+, which is similar to what has been described for other species.

The low frequency of arrhythmias observed in our study indicate that although low serum concentrations of magnesium and calcium were measured, they did not potentiate a disturbance in the cardiac cycle that could lead to an arrhythmia. Although this may suggest that horses have a higher threshold for developing arrhythmias in the face of low serum concentrations of magnesium and calcium, it also may be attributable to the small number of horses that were included in our study. In addition, further diagnostic modalities, including echocardiography, are needed together with ECG analysis to better assess cardiac function in the presence of low cation concentrations. Our study provided inadequate statistical power to detect a difference in serum concentrations of magnesium and calcium between horses with and without arrhythmias.

Early recognition and correction of magnesium and calcium deficiencies may help to reduce morbidity and mortality in horses with colic. Although intestinal motility was not specifically measured in our study, the role of magnesium and calcium in intestinal motility suggests that deficiencies could contribute to ileus. This was supported by lower serum concentrations of magnesium and calcium in horses with postoperative ileus. Therefore, supplementation of both cations may restore normal intestinal motility sooner. Correction of magnesium deficiencies alone may also, by itself, help to restore normal serum concentration of calcium by acting on the calcium ATPase pump.

On the basis of the results of our study, empirical magnesium and calcium supplementation is recommended for the perioperative treatment of horses with colic. To date there are no guidelines, to our knowledge,
for magnesium replacement therapy in horses. Further studies of the potential benefits of magnesium and calcium supplementation and optimal administration guidelines for horses with colic are warranted.

References


