Tutorial Article

Electrolyte disorders in horses with colic. Part 2: calcium, sodium, chloride and phosphate

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Introduction

In the first part of this article (Borer and Corley 2006), we covered potassium and magnesium. In this second part, we turn our attention to calcium, sodium, chloride and phosphate. Table 1 gives the normal ranges utilised for these electrolytes at the authors’ hospital.

Calcium

Calcium abnormalities are common in horses with colic (Dart et al. 1992; Garcia-Lopez et al. 2001). Calcium is involved in excitation and contraction of cardiac muscle and the maintenance of vascular tone. It is a positive inotrope, causing an increase in smooth muscle contractility (Gasthuys et al. 1991; Grubb et al. 1996; Garcia-Lopez et al. 2001). It also has important effects on the action potential, which is shortened with hypercalcaemia and prolonged with hypocalcaemia (Atkins 1999). Other functions of calcium in the body include neuromuscular transmission, enzyme and hormone production and coagulation (Grubb et al. 1996). It is also involved in cell messaging and receptor coupling (Zaloga et al. 1992).

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Calcium is primarily extracellular, with 99% being found in bones and teeth (Dart et al. 1992). Only 1% is found in the extracellular fluid, of which roughly half is protein bound, and approximately 47% ionised in the plasma (Dart et al. 1992). Many commonly used analysers measure total plasma calcium, which may not be related to ionised calcium, the biologically active form (Garcia-Lopez et al. 2001). Acid-base alterations will affect the protein binding of calcium; with acidosis increasing ionised calcium as it is displaced from protein bound sites by hydrogen ions (Cooper et al. 1992; Dart et al. 1992; Garcia-Lopez et al. 2001).

Hypocalcaemia

There is a very high prevalence (66%) of hypocalcaemia in post operative colic patients, which is significantly different from the prevalence (17%) in horses undergoing elective surgery (Protopapas 2000). Calcium is heavily bound to albumin in the plasma, so hypoalbuminaemia may artefactually decrease serum total calcium concentrations. Volatile anaesthetics are also associated with a fall in plasma calcium concentrations (Dart et al. 1992; Grubb et al. 1999). Agents such as halothane and isoflurane inhibit the flow of calcium through ion channels in the myocardium and alter calcium balance in the sarcoplasmic reticulum (Gasthuys et al. 1991; Grubb et al. 1999). Endotoxaemia, sepsis and diarrhoea also result in low serum calcium concentrations (Dart et al. 1992; Grubb et al. 1996). High plasma lactate concentrations are associated with low ionised calcium in patients in shock, and it is possible that lactate may chelate the calcium ions (Cooper et al. 1992).

Signs of hypocalcaemia are often nonspecific and include muscle weakness or fasciculations, tetany (Atkins 1999), synchronous diaphragmatic flutter, ileus and convulsions (Grubb et al. 1996). Sweating, tachycardia and tachypnoea are also reported. In horses following colic surgery, decreasing ionised calcium concentrations were correlated with the following changes on the electrocardiogram: increased heart rate, increased QT interval (corrected for heart rate), decreased PR interval, and decreased QRS interval (Fig 1: Atkins 1999; Garcia-Lopez et al. 2001) although other arrhythmias

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Normal range (mmol/l)</th>
<th>Treat if falls below (mmol/l)</th>
<th>Treat if rises above (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (ionised)</td>
<td>1.40–1.79</td>
<td>0.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Sodium</td>
<td>132–146</td>
<td>128</td>
<td>155</td>
</tr>
<tr>
<td>Chloride</td>
<td>99–109</td>
<td>95</td>
<td>120</td>
</tr>
<tr>
<td>Phosphate</td>
<td>0.52–1.2</td>
<td>0.30</td>
<td>not known</td>
</tr>
</tbody>
</table>

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including atrioventricular block, ventricular tachycardia and premature depolarisations may also occur in horses (Glazier et al. 1979). Experimentally induced hypocalcaemia (<0.83 mmol/l) induced cardiac arrhythmias in 4 out of 7 ponies, which were fatal in 2 (Glazier et al. 1979). Hypocalcaemia has been implicated in the development of post anaesthetic myopathy, due to reduced myocardial contractility and tissue blood flow (Grubb et al. 1999).

Hypocalcaemia is associated with heart failure and reduced cardiac output in man, due to reduced myocardial contractility (Atkins 1999). Lang et al. (1988) showed that left ventricular contractility was directly related to calcium concentration in man. Increasing plasma calcium concentrations resulted in reduced afterload, increased fractional shortening and increased aortic systolic pressure, associated with improved cardiac performance (Lang et al. 1988). No change in heart rate was noted in this study. Studies in horses have shown a fall in heart rate associated with calcium supplementation (Gasthuys et al. 1991; Grubb et al. 1996, 1999). Gasthuys et al. (1991) hypothesised that this was due to vagal stimulation, but it may also be a reflex response to the higher arterial pressure achieved after calcium administration (Grubb et al. 1999).

There are conflicting results on other haemodynamic variables in response to calcium administration. Gasthuys et al. (1991) found an increase in stroke volume but no change in cardiac output. These authors also noted an increase in systemic vascular resistance and mean arterial blood pressure, associated with vasoconstriction. Grubb et al. (1996) reported an increase in stroke volume and cardiac output with no change in systemic vascular resistance or arterial pressures in conscious horses (Grubb et al. 1999). The difference in results obtained by the above studies may reflect differences in the formulation of calcium given (calcium chloride or gluconate), or different doses. A generalised increase in systemic vascular resistance and vasoconstriction due to calcium may be offset by regional vasodilation, preserving blood flow to vital areas (Grubb et al. 1996).

Experiments in laboratory rats have shown that even relatively low doses of intravenous calcium increase mortality in endotoxaemia (Malcolm et al. 1989; Zaloga et al. 1992). Rats with increased ionised calcium concentrations, 24 h after endotoxin administration, had a mortality rate of 80%, compared to 20% in normocalcaemic rats. This difference in mortality occurred despite an increased mean arterial blood pressure in rats with higher ionised calcium concentrations. Zaloga et al. (1992) found only 44% survival in rats treated with calcium after endotoxaemia was induced by caecal ligation. Higher plasma calcium concentrations were associated with increased concentrations of endotoxin in the plasma. It was hypothesised that calcium might increase translocation of endotoxin across the intestinal wall, or reduce clearance of endotoxin from the body (Zaloga et al. 1992). The relevance of these findings to the horse is, as yet, unknown.

**Hypercalcaemia**

Hypercalcaemia is uncommon in horses following colic surgery. Protopapas (2000) reported a prevalence of 0% in post operative colic patients, and the condition usually occurs in horses with chronic renal failure or neoplasia. It can cause muscle weakness, depression and seizures due to elevated CSF calcium concentrations (Grubb et al. 1996). Hypercalcaemia causes a shortened Q-T interval and S-T depression (Fig 1). Intracardiac conduction may be slowed, resulting in atrio-ventricular block (Atkins 1999), but tachycardia may also occur (Reef 1999). Experimentally induced hypercalcaemia in ponies resulted in ventricular fibrillation or cardiac arrest at ionised calcium concentrations of 4.55–10.0 mmol/l (Glazier et al. 1979).

**Sodium**

Sodium is one of the major extracellular cations and is functionally impermeable, being unable to cross cell
membranes (Adrogué and Madias 2000a). It is a major contributor to plasma tonicity and osmolality, inducing movement of water across cell membranes. Disruptions in water homeostasis result in abnormalities of serum sodium (Adrogué and Madias 2000a).

**Hyponatraemia**

The prevalence of hyponatraemia in post operative colic patients is 30% (Protopapas 2000). Both sodium loss and water gain can result in hyponatraemia. One cause of water gain is excessive secretion of antidiuretic hormone, which can occur post operatively or due to pain (Schaer 1999). Disorders resulting in hyponatraemia include diarrhoea, renal failure, urinary bladder rupture, severe blood loss, diuretic administration (for example mannitol) and overloading with water (Ayus et al. 1982; Lakritz et al. 1992; Adrogué and Madias 2000b). Repeated nasogastric administration of plain water, instead of a salt solution, for relief of a large colon impaction can result in a marked hyponatraemia (Lopes 2003). Sequestration of fluid in a ‘third space’, as occurs with intestinal obstruction or peritonitis may also result in hyponatraemia (Adrogué and Madias 2000b). Mortality associated with severe hyponatraemia in man is extremely high and can reach 50% (Ayus et al. 1982).

Clinical signs of hyponatraemia include neurological signs such as decreased mentation, seizures, weakness, lethargy, hypotension and tachycardia (Ayus et al. 1982; Schaer 1999). Brain oedema and subsequent cerebral hypoxia have also been reported (Lakritz et al. 1992; Adrogué and Madias 2000b).

**Hypernatraemia**

Hypernatraemia is reported to occur in 12% of post operative colic patients (Protopapas 2000). It results in hypertonicity, hyperosmolality and cellular dehydration (Adrogué and Madias 2000a). Hypernatraemia usually occurs due to water loss, but may result from a net gain of sodium (Schaer 1999; Adrogué and Madias 2000a). Diarrhoea, drainage of gastric reflux, renal failure and diuresis can all cause hypernatraemia. Prolonged water restriction or excess administration of salt or sodium bicarbonate may also result in iatrogenic hypernatraemia (Schaer 1999; Adrogué and Madias 2000a).

Hypernatraemia results in central nervous system dysfunction. The severity of the signs depends mainly on the magnitude and rapidity of the increase in sodium concentration (Adrogué and Madias 2000a). Hyperpnoea, muscle weakness and lethargy are commonly seen. Convulsions usually only occur in adult humans when a large sodium load is administered (Adrogué and Madias 2000a). Hypovolaemia may be present resulting in hypotension and tachycardia. Most seriously, brain shrinkage occurs in response to hypernatraemia. This can result in cerebral haemorrhage and permanent neurological damage (Adrogué and Madias 2000a).

**Chloride**

Chloride ions are important in maintaining acid-base balance, renal tubular function and production of gastric acid (Maloney et al. 2002). Chloride is the major anion in the extracellular fluid (de Morais 1993). High concentrations of chloride are found in gastric acid and small intestinal secretions and it is normally absorbed from the upper small intestine (de Morais 1993). Large quantities of chloride can be lost via intestinal secretions in patients with diarrhoea (Maloney et al. 2002). In the kidney, its reabsorption is heavily influenced by both plasma sodium concentration and acid-base balance. Both active and passive chloride transport mechanisms contribute to its reabsorption (de Morais 1993). Renal reabsorption of chloride is affected by a number of hormones including parathyroid hormone, calcitonin, anti-diuretic hormone and angiotensin II (de Morais 1993).

Chloride ion concentration is dependent on whole body water balance. Therefore, plasma chloride concentrations must be interpreted relative to plasma sodium ion concentrations (de Morais 1993; Corley and Marr 1998). The presence of lipaemia can cause artefactual changes in the chloride concentration measured by the analyser, depending on the method of analysis used (de Morais 1993).

**Hypochloraemia**

Hypochloraemia can occur in horses that are losing large amounts of gastric fluid in reflux, and the condition has a reported prevalence of 12% in post operative colic patients (Protopapas 2000). Gastric reflux is rich in hydrogen and chloride ions, and the resultant hypochloraemia is usually accompanied by a metabolic alkalosis (de Morais 1993; Schaer 1999). Administration of diuretics, sodium penicillin or bicarbonate containing fluids can also result in hypochloraemia (de Morais 1993). Concurrent hypokalaemia may occur, due to intracellular shift of potassium ions in an attempt to correct the acid-base disturbance.

**Hyperchloraemia**

There is a high prevalence (54%) of hyperchloraemia in post operative colic patients (Protopapas 2000). Hyperchloraemia can occur due to loss of water in excess of electrolytes, in which case it occurs in concert with hypernatraemia. Hyperchloraemia may also result from metabolic compensation for respiratory alkalosis, renal tubular acidosis and due to loss of water and sodium in diarrhoea (de Morais 1993; Corley and Marr 1998). Administration of 0.9 or 7.2% sodium chloride solutions can also result in hyperchloraemia, with increases in chloride concentration often exceeding those in sodium concentration (Corley 2004). Long-term administration of parenteral nutrition solutions may also result in hyperchloraemia (de Morais 1993). Hyperchloraemia contributes to a metabolic acidosis (Corley and Marr 1998). Potassium metabolism may also be affected, resulting in hypokalaemia or hyperkalaemia.
Phosphate

The majority of phosphorus in the body is found in bone, with only 1% in blood (Bugg and Jones 1998). Phosphate (inorganic phosphorus) is the most abundant intracellular anion (Maloney et al. 2002). Phosphate homeostasis is controlled by parathyroid hormone, calcitonin and vitamin D, involving the intestine, kidneys and bone. Absorption of phosphate from the intestine is affected by calcium, which binds to intraluminal phosphate to form insoluble complexes, thereby reducing bioavailability of both ions (Bugg and Jones 1998). Phosphate in the body is important as an enzyme cofactor, a buffer and in the production of adenosine triphosphate (ATP) for energy. It is an important part of proteins and lipids, and is also essential for normal functioning of the coagulation cascade and the immune system (Maloney et al. 2002).

Hypophosphataemia

The prevalence of hypophosphataemia in post operative colic patients is 44% (Protopapas 2000). It is reported as a poor prognostic indicator in man (Maloney et al. 2002). However, as phosphate is primarily intracellular, hypophosphataemia is not necessarily indicative of total body depletion. Muscle phosphate concentration may provide a more accurate measure of chronic phosphate depletion.

One of the commonest causes of hypophosphataemia is inadequate intake during starvation. Parenteral nutritional products may also be deficient in phosphorus (Bugg and Jones 1998). Extensive bowel resection can result in hypophosphataemia, because the distal small intestine is a major site of phosphate absorption in the horse (Schryver et al. 1970). Phosphate absorption may also be reduced by binding to aluminium and magnesium compounds in the intestine. Long term use of sucralfate (containing aluminium) and many antacids have been associated with hypophosphataemia (Bugg and Jones 1998). Intracellular shifts of phosphate can occur, leading to hypophosphataemia with no change in total body phosphate. Factors associated with intracellular shifts of phosphate include increases in circulating catecholamine and glucose concentrations, and alkalosis, all of which can occur in critical illness (Bugg and Jones 1998; Maloney et al. 2002). Glucocorticoids may increase renal phosphate loss and hypocalcaemia and hypomagnesaemia also predispose to hypophosphataemia (Bugg and Jones 1998).

Hypophosphataemia can result in respiratory muscle dysfunction, due to a lack of substrate for energy production, and, in man, an improvement in diaphragmatic function has been reported following phosphate therapy (Bugg and Jones 1998). An increased incidence of ventricular dysrhythmias and myocardial dysfunction has been associated with hypophosphataemia in man (Maloney et al. 2002). Neuropathies and myopathies are also reported (Bugg and Jones 1998). Red cell fragility and reduced leucocyte function may occur with hypophosphataemia (Bugg and Jones 1998; Maloney et al. 2002).

Phosphorus replacement therapy can result in problems itself, associated with iatrogenic hyperphosphataemia and hypocalcaemia. Many preparations are formulated with potassium, and over-zealous replacement may lead to hyperkalaemia (Bugg and Jones 1998).

Hyperphosphataemia

The prevalence of hyperphosphataemia in horses following colic surgery is 12% (Protopapas 2000). Large quantities of phosphate are found in intestinal tissue. Ischaemic damage to the intestinal wall leads to leakage of phosphate into both the intestinal lumen and peritoneal fluid, which occurs at an early point after onset of intestinal ischaemia. The phosphate in the peritoneal space may reach the systemic circulation via the portal system and lymphatics (Arden and Stick 1988). Supporting this, the correlation between serum and peritoneal fluid phosphate concentrations was high in horses with colic (Arden and Stick 1988). Furthermore, phosphate concentrations in peritoneal fluid and serum have been used as indicators of the need for resection of ischaemic bowel (Arden and Stick 1988). Increased phosphate concentrations were found in horses that required extensive intestinal resection, compared to those with medical colic or lesions that did not require resection. In experimental rats, endotoxin administration results in increased renal excretion of phosphate (Mimura et al. 1997). If this is also true in horses, this may, to some degree, counteract the increased phosphate seen with intestinal injury. Foals have higher phosphate concentrations than adult horses due to rapid bone growth, and peritoneal fluid and serum concentrations are not diagnostic in these animals.

Signs of hyperphosphataemia are usually nonspecific and can include arrhythmias, hypotension and renal failure. Abnormalities in calcium balance can occur, resulting in hypocalcaemia or, when chronic, ectopic calcification (Maloney et al. 2002). Hyperphosphataemia is usually well tolerated by the patient. Treatment is aimed at the underlying cause, but antacids that bind phosphate in the intestinal tract may be useful to decrease absorption (Maloney et al. 2002). Fluid therapy and diuretics increase renal excretion of phosphate, whilst administration of dextrose will cause an intracellular shift of phosphate.

Prevention and treatment

The main principles of electrolyte administration have been discussed in part 1 (Borer and Corley 2006).

Hypocalcaemia

Doses recommended for treatment of hypocalcaemia vary. Atkins (1999) used 10% calcium gluconate given at 1–1.5 mg/kg bwt intravenously over 10–20 min. Grubb et al. (1996, 1999) used an infusion of 0.1–0.4 mg/kg bwt/min calcium gluconate. Reef (1999) also recommends a dose of 0.4 mg/kg bwt/min of calcium gluconate, whereas Gasthuys et al. (1991) reported the use of calcium chloride at a dose of
TABLE 2: Replacement guidelines

<table>
<thead>
<tr>
<th>Measured value</th>
<th>Amount to add to 5 l bag of balanced electrolyte solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypocalcaemia</td>
<td>Ca gluconate 40% 0.1–0.5 ml/kg bwt over 2–3 h</td>
</tr>
<tr>
<td>Hypercalcaemia</td>
<td>Mg sulphate 4–16mg/kg bwt</td>
</tr>
<tr>
<td>Hypophosphataemia</td>
<td>0.25–1.0 mmol/kg bwt over 12 hours</td>
</tr>
</tbody>
</table>

0.1–0.3 mg/kg bwt/min. Once calcium treatment is discontinued, the effects wane rapidly, therefore a constant infusion is recommended to maintain plasma concentrations (Grubb et al. 1999). Care should be taken to dilute the solution before administration to avoid irritation of the veins. Calcium should also not be mixed with bicarbonate solutions or whole blood. Recommendations based on experience at the authors’ hospital are given in Table 2.

**Hypercalcaemia**

Treatment of hypercalcaemia includes fluid therapy with sodium chloride, magnesium, glucocorticoids (prednisolone 1–1.5 mg/kg bwt per os b.i.d.) and frusemide (2–4 mg/kg bwt per os b.i.d.) (Table 2; Atkins 1999).

**Hyponatraemia**

In hypovolaemic patients, treatment should be aimed at restoring intravascular volume using 0.9% saline (Adrogué and Madias 2000b). Hypertonic saline has also been given as a bolus to correct severe hyponatraemia (Ayus et al. 1982; Lakritz et al. 1992). Diuretics such as frusemide are used in normovolaemic or hypervolaemic patients to avoid volume overload (Ayus et al. 1982; Adrogué and Madias 2000b).

The rate at which sodium concentration in the plasma should be changed is controversial. Schaer (1999) recommends a slow rate of change to avoid neurological complications, such as central pontine myelinolysis, associated with rapidly increasing plasma sodium concentrations and shrinkage of the brain (Adrogué and Madias 2000b). These authors recommend correction rates of 0.5–1 mEq/l/h, not to exceed a total of 8 mEq/l in the first 24 h (Schaer 1999; Adrogué and Madias 2000b). Conversely, Ayus et al. (1982) reported a case series of 7 human patients where the sodium deficit was corrected in less than 24 h at an average rate of 2.4 mEq/l/h. The sodium concentration was raised an average 29 mEq/l in this time (Ayus et al. 1982). No neurological complications were observed in these patients, and these authors hypothesised that the neurological sequelae noted in other studies, when sodium deficit was corrected over more than 24 h, was due to prolonged exposure of the central nervous system to hyponatraemia, resulting in injury (Ayus et al. 1982).

**Hypernatraemia**

Low solute fluids should be given to correct the water deficit. Suitable fluids include 5% dextrose solution, 0.45% sodium chloride/2.5% dextrose solution and maintenance fluid formulas, such as Plasmalyte-M1. The deficit should be corrected slowly to prevent CNS problems such as cerebral oedema and convulsions, ideally lowering the plasma sodium concentration by 0.5 mEq/l/h, with a maximum decrease of 12 mEq/l over the first 24 h (Schaer 1999; Adrogué and Madias 2000a).

**Conclusion**

There is a high prevalence of electrolyte abnormalities in horses with colic. However, restoring electrolyte concentrations to the range found in normal animals is not always appropriate, and the side-effects of exogenously administered electrolytes must be taken into consideration in any supplementation plan. Administering electrolytes at a standard rate and frequently re-measuring the plasma concentration is preferable to calculation of a theoretical deficit, and supplementation without frequent monitoring.

Marked increases or decreases in plasma electrolyte concentrations can have profound effects on normal physiological functions, which may result in increased morbidity and mortality in horses with colic.

**Manufacturer’s address**

1Baxter, Deerfield, Illinois, USA.

**References**


