ADVANCES IN ORAL AND INTRAVENOUS FLUID THERAPY OF CALVES WITH GASTROINTESTINAL DISEASE

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1. INTRODUCTION

Diarrhea, ruminal acidosis (ruminal drinkers) and the acidosis without dehydration syndrome are the major causes of morbidity and mortality in neonatal calves. Acidemia, often due to D-lactic acidosis, is an important part of all these conditions. This paper reviews the importance of D-lactic acid to the development of clinical signs and describes the use of therapy to treat these syndromes.

Before discussing the current state of fluid therapy it is appropriate to recognize how advances in fluid therapy have improved the outcome for calves. Over the past 30 years a number of surveys have determined the prevalence of morbidity and mortality from diarrhea in neonatal calves in the western Canada. These surveys used slightly different methodology so they are not strictly comparable. However, they document a marked and systematic reduction in the prevalence of neonatal diarrhea in calves and an improvement in case fatality rates, Table I. Improvements in oral and intravenous (IV) therapy are likely partly responsible for the reduction in mortality rates.

Table I. Morbidity and mortality rates for calf diarrhea in Saskatchewan and Alberta at selected time points

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Source</th>
<th>Morbidity</th>
<th>Case fatality rate</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1973-1975</td>
<td>Saskatchewan, Alberta</td>
<td>Random sample of farmers belonging to stock-growers association</td>
<td>17%</td>
<td>9%</td>
<td>Acres, 1976</td>
</tr>
<tr>
<td>1975</td>
<td>Saskatchewan</td>
<td>Random sample based on Agriculture Canada census Provincial survey</td>
<td>22%</td>
<td>14%</td>
<td>Church, 1978</td>
</tr>
<tr>
<td>1988</td>
<td>Alberta</td>
<td>Random sample of farms with a relationship with a veterinary practice, Provincial survey</td>
<td>11%</td>
<td>7%</td>
<td>Naylor et al. 1990</td>
</tr>
<tr>
<td>2004</td>
<td>Alberta</td>
<td>Random sample of farms Provincial survey</td>
<td>6%</td>
<td>7%</td>
<td>Waldner, 2005</td>
</tr>
</tbody>
</table>
2. **CAUSES OF MORBIDITY AND MORTALITY IN NEONATAL GASTRO-INTESTINAL DISEASE**

Calves with gastrointestinal disorders can show systemic signs of central nervous system (CNS) depression, weakness, and reduced food intake. These systemic signs are referred to collectively in this paper as malaise and may result from dehydration, acidemia, endotoxemia or sepsis. More recently, D-lactic acidemia has been detected in diarrheic calves, in ruminal acidosis and in acidosis without dehydration syndrome. There is an increasing body of evidence that D-lactate plays a major role in the development of malaise in sick calves. The relative contributions of dehydration, acidemia, D-lactate, endotoxemia and sepsis are partly understood. The following review integrates this information and describes the relative importance of these factors as causes of malaise or death.

2.1 **Endotoxemia**

Endotoxemia probably plays a small to moderate role in calf digestive diseases. Many calves with severe diarrhea have markedly inflammatory hemograms even though the primary etiologic agents isolated are often viral or protozoal. Endotoxin is known to produce severe inflammatory changes in calves (Deldar et al. 1984). Translocation of endotoxin across damaged intestinal mucosa may be the cause of these hemogram changes. Similarly, endotoxemia may play a role in ruminal acidosis with the absorption of gram negative toxins through damaged ruminal mucosa. Leukocytosis has been described in acute experimental ruminal carbohydrate overload in calves but no changes in the differential cell count were noted (Halimi et al. 1991). Leukocytosis and left shift have also been described in cases of acidosis without dehydration, again suggesting a possible role for endotoxemia (Kasari & Naylor, 1986b). Endotoxemia can cause fever, malaise and death (Baile et al. 1981; Naylor & Kronfeld, 1985; Naylor & Kronfeld, 1986). However, the success of IV or oral fluid therapy in resuscitating many calves with gastrointestinal disease argues for a major role for dehydration and acidemia, but not endotoxemia, in the pathogenesis of malaise and mortality.

2.2 **Sepsis and bacteremia**

Irrespective of the initial cause, bacteremia or sepsis can complicate enteritis. In experimentally induced viral diarrhea of calves, some dying calves have evidence of septicaemia with focal infection of various parts of the body (Naylor et al. 1990). Bacteremia and septicaemia, frequently with *E. coli*, are common complications of neonatal diarrhea (Fecteau et al. 1997; Lofstedt & Dohoo, 1996). It is assumed that most of these organisms are normally resident in the gastrointestinal tract and gain entry across the damaged gut mucosal barrier. In addition, enteric bacterial overgrowth is common in diarrheic calves, irrespective of the initial cause (Constable, 2004) and this likely facilitates systemic translocation. Septicaemia is not a common complication of the acidosis without dehydration syndrome in calves. However in a series of 7 cases in goat kids, one case that failed to respond to therapy was septicemic (Tremblay et al. 1991).

2.3 **Dehydration**

Experimental studies using IV diuretics and orally administered sucrose show that calves can endure dehydration of at least a 14% loss of body weight without becoming profoundly depressed or loosing the ability to stand or suck. As in naturally occurring diarrhea, the majority of fluid loss is from the extracellular space. Despite the severe dehydration there were only minor changes in blood pH; L-lactate levels rose from 1.1 to 2.8 mmoles/l. (Constable et al. 1998; Walker et al. 1998). In contrast, a study of naturally occurring cases of severe calf diarrhea in which most calves were profoundly depressed with involuntary lateral recumbency had a mean level of dehydration of 7.5% and only a few calves were more than 14% dehydrated (Naylor, 1989). The discrepancy
between the degree of dehydration commonly seen in the field and the maximum amount of dehydration a calf can endure reflects the influence of other factors that work in concert with dehydration to limit life. For example, many dehydrated calves are also acidic and this combination is likely to be more lethal than dehydration alone.

Dehydration is a common feature of ruminal acidosis in calves (Gentile et al. 2004; Halimi et al. 1991). In the acidosis without dehydration syndrome, clinical signs of dehydration are not present. However, serum creatinine concentrations may be elevated suggesting impaired renal function. This may be secondary to mild hypovolemia and decreased renal blood flow (Kasari & Naylor, 1986b).

### 2.4 Acidemia

Acidemia is common in diarrheic calves (Table II). Calves dying with diarrhea tend to have venous blood pH’s between 6.50 and 7.05. The importance of correcting acidemia in diarrheic calves has been documented in several, severe, controlled, experimental challenge models. In general, these show that correcting acidemia is at least as important as correcting dehydration (Table III).

Table II. **D-lactic acidosis and selected blood gas values in healthy calves and calves with the acidosis without dehydration syndrome, diarrhea or ruminal acidosis.** Values are mean ± SD unless otherwise noted.

<table>
<thead>
<tr>
<th>Condition</th>
<th>pH</th>
<th>Bicarbonate (mmol/l)</th>
<th>Anion gap (mmol/l)</th>
<th>D-lactate (mmol/l)</th>
<th>L-lactate (mmol/l)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>7.51 ± 0.20</td>
<td>27.9 ± 3.48</td>
<td>23.6 ± 5.15</td>
<td>2.31 ± 1.61</td>
<td>2.53 ± 1.93</td>
<td>Schelcher et al. 1998</td>
</tr>
<tr>
<td>Acidosis with minimal dehydration</td>
<td>7.251 ± 0.18</td>
<td>12.3</td>
<td>35.14 ± 3.68</td>
<td>10.21 ± 2.65</td>
<td>1.28 ± 0.24</td>
<td>Schelcher et al. 1998</td>
</tr>
<tr>
<td>Control (n = 21)</td>
<td>7.36 ± 0.03</td>
<td>32.6 ± 2.1</td>
<td>5.6 ± 3.5</td>
<td>&lt; 0.5</td>
<td>2.0 ± 1.1</td>
<td>Omole, 2001</td>
</tr>
<tr>
<td>Diarrhea (n = 21)</td>
<td>7.17 ± 0.14</td>
<td>18.0 ± 8.8</td>
<td>19.7 ± 8.6</td>
<td>5.2 ± 5.7</td>
<td>4.1 ± 3.4</td>
<td>Omole, 2001</td>
</tr>
<tr>
<td>Control (n = 11)</td>
<td></td>
<td></td>
<td>1.4 (0.8-3.8)</td>
<td>1.7 (1.2-2.9)</td>
<td></td>
<td>Ewaschuk &amp; Zello, 2004</td>
</tr>
<tr>
<td>Diarrhea (n = 16)</td>
<td></td>
<td></td>
<td>13.9 (1.2-22.7)</td>
<td>1.6 (0.9- 3.5)</td>
<td></td>
<td>Ewaschuk &amp; Zello, 2004</td>
</tr>
<tr>
<td>Control (n = 9)</td>
<td></td>
<td></td>
<td>12.8 ± 1.95</td>
<td>0.2 ± 0.1</td>
<td>0.7 ± 0.2</td>
<td>Gentile et al. 2004</td>
</tr>
<tr>
<td>Ruminal acidosis (n = 8)</td>
<td></td>
<td></td>
<td>20.3 ± 1.65</td>
<td>5.9 ± 1.8</td>
<td>0.5 ± 0.2</td>
<td>Gentile et al. 2004</td>
</tr>
</tbody>
</table>

*Values are median (range)*

Table III. **Effect of adding alkalinizing agents to oral fluids used to treat diarrheic calves**

<table>
<thead>
<tr>
<th>Animals</th>
<th>Treatment Regime</th>
<th>Outcome, no alkalinizing agent</th>
<th>Outcome, alkalinizing agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental rotavirus, coronavirus diarrhea, 12 calves per treatment</td>
<td>Calves fed milk, 5% body weight and oral electrolytes 4 to 6 L a day</td>
<td>Ion-Aid oral electrolyte, 33% survival</td>
<td>Life-Guard oral electrolyte (bicarbonate alkalinizing agent), 83% survival. Revibe oral electrolyte (acetate alkalinizing agent), 92% survival</td>
</tr>
<tr>
<td>Experimental rotavirus, coronavirus, cryptosporidium, K99 positive E. coli</td>
<td>Fed milk at 0, 0.75 or 1.5 x maintenance and oral electrolytes at 4 L a day</td>
<td>3/10 calves on oral electrolyte containing 105 mmol/l of chloride died</td>
<td>1/9 calves on oral electrolyte containing 25 mmol/l chloride and 80 mmol/l bicarbonate died</td>
</tr>
</tbody>
</table>
From data in (Heath et al. 1989; Naylor et al. 1990)

In calves with the acidosis without dehydration syndrome a controlled comparison of equal volumes (approximately 2 L per 50 kg calf) of isotonic saline or sodium bicarbonate solution showed that isotonic sodium bicarbonate markedly improved blood pH and demeanour. In contrast simply providing IV saline resulted in only small improvements in blood pH and calf demeanour (Kasari & Naylor, 1986b). Correction of systemic acidosis is also thought to be helpful in the treatment of ruminal acidosis.

2.5 D-lactic acidosis

D-lactic acidosis has been reported in ruminal acidosis, acidosis without dehydration syndrome and in calves with neonatal diarrhea since the late 1990’s (Gentile, 1995; Grude et al. 1999; Schelcher et al. 1998; Zello et al. 1998; Zello et al. 1999). In the acidosis without dehydration syndrome D-lactic acid is responsible for all of the systemic acidosis (Schelcher et al. 1998). It arises from gastrointestinal fermentation of nutrients by bacteria. In severely diarrheic calves it accounts for a major portion of the acidemia and is a more important contributor to acidemia than L-lactic acid. (Constable, 2004; Ewaschuk & Zello, 2004; Omole, 2001; Zello et al. 1998; Zello et al. 1999). D-lactic acidosis also occurs in ruminal carbohydrate overload in calves (Gentile, 1995; Gentile et al. 2004; Grude, 2003; Grude et al. 99) (Table II).

D-lactic acidosis has also been implicated in a variety of gastro-intestinal disorders in other neonatal ruminant species, propylene glycol intoxication in cats and people (Christopher et al. 1990; Jorens et al. 2004), as an unusual complication of exocrine pancreatic insufficiency in cats (Packer et al. 2005) and as a complication of short bowel syndrome in humans (Hudson et al. 1990; Mayr et al. 1999; Uribarri et al. 1998).

The presence of severe D-lactic acidemia is always associated with signs of neurological dysfunction including ataxia and a drunken appearance. There has been, and continues to be, discussion as to whether these changes are a direct effect of the D-lactate ion. Recently Lorenz and Gentile found that IV sodium D-lactate produced signs of ataxia, somnolence and an impaired palpebral response (Lorenz et al. 2005). However, this experiment was criticized on the grounds that the calves also became hypernatremic and the infusion was about 15 times hypertonic (Stampfl, 2005). We recently compared the effects of equimolar concentrations of 0.3 M DL-lactic acid, L-lactic acid, hydrochloric acid and isotonic saline on neurological function in healthy calves (Zello et al. 2005). Hydrochloric acid produced the more severe acidosis. However, DL-lactic acid had by far the most profound neurological effects. Between four and six hours of infusion 6/6 calves receiving DL-lactic acid became involuntarily recumbent; many were comatose with a neurologic depression score close to 8 (0 = normal). In contrast during hydrochloric acid infusion all calves retained the ability to stand. During L-lactic acid infusion only one calf became involuntarily recumbent and this was for one time period only. Similarly, only DL-lactic acid infusion completely abolished the menace reflex. Mean depression scores during L-lactic acid or hydrcloric acid infusion were < 2 (Naylor et al. unpublished). This experiment also demonstrated that D-lactate readily penetrates into the CSF space with concentrations similar to those in serum. Overall, loss of the menace reflex, palpebral reflex, panniculus reflex and ability to stand were highly correlated with CSF D-lactate concentration. Interestingly, loss of the suck reflex correlated poorly with D-lactate concentration and, unlike the other reflexes, correlated better with the degree of acidemia. This experiment shows that D-lactate can acutely produce severe and wide ranging neurological disturbances. However, the correlation of the suck reflex with acidemia keeps open the possibility that acidemia may be directly toxic to some regions of the brain. This may be
particularly true in chronic acidemia, where there is more time for CSF and serum pH to equilibrate, and this should be investigated further.

2.6 Relative contribution of dehydration, acidemia and D-lactic acid to clinical signs in gastrointestinal disease

At the present time blood D-lactate accumulation appears to be one of the most important factors in the pathogenesis of systemic signs of weakness and CNS depression in calves with gastro-intestinal disease. In the acidosis without dehydration syndrome signs of neurological compromise (weakness, ataxia, and decreased menace, suck and panniculus reflexes) are highly correlated with the severity of metabolic acidosis (Kasari & Naylor, 1986b). Later work showed that D-lactate was almost entirely responsible for the acidosis (Schelcher et al. 1998). Both our studies, and those of Lorenz and Gentile, show that D-lactate produces these clinical signs when administered to calves (Lorenz et al. 2005). Overall this suggests that D-lactate is responsible for the majority of clinical signs in calves with the acidosis without dehydration syndrome. The only clinical sign that may not be produced by D-lactate is the decreased suck reflex, which may be a direct result of acidemia.

In calves with enteritis and diarrhea, dehydration is a contributory factor to CNS depression. However, it cannot alone produce the profound depression seen in some diarrheic calves (Walker et al. 1998). Given the ability of D-lactate to produce profound weakness, ataxia and CNS depression, and the known presence of D-lactate in calves with severe diarrhea, it seems likely that D-lactate is partly responsible for these clinical signs in diarrheic calves. D-lactate can be efficiently cleared by the kidneys, so dehydration may have an indirect role in increasing the toxicity of D-lactate produced by limiting renal excretion (Ewaschuk & Zello, 2004).

The role of acidemia is less clear. Several experiments document that correction of acidosis, or prevention of acidemia, improves survival in diarrheic calves (Booth & Naylor, 1987; Heath et al. 1989; Naylor et al. 1990). The mechanism is not understood and it is possible that correction of acidemia simply speeds the removal of D-lactate from the body. In our experiments, induction of acute acidemia is associated with weakening of the suck reflex so acidosis may directly affect some regions of the brain. Chronic acidosis may have more profound effects than acute acidosis. CSF pH falls more slowly than blood pH and it may take some time before the full affects of acidemia are felt. Acidemia is also important as a result of its affects on intra- and extra-cellular potassium concentrations. Acidosis favors the movement of potassium from cells to serum. These alterations in potassium concentration predispose to the development of cardiac arrhythmia, including bradycardia, which would be expected to reduce CNS perfusion and produce weakness or death.

In ruminal acidosis it is likely that the relative contributions of dehydration, acidemia and D-lactate are similar to those in diarrheic calves.

2.7 Mortality

The final mechanisms by which death is induced are variable. For example, both dehydration and endotoxemia can produce shock with death from failure of cellular metabolism secondary to impaired delivery of nutrients or hypothermia. Hypothermia is well recognized in diarrheic calves (Naylor, 1989). Some diarrheic calves die from cardiac arrhythmia related to imbalances in intra- and extracellular potassium concentration bought on by dehydration and acidemia (Fisher, 1965; Fisher & McEwan, 1967; Weldon et al. 1992). In addition, chronic cases may die from emaciation or secondary sepsis.
3. FLUID THERAPY

The objectives of fluid therapy in calves with gastrointestinal disease are to correct dehydration, correct acidemia and reduce serum D-lactate concentrations below 1 mmol/l.

3.1 Calculating Total Fluid Requirements

The principles of rehydration therapy have been understood for over three decades. Dehydration is assessed from clinical signs of enophthalmos, the color and dryness of the mucous membranes and skin elasticity over the neck and thorax. Skin tenting over the eyelid is an unreliable indicator of dehydration (Constable et al. 1998). Clinical trials also indicate that many of the older schemes used to assess dehydration overemphasized the severity of dehydration (Naylor, 1992). Guidelines for estimating dehydration based on the more recent evidence are shown in Table IV.

Table IV. Predicting dehydration from clinical signs (Constable et al. 1998; Naylor, 1987b)

<table>
<thead>
<tr>
<th>Dehydration</th>
<th>Eyeball sunkenness</th>
<th>Mild cervical skin tent (seconds)</th>
<th>Mucous membranes</th>
<th>Extremities</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>None</td>
<td>≤ 2</td>
<td>Moist, pink</td>
<td></td>
</tr>
<tr>
<td>2%</td>
<td>Slight, 1 mm</td>
<td>3</td>
<td>Dry</td>
<td></td>
</tr>
<tr>
<td>4%</td>
<td>Slight, 2 mm</td>
<td>4</td>
<td>Dry</td>
<td></td>
</tr>
<tr>
<td>6%</td>
<td>Moderate, 3 mm (separation of eyeball from orbit)</td>
<td>5</td>
<td>Dry</td>
<td></td>
</tr>
<tr>
<td>8%</td>
<td>Moderate, 4 mm</td>
<td>6</td>
<td>Dry</td>
<td>Cold</td>
</tr>
<tr>
<td>10%</td>
<td>Severe, 6 mm</td>
<td>7</td>
<td>Dry</td>
<td>Cold</td>
</tr>
<tr>
<td>12%</td>
<td>Severe, 7 mm</td>
<td>&gt; 8</td>
<td>Dry</td>
<td>Cold</td>
</tr>
<tr>
<td>≥ 14%</td>
<td>Severe, &gt; 8 mm</td>
<td>&gt; 10</td>
<td>Dry, white</td>
<td>Cold</td>
</tr>
</tbody>
</table>

When calculating fluid requirements it is customary to add amounts for ongoing losses and maintenance requirements. In diarrheic calves fed milk and oral electrolyte solutions, ongoing fecal water losses are generally between 1 and 4 L of a day (Heath et al. 1989). In the acidosis without dehydration syndrome there are no unusual fluid losses. Ongoing losses for calves with ruminal acidosis may be similar to those in diarrheic calves. Maintenance water requirements for calves are not fully documented but 70 ml/kg body weight prevented the development of dehydration and hypovolemia in one experiment (Gottardo et al. 2002).

Table V shows the application of these principles. In the first example, the calf is not clinically dehydrated and requires 5.5 L of fluid a day. This could be met with 4L of oral electrolyte solution and 2 L of milk. Although the absorption of oral electrolyte solutions is less than 100%, this amount of fluid will be sufficient since the values for fecal fluid loss were generated using calves receiving oral electrolyte solution and milk. In the second example, a 10% dehydrated calf requires 11.5 L of fluid. This will be best supplied by giving all or part of the fluid intravenously. The IV route allows for the administration of relatively large volumes of fluid without inefficiencies due to incomplete absorption. It also avoids problems with poor suck reflex and ileus. Ileus delays or prevents the absorption of oral fluids. Diarrheic calves fed either no or small amounts of fluid orally often rapidly develop formed feces, so in this example 3 L was chosen as the likely fecal output.

Table V. Examples of 24 hours fluid requirements for a 50 kg diarrheic calf in two different scenarios

<table>
<thead>
<tr>
<th>Item</th>
<th>No clinical dehydration (moderate diarrhea)</th>
<th>Dehydration 10% (severe diarrhea)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Replacement, L</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Ongoing losses, L</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Maintenance (70 ml/kg), L</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>Total 24 hour requirement</td>
<td>5.5</td>
<td>11.5</td>
</tr>
</tbody>
</table>
3.2 Rate of fluid administration

The ideal rate of oral fluid administration has not been determined. In general, the maximum amount of oral fluid I give to a 50 kg diarrheic calf in a 24 hour period is 8 L divided into at least 4 feeds of 2 L or less.

Studies in healthy sheep and cats indicate that fluid overload occurs at administration rates of about 90 ml/kg body weight for periods longer than one hour. Rates of 30 ml/kg for a number of hours produce no toxic side effects (Bjorling & Rawlings, 1983; Broaddus et al. 1990; Gottardo et al. 2002). Some sick calves hypoproteinemic or have increased vascular permeability and are likely to be more susceptible to volume overload. In practice very rapid rates of IV fluid infusion, 100 ml/kg.h can be employed for short periods of time (20 minutes) in the initial resuscitation of severely dehydrated calves. The objective of this initial high rate of infusion is to rapidly improve circulation by restoring blood volume, which can be preferentially depleted (Naylor, 1987b). Based on a plasma volume of 7.2% of body weight (Wagstaff et al. 1992) fluid administration at these rates will increase plasma volume by almost 50%. IV infusion rates should then be limited to 20 to 40 ml/kg.h. The usual aim is to correct dehydration in about 6 to 8 hours and then gradually administer the remaining fluids required for maintenance and ongoing losses.

3.3 Correction of acidosis

Although different philosophies regarding the control of acid-base balance exist, there is agreement that base deficit is the most useful parameter for quantifying metabolic acidosis. It is routinely used to experimentally determine therapeutic bicarbonate requirements in sick calves.

Base deficit (sometimes expressed as a negative base excess) is defined as the total titratable acidity at a pCO₂ of 40 mm Hg (Sigaard-Andersen, 1966). A similar definition is the amount of alkali required to restore one liter of blood to a pH of 7.4 at a pCO₂ of 40 mm Hg (Ganong, 1987). Thus normal base deficit values are close to 0. Bicarbonate measurements are a less accurate basis for calculating therapeutic bicarbonate requirements as they are affected by both metabolic and respiratory changes. Changes in pCO₂ have a small effect on bicarbonate concentration as they shift the dissociation of carbonic acid to the right or left. Since base deficit is measured after the blood has been tonometered to a pCO₂, these respiratory effects are removed.

Blood gas machines do not tonometer blood and do not measure bicarbonate concentrations directly. Instead they measure pH and pCO₂ and calculate bicarbonate at the actual blood pCO₂ and also at a pCO₂ of 40 using equations related to the Henderson-Hasselbach equation. The definition of base deficit implies this parameter should be sensitive to changes in all blood buffers. However, only hemoglobin concentration is taken into account when blood gas machines calculate base deficit (Sigaard-Andersen, 1966). Hemoglobin is by far the largest component of blood protein; it exerts an important buffering effect on plasma secondary to the movement of ions and carbon dioxide across the erythrocyte membrane. Most calculated values for base deficit do not take into account buffering by plasma proteins. Studies in calves show the net charge on plasma protein is approximately 10 meq/l. There is little overall difference in the charge on plasma proteins between diarrheic and healthy calves since the effects of hemoconcentration are offset by an almost equal decrease in charge due to acidemia (Constable et al. 2005). When a blood gas machine is not available, base deficit can be predicted empirically in diarrheic calves from clinical signs, Table VI.

Table VI. Predicted base deficit, mmol/l, of diarrheic calves based on their age and clinical signs (Naylor, 1989)
Sodium bicarbonate is an effective alkalinizing agent; a fact that has been empirically proven in randomized, controlled, blinded trials in diarrheic calves and in calves with the acidosis without dehydration syndrome (Booth & Naylor, 1987; Kasari & Naylor, 1986a; Kasari & Naylor, 1986b).

The amount of sodium bicarbonate required to correct metabolic acidosis is given by the formula: 

\[
\text{Sodium bicarbonate requirement, mmol} = \text{Body weight, Kg} \times \text{Base Deficit} \times Vd
\]

Where Vd is the volume of distribution of bicarbonate and has been empirically determined in healthy calves, calves with diarrhea and calves with the acidosis without dehydration syndrome (Kasari & Naylor, 1986a; Kasari & Naylor, 1986b; Naylor & Forsyth, 1986). These studies yield values for Vd that range from 0.45 to 0.75. In general a value of 0.5 is used for clinical purposes. However, this is only a general guideline. Individual variations arise due to differences in plasma protein and phosphate buffering systems between calves and to differences in the degree of intracellular acidosis. Bicarbonate requirements may also be affected by needs to buffer gastrointestinal acids. In general, calves with the deepest acidosis tend to depart from the general trend. Severely acidemic calves that do not respond to bicarbonate therapy should have their acid-base status rechecked.

If only a serum bicarbonate is available, bicarbonate requirement can be calculated from serum bicarbonate concentrations using the following formula and a Vd of 0.6 to compensate for buffering by non-bicarbonate systems (Naylor, 1987a). 

\[
\text{Sodium bicarbonate requirement, mmol} = \text{Body weight, kg} \times (30 - \text{Patient Bicarbonate}) \times Vd
\]

Typically correction of acidosis requires 1 to 4 L (25 to 100 ml/kg), of isotonic 1.3% sodium bicarbonate administered over about 4 to 8 hours. It is unknown whether this rapid correction leads to paradoxic CSF acidosis. Paradoxic CSF acidosis is most likely to occur following rapid correction of chronic, deep acidosis with respiratory compensation. In severely acidic calves treated with sodium bicarbonate, there can be residual depression that takes 12 to 18 hours to resolve. This may represent correction of CSF acidosis, clearance of D-lactate or some other factor.

There has been interest in whether hypertonic sodium bicarbonate can be used to correct acidemia in calves. Hypertonic solutions have been tested in neonatal calves with experimentally induced respiratory acidosis. Sodium bicarbonate, 8.4% was given at 5 ml/kg over 5 minutes. It changed base excess by 6.5 mmol/l and improved cardiac output and contractility (Berchtold et al. 2005). This suggests that small amounts of hypertonic sodium bicarbonate may also be useful in the initial resuscitation of diarrheic calves. However, many modern oral electrolyte solutions contain relatively high concentrations of sodium (> 110 mmol/l). On average, diarrheic calves presented to the University of Saskatchewan for treatment have normal serum sodium concentrations. Some fit the traditional pattern and are hyponatremic. Others, however, are severely hypernatremic; this is presumably the result of prior oral electrolyte therapy and limited water or milk intake. In consequence, hypertonic sodium bicarbonate should be used cautiously in previously treated calves unless the serum sodium concentration has been measured.

Although sodium bicarbonate is the agent of choice for IV correction of acidemia a variety of other sodium salts can also be used including sodium L-lactate and sodium acetate. Protons are removed when these bases are metabolized. Shock interferes with cellular metabolism and the effectiveness of these bases (Kasari & Naylor, 1986a).
Oral correction of acidemia can be achieved with electrolyte solutions containing bicarbonate, acetate, citrate or other metabolizable bases. Orally administered bicarbonate is not directly effective, it is first neutralized by abomasal acidity. Systemic alkalinization occurs as the abomasal proton pumps regenerate abomasal acid with an equal addition of bicarbonate to the systemic circulation. Since oral electrolyte therapy is only recommended for calves that are not severely compromised, the metabolism of bases such as acetate is unlikely to be impaired. In a small scale trial an oral electrolyte solution containing acetate was slightly more effective than an identical solution containing bicarbonate in correcting acidemia (Naylor, unpublished observations). In general, bicarbonate is avoided in oral electrolyte solutions because of concerns it will raise abomasal pH and thereby facilitate entry of pathogens to the intestinal tract. Bicarbonate and citrate also interfere with milk clotting which is a concern in calves sucking whole cow’s milk.

3.4 Correction of D-lactic acidosis

Several important questions still need to be answered about the correction of D-lactic acidosis. One of the more important is whether or not correction of acidemia speeds the clearance of D-lactate. Conventional IV fluid therapy with saline and sodium bicarbonate given in accordance with the preceding principles has been shown to rapidly correct hyper D-lactatemia in diarrheia calves (Ewaschuk et al. 2006). This is also associated with the excretion of D-lactate in urine (Ewaschuk & Zello, 2004). In a controlled trial in calves with the acidosis without dehydration syndrome sodium bicarbonate was more effective than an equal volume of saline in correcting CNS depression suggesting that sodium bicarbonate therapy helps speed removal of D-lactate (Kasari & Naylor, 1986b).

4. SUMMARY

Enteritis and ruminal acidosis are long recognized causes of illness in neonatal calves. Over the last three decades a new gastro-intestinal disorder of calves has been recognized - acidosis without dehydration syndrome. Dehydration and acidosis are important in the pathogenesis of these syndromes. Recently, D-lactic acidosis has been documented as a major cause of acidemia. It is an important cause of systemic signs of CNS depression.

Correction of gastro-intestinal disturbances in calves depends on correction of dehydration, acidemia and the removal of D-lactate from blood and CSF. Early clinical algorithms for assessing dehydration emphasized the degree of dehydration and the reliability of eyelid skin tenting. Eyeball recession and neck skin tent remain reliable indicators of dehydration. Correction of acidemia is based on the calf’s body weight and base deficit which can either be directly measured using a blood gas machine and the calf’s hemoglobin concentration or can be estimated from clinical signs and the calf’s age. The factors that influence the clearance of D-lactate from the blood are not fully elucidated but D-lactate is rapidly cleared in calves receiving antibiotics and IV fluid therapy formulated to correct dehydration and acidemia.

5. KEY WORDS

Bovine, calf, diarrhea, acidosis without dehydration, ruminal acidosis, D-lactic acidosis, D-lactate, fluid therapy, acidemia, clinical signs.

6. RESUME

L’entérite et l’acidose ruminale sont des affections connues depuis longtemps chez le veau nouveau-né. Ces trois dernières décennies, une nouvelle affection gastro-intestinale a été identifiée, à savoir une acidose sans syndrome de déshydratation. La déshydratation et l’acidose métabolique
sont deux composantes majeures dans la physiopathologie de ces syndromes. Récemment, l’acidose par le D-lactate a été reconnue comme une cause majeure d’acidose sanguine, responsable de signes cliniques systémiques associés à une atteinte dépressive du système nerveux central.

La correction des troubles gastro-intestinaux chez le veau nécessite une correction de la déshydratation et de l’acidose sanguine ainsi que l’élimination du D-lactate du sang et du liquide céphalo-rachidien. Les algorithmes cliniques pour évaluer précocement la déshydratation soulignent l’importance de la relation entre degré de déshydratation et tension de la paupière. L’enfoncement du globe oculaire et la persistance du pli de peau de l’encolure restent aussi des indicateurs fiables d’une déshydratation. La correction de l’acidose dans le sang prend en compte le poids du veau et le déficit en bases qui peut être, soit directement mesuré avec un automate qui mesure les gaz sanguins et la concentration en hémoglobine du veau, soit estimé à partir des signes cliniques et de l’âge de l’animal. Les facteurs qui favorisent l’élimination du D-lactate sanguin ne sont pas totalement identifiés mais le D-lactate est rapidement éliminé chez les veaux qui reçoivent un traitement antibiotique et une fluidothérapie intraveineuse destinée à corriger la déshydratation et l’acidose métabolique.

7. MOTS CLES

Bovin, veau, diarrhée, acidose sans déshydratation, acidose ruminale, acidose D-lactique, D-lactate, fluidothérapie, acidémie, signes cliniques.

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