The Veterinary Journal 195 (2013) 350–356

Contents lists available at SciVerse ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

The prevalence and clinical relevance of hyperkalaemia in calves with neonatal diarrhoea

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ARTICLE INFO

Article history:
Accepted 2 July 2012

Keywords:
Potassium
Neonatal diarrhoea
Calves
D-lactate
Dehydration

ABSTRACT

One hundred and twenty-four calves with neonatal diarrhoea were investigated in order to assess the prevalence of hyperkalaemia and the associated clinical signs. Hyperkalaemia (potassium concentration >5.8 mmol/L) was recognized in 42 (34%) calves and was more closely associated with dehydration than with decreases in base excess or venous blood pH. In 75 calves with normal blood concentrations of D-lactate (i.e. ⩽3.96 mmol/L), K concentrations were moderately correlated with base excess values ($r = -0.48$, $P < 0.001$). In contrast, no significant correlation was observed in 49 calves with elevated D-lactate. Only three hyperkalaemic calves had bradycardia and a weak positive correlation was found between heart rate and K concentrations ($r = 0.22$, $P = 0.014$). Ten of the 124 calves had cardiac arrhythmia and of these seven had hyperkalaemia indicating that cardiac arrhythmia had a low sensitivity (17%) but a high specificity (96%) as a predictor of hyperkalaemia.

In a subset of 34 calves with base excess values ⩽−5 mmol/L and D-lactate concentrations <5 mmol/L (of which 22 had hyperkalaemia), changes in posture/ability to stand could be mainly explained by elevations of K concentrations ($P < 0.001$) and to a lesser extent by increases in L-lactate concentrations ($P = 0.024$). Skeletal muscle weakness due to hyperkalaemia alongside hypovolaemia may produce a clinical picture that is similar to that in calves with marked D-lactic acidosis. However, since reductions in the strength of the palpebral reflex are closely correlated with D-lactate concentrations, a prompt palpebral reflex can assist the clinical prediction of hyperkalaemia in calves presenting with a distinct impairment in their ability to stand (specificity 99%, sensitivity 29%).

Introduction

In the last decade, scientific work has changed our view of the pathophysiology of neonatal calf diarrhoea, with D-lactate being identified as the cause of most of the clinical signs that had traditionally been attributed to metabolic acidosis (Lorenz, 2004; Lorenz et al., 2005). In experimental settings, neither artificially induced severe dehydration up to 20% of body mass (Constable et al., 1998) nor artificially induced severe metabolic acidosis by administration of hydrochloric acid with base excess values as low as −33 mmol/L (Gentile et al., 2008) was accompanied by a deterioration in general condition. Only intravenous (IV) administration of sodium D-lactate has enabled researchers to reproduce the majority of clinic findings regularly observed in calves with naturally acquired diarrhoea and metabolic acidosis, such as changes in posture, behaviour and a reduction in the strength of the palpebral reflex (Lorenz et al., 2005).

In hospitalised diarrhoeic calves with metabolic acidosis we have often observed clinically important alterations in the animals' ability to stand, and disturbances in general condition that could not been explained by elevations of serum D-lactate. This has led us to the conclusion that factors other than D-lactate can influence the clinical picture in diarrhoeic calves.

Hyperkalaemia has been shown to be an important electrolyte disturbance in many studies of calf diarrhoea (Lewis and Phillips, 1973; Groutides and Michell, 1990; Grove-White, 2007; Koch and Kaske, 2008). The hyperkalaemia occurs despite diarrhoea causing a significant net loss of K^+ (Lewis and Phillips, 1972) because the buffering required to counteract the acidaemia resulting from the diarrhoea means that K^+ leaves the cells in order to maintain intracellular electroneutrality (Lewis and Phillips, 1973; Kaske, 1994; Sweeney, 1999). This is exacerbated by dysfunction of the Na^+/K^+-ATPase, which distributes K^+ between the intracellular and extracellular space (Constable, 2002) and impairment of renal excretion of K ions as a result of the hypovolaemia (Sweeney, 1999; Carlson and Bruss, 2008).

The aims of the present study were to assess the prevalence of hyperkalaemia in calves with neonatal diarrhoea, to assess the

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http://dx.doi.org/10.1016/j.tvjl.2012.07.002

clinical signs associated with that condition and to assess the predictability of hyperkalaemia in a clinical setting.

Materials and methods

Calves admitted to the Clinic for Ruminants, LMU Munich, between September 2009 and April 2010 with a diagnosis of neonatal diarrhoea ($n = 150$) were included in the study. Calves were excluded from the study because of death or euthanasia (due to severe concurrent health problems) during the first 24 h of hospitalisation ($n = 16$), need for surgical intervention ($n = 2$), marked hypernatraemia (> 170 mmol/L, $n = 4$) and a history of repeated force-feeding prior to admission ($n = 1$). Additionally, three calves that were euthanased at a later point in time were excluded retrospectively because of post mortem findings (i.e. bovine viral diarrhoea infection, peritonitis, caecocolic intussusception). Thus data were available for 124 calves. Most of the calves ($n = 113$, 91%) were Simmentals, the most common dairy breed in Bavaria.

Clinical examinations were performed immediately after admission by the same investigator who was blinded to all laboratory values. The following parameters were categorized: (1) posture/ability to stand (standing securely, standing insecurely – able to correct position if pushed, standing insecurely – unable to correct position if pushed, recumbent/unable to stand); (2) palpebral reflex (prompt, delayed, absent), and (3) colour of the mucous membrane and muzzle (hyperaemic, normal, pale, pale-cyanotic, white).

The clinical assessment of posture/ability to stand included lifting the animal if it was not able or willing to stand up. The degree of enophthalmos (which has been identified as the best predictor of degree of dehydration) was assessed by measuring the distance between the eyeball and the palpebral conjunctiva in millimetres (Constable et al., 1998; Niethammer, 2007). Heart rate and presence of cardiac arrhythmias was assessed by auscultation for a period of 30 s.

Blood samples were taken from the jugular vein following admission examination. Blood for blood gas analysis was collected anaerobically into 2 mL heparinised plastic syringes (Monovette, Sarstedt) and was immediately examined for base excess, pH, Na and K using a blood gas analyser (Rapidlab 865, Bayer). Blood gas determinants were corrected for rectal temperature and actual bicarbonate concentration (HCO_3^-) was calculated by using the Henderson–Hasselbalch equation ($\log HCO_3^- = pH + \log(PCO_2 \times S) - pK_1'$).

Values for the negative logarithm of dissociation constant of carbonic acid (pK_1') and solubility of carbon dioxide (S) for plasma at 37 °C were 6.105 and 0.0307 mmol/L per mm Hg, respectively. After measuring the haemoglobin concentration (Hb) photometrically, blood base excess (in vitro base excess) was calculated by the unit using the following formula:

$$\text{Base excess (mmol/L)} = (1\text{—}0.014 \times Hb) \times [(HCO_3^- - 24.8) + (1.43 \times Hb + 7.7) \times (pH - 7.4)]$$

Automatic analysers were used for haematology (F-820, Sysmex) and blood biochemistry analysis (Automatic Analyzer Hitachi 911, Roche Diagnostics). Concentrations of D-lactate, L-lactate and glucose were determined from heparinised blood samples containing sodium fluoride as a glycostatic agent. An additional serum sample was assayed for concentrations of urea, creatinine, total protein, inorganic phosphorus and activities of creatine kinase (CK) and aspartate aminotransferase (AST). D-lactate concentrations were determined using D-lactate dehydrogenase and hyper-D-lactataemia was defined as D-lactate concentration >3.96 mmol/L (Lorenz et al., 2003). Plasma K concentrations of 3.9–5.8 mmol/L were defined as normokalaemic (Kaneko et al., 2008).

PASW 18.0 (SPSS) was used for the statistical analysis. Normal distribution was assessed visually using box-and-whisker plots and QQ plots. Since most of the data were not distributed normally, non-parametric tests were employed and data are reported as medians and 25-/75-quartiles (Q_{25}/Q_{75}). The Mann–Whitney U test was used for comparisons between groups. Associations between parameters were determined using Spearman's coefficient of correlation. Locally weighted scatterplot smoother lines have been included in the graphical display (Cleveland, 1979). Sensitivity, specificity and positive predictive values (PPV) were calculated for clinical signs that could be used for the prediction of hyperkalaemia.

Calves with base excess values ⩽−5 mmol/L and D-lactate concentrations <5 mmol/L ($n = 34$) were used to evaluate the association between K and other variables on the one hand and posture/ability to stand on the other hand. Statistically significant differences of several relevant measures between the four clinical categories of posture were identified using a Kruskal–Wallis test. Those variables with P values ⩽0.2 in preliminary univariate analysis were entered in a multivariate proportional-odds logistic regression model. If two variables were closely correlated with each other ($r > 0.65$), the variable which had the lowest P-value in the preliminary univariate analysis was the only one entered into the model. A backwards approach was used to eliminate non-significant variables from the model until the remaining variables were all significant ($P \leqslant 0.05$). Odds ratios (OR) and their 95% confidence interval (95% CI) were calculated for those variables remaining in the model. Interactions between these variables were tested by including those interactions in the model and testing for their significance.

Results

The median (Q_{25}/Q_{75}) age of the calves was 9.0 (6.0/13.0) days. Hyperkalaemia was found in 42 calves (34%), normokalaemia in 70 (56%) and hypokalaemia in 12 (10%). Table 1 shows the association between plasma K concentrations and selected clinical and laboratory parameters. K concentrations were much better correlated with clinical and laboratory hydration status than with decreases in base excess or venous blood pH. A moderate correlation ($r = -0.48$, $P < 0.001$) between base excess and K concentrations was found in the 75 calves which had normal concentrations of D-lactate (Fig. 1), whereas no such correlation ($r = -0.11$, $P = 0.44$) was found in the 49 calves with hyper-D-lactataemia. In the latter group, K concentrations varied widely ranging from 2.9 to 8.5 mmol/L while base excess values ranged from −10 to −30 mmol/L (Fig. 2). Hyperkalaemia was associated with a higher extent of dehydration (Table 2) and a negative correlation ($r = -0.29$, $P = 0.043$) between D−lactate and K concentrations was seen in calves with hyper-D-lactataemia.

Of the 42 calves with hyperkalaemia, only three had bradycardia (<85 beats per minute). In addition there was a weak positive correlation between heart rate and K concentrations ($r = 0.22$, $P = 0.014$). Cardiac arrhythmias were observed in 10/124 calves. These calves had significantly higher K and lower Na concentrations resulting in significantly lower Na to K ratio than calves with a normal heart rhythm (Table 3). Cardiac arrhythmias had a low sensitivity (17%) but a high specificity (96%) as a predictor of hyperkalaemia.

Other signs which were highly specific predictors of hyperkalaemia were pale-cyanotic muzzle or mucous membranes and the finding of a prompt palpebral reflex in calves that were barely able or unable to stand. Hyperkalaemia was found in 76% of calves with severe clinical dehydration (enophthalmos ⩾7 mm) (Table 4).

The association between biochemistry and ability to stand is summarised in Table 5 for 34 calves with base excess values ⩽−5 mmol/L and D-lactate concentrations <5 mmol/L. PCV and inorganic P ($r = 0.71$), urea and creatinine ($r = 0.78$) and AST and CK ($r = 0.66$) were all significantly correlated, so only PCV, urea and CK were entered into the multivariate model. The degree of enophthalmos, CK, PCV, total protein, Na, glucose, and urea were eliminated from the final model. In the final model higher K and L-lactate concentration were associated with an increased likelihood of impairment of ability to stand in spite of normal or negligibly elevated D-lactate concentrations. Odds ratios for the remaining variables are given in Table 6. The model explained 65.2% of the variation of posture/ability to stand in these 34 calves. Interactions between the remaining variables were not significant.

Table 1
Coefficients of correlation between selected clinical and laboratory variables and the plasma potassium concentration in 124 calves with neonatal diarrhoea.

Variable	Plasma potassium
Creatinine	$r = 0.66^{**}$
Phosphorus	$r = 0.65^{**}$
L-lactate	$r = 0.65^{**}$
Clinical hydration status (enophthalmos)	$r = 0.59^{**}$
Urea	$r = 0.51^{**}$
Total protein	$r = 0.48^{**}$
PCV	$r = 0.48^{**}$
Body temperature	$r = -0.31^{**}$
Venous blood pH	$r = -0.26^{*}$
Base excess	$r = -0.15^{NS}$

* $P < 0.05$.
** $P < 0.001$.
^{NS} Not significant.