Turkish Journal of Veterinary & Animal Sciences

Volume 39 | Number 5 Article 17

1-1-2015

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TÜBİTAK

Turkish Journal of Veterinary and Animal Sciences

http://journals.tubitak.gov.tr/veterinary/

Research Article

Turk J Vet Anim Sci
(2015) 39: 615-620
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doi:10.3906/vet-1502-42

Analysis of acid–base disorders in calves with lactic acidosis using a classic model and strong ion approach

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Received: 13.02.2015 • **Accepted/Published Online:** 30.06.2015 • **Printed:** 30.10.2015

Abstract: The objective of this study was to analyze the disorders of acid–base balance in calves with lactic acidosis using the classic model and the strong ion approach. The study included 40 calves: group I was the control group (n = 20) and group II consisted of calves with diarrhea and lactic acidosis (n = 20). The highest lactate concentration (5.49 ± 2.58 mmol/L) was documented in diarrheic calves. The diarrheic calves presented with significantly lower pH, pCO_2, and concentrations of HCO_3^- ($P < 0.01$), and with higher anion gap (AG), strong ion difference (SID_3, SID_7), and strong ion gap (SIG) ($P < 0.01$) than the controls. In the group of diarrheic calves lactic acid correlated with AG ($r = 0.684$, $P < 0.01$), SID_3 ($r = 0.718$, $P < 0.01$), SID_7 ($r = 0.494$, $P = 0.03$), and SIG ($r = 0.561$, $P = 0.01$). There was a negative correlation between lactate and effective SID (SID_{Eff}) ($r = -0.499$, $P = 0.02$), and total plasma concentration of nonvolatile buffers (A_{Tot}) ($r = -0.361$, $P = 0.04$). The results indicated that in lactic acidosis there were specific disturbances with an increased concentration of unmeasured strong ions.

Key words: Calves, diarrhea, acid–base balance, strong ion difference, lactic acidosis

1. Introduction

Neonatal calf diarrhea is a common disorder affecting calves and is an important cause of economic losses. The diarrhea of neonatal calves is usually associated with bacterial (enterotoxigenic strains of *E. coli*), rotaviral, and coronaviral infections and/or feeding factors (1,2). Clinical signs of diarrhea include loose watery stools, lack of appetite, and abdominal pain. This condition may result in dehydration, acid–base disorders, and electrolyte imbalances like metabolic acidosis, hyperkalemia, prolonged malnutrition, hypoglycemia, and hypothermia (3,4). The clinical status of an animal may further deteriorate due to lactic acidosis, which has been reported in diarrheic calves (5,6). Lactic acidosis is the result of elevated concentrations of L-lactate or/and D-lactate in the blood serum. L-lactate is produced by anaerobic metabolism due to tissue hypoperfusion or low oxygen supply to the tissue, while D-lactate is a byproduct of bacterial metabolism (5–7). Although levels of L-lactate or/and D-lactate can be elevated, only the nonstereospecific assay is routinely used in clinical practice.

The interpretation of an acid–base balance is traditionally based on changes in pH, bicarbonate concentration (HCO_3^-), base excess (BE), and anion gap (AG) in plasma. This model characterizes four primary acid–base disturbances (i.e. respiratory acidosis and alkalosis, metabolic acidosis, and alkalosis) (8). The Stewart model (strong ion model) represents an alternative method of evaluation of acid–base status. This model is based on three independent variables to determine the acid–base balance: the strong ion difference (SID)—the difference between all completely dissociated cations and anions; the plasma partial pressure CO_2 (pCO_2), and the total nonvolatile weak acid concentration, mainly inorganic phosphate and albumin. The Stewart approach describes six primary acid–base disturbances (i.e. respiratory acidosis and alkalosis, strong ion acidosis and alkalosis, and nonvolatile buffer ion acidosis and alkalosis). Although the Stewart approach may give a better understanding of the mechanisms that underlie an acid–base disorder, the traditional methods are more convenient in daily practice (4,8–10). Previous studies evaluated the use of two models for description of acid–base disturbances in cases of acute diarrhea, after intravenous fluid therapy or oral rehydration therapy (3,4,11,12).

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To the best of our knowledge none of the previous studies analyzed the acid–base balance disorders using the classic model and Stewart approach in calves with lactic acidosis. In previous studies, the acid–base balance of calves with lactic acidosis was determined using only the classic model and only the association between lactate (L-lactate or/and D-lactate) and the anion gap have been investigated (8–10).

Therefore, the aim of this study was to compare the classic model and the strong ion approach in calves with lactic acidosis and prolonged diarrhea. We hypothesized that acid–base analysis according to the strong ion approach could result in important changes in diagnosis. We also analyzed the association between lactate and strong ion approach parameters in neonatal calves.

2. Materials and methods

2.1. Study design

The study included 40 Holstein–Friesian calves, aged between 7 and 21 days. Animals were housed in individual calf boxes with straw bedding. Calves were fed two times daily (at 0800 and 1700). Calves had ad libitum access to water and were provided with hay and calf starter concentrates. The calves were allocated to two groups: group I (control group) consisted of healthy calves with an appropriate acid–base balance (n = 20), and group II consisted of calves (n = 20) with uncomplicated diarrhea (yellow or gray-yellow stool and the absence of fever or other clinical signs) lasting for 3–4 days and lactic acidosis (concentration of serum lactate higher than 2.0 mmol/L). All animals were subjected to clinical examination. Dehydration status was determined by examining posture, behavior, elasticity of skin, and the distance between the eyeball and the palpebral conjunctiva in millimeters (13). The protocol of the study was approved by the 2nd Local Ethical Committee for Experiments on Animals in Wroclaw (decision no. 23/2011).

2.2. Measurements and analyses

Heparinized jugular venous blood samples were collected anaerobically, and acid–base parameters were determined using a VetStat analyzer (Idexx, USA). The plasma concentrations of sodium, potassium, chloride, calcium, magnesium, inorganic phosphorous, albumin, and lactate were measured with a Pentra 400 analyzer (Horiba ABX, France). The anion gap (AG) was calculated as follows (3,8):

$AG = ([Na^+] + [K^+]) - ([HCO3^-] + [Cl^-])$

In the strong ion model, the acid–base balance was determined on the basis of the strong ion difference (SID), total plasma concentration of nonvolatile buffers (A_{Tot}), effective strong anion difference (SID_{Eff}), and strong ion gap (SIG), calculated according to the following formulas (8,9):

$SID_3 = [Na^+] + [K^+] - [Cl^-]$,

$SID_7 = ([Na^+] + [K^+] + [Mg^{2+} + [Ca^{2+}]) - ([Cl^-] + [lactate])$,

A_{Tot} = [albumin in g/dL] × [0.123 × pH – 0.631] + [P in mmol/L × {pH – 0.469}],

$SID_{Eff} = 2.46 \times 108 \times pCO_2/10\ pH + A_{Tot}$,

$SIG = SID_7 - SID_{Eff.}$

2.3. Statistical analysis

The results were subjected to statistical analysis with Statistica ver. 10 software. The significance of intergroup differences in the analyzed parameters was verified using Duncan's post-hoc test. The correlation analysis between the serum lactate and anion gap and strong ion approach parameters was carried out with Pearson's test and simple linear regression analysis.

3. Results

All the calves with diarrhea presented with loose, yellow or gray-yellow stools, and normal or slightly decreased rectal body temperature (with a mean of 38.6 °C and a range of 37.8–38.9 °C). Animals from group II were weak, not able to stand, but continued to nurse. Nine calves presented with more than 5% dehydration.

The acid–base balance parameters of the study calves, estimated with the Henderson–Hasselbach equation, are presented in Table 1. The pH, plasma partial pressure CO_2 (pCO_2), and concentrations of HCO_3^- of calves with diarrhea were significantly lower ($P < 0.01$) than those in the controls. The highest lactate concentration (5.49 mmol/L) was documented in calves from group II (animals with chronic diarrhea). The calves from group II showed significantly lower plasma concentrations of chloride and phosphorus and significantly higher potassium. Diarrheic animals had significantly higher anion gap values and corrected anion gap values than healthy animals ($P < 0.01$).

The acid–base balance parameters of the strong ion model are presented in Table 2. The diarrheic calves presented with significantly higher SID_3 ($P < 0.01$), SID_7 ($P < 0.01$), and SIG ($P < 0.01$) values than animals from the control group, whereas A_{Tot} ($P < 0.01$) and SID_{Eff} ($P < 0.01$) were significantly lower.

Table 3 shows the association between serum lactate and the anion gap and parameters of the strong ion approach for healthy and diarrheic calves. Data analysis showed that the anion gap ($r = 0.684$, $P < 0.01$, Figure 1), SID_3 ($r = 0.718$, $P < 0.01$), SID_7 ($r = 0.494$, $P = 0.03$), and SIG ($r = 561$, $P = 0.01$, Figure 2) correlated with lactate concentrations in group II (diarrheic calves). In addition, there was a negative correlation between SID_{Eff} and lactate parameters in this group ($r = –0.499$, $P = 0.02$), and between lactate and A_{Tot} ($r = –0.361$, $P = 0.04$). The anion gap and the Stewart model parameters did not correlate with blood serum lactate in healthy calves.

Table 1. Mean values of acid–base balance parameters (classic model) and electrolytes level in calf blood.

Parameters	Group I (control) Mean ± SD	Group II (diarrhea) Mean ± SD	P-value
pH	7.38 ± 0.04	7.27 ± 0.08	<0.01
pCO_2 kPa	5.93 ± 0.41	4.99 ± 0.61	<0.01
$HCO3^-$ (mmol/L)	26.65 ± 1.92	23.73 ± 1.85	<0.01
BE (mmol/L)	0.73 ± 1.12	–2.11 ± 2.01	<0.01
Na (mmol/L)	138.28 ± 2.9	136.55 ± 3.12	0.17
K (mmol/L)	4.69 ± 0.31	5.01 ± 0.54	<0.01
Cl (mmol/L)	102.99 ± 3.61	96.12 ± 4.15	<0.01
Albumins (g/L)	28.36 ± 1.94	25.13 ± 2.22	0.29
Lactate (mmol/L)	1.03 ± 0.40	5.49 ± 2.58	<0.01
Mg (mmol/L)	0.83 ± 0.11	0.84 ± 0.12	0.39
Ca (mmol/L)	2.27 ± 0.18	2.29 ± 0.31	0.40
P (mmol/L)	1.68 ± 0.21	1.46 ± 0.28	<0.01
AG (mmol/L)	13.24 ± 3.76	23.01 ± 3.15	<0.01

Table 2. Mean values of acid–base balance parameters of the strong ion approach.

Parameters	Group I (control) Mean ± SD	Group II (diarrhea) Mean ± SD	P-value
SID_3 (mmol/L)	39.89 ± 2.32	46.90 ± 3.19	<0.01
SID_7 (mmol/L)	41.39 ± 2.46	44.02 ± 3.75	<0.01
A_{Tot} (mmol/L)	11.83 ± 0.49	10.83 ± 0.99	<0.01
SID_{Eff} (mmol/L)	36.27 ± 1.79	33.06 ± 1.93	<0.01
SIG (mmol/L)	2.40 ± 3.71	10.96 ± 3.11	<0.01

Table 3. Correlation coefficients between serum lactate concentrations and the anion gap (AG) and the strong ion approach.

Parameters		Group I (control)	Group II (diarrhea)
AG	r P-value	–0.032 0.894	0.684 <0.01
SID_3	r P-value	0.138 0.561	0.718 <0.01
SID_7	r P-value	–0.001 0.993	0.494 0.03
A_{Tot}	r P-value	–0.334 0.149	–0.361 0.04
SID_{Eff}	r P-value	–0.054 0.820	–0.499 0.02
SIG	r P-value	0.037 0.873	0.561 0.01

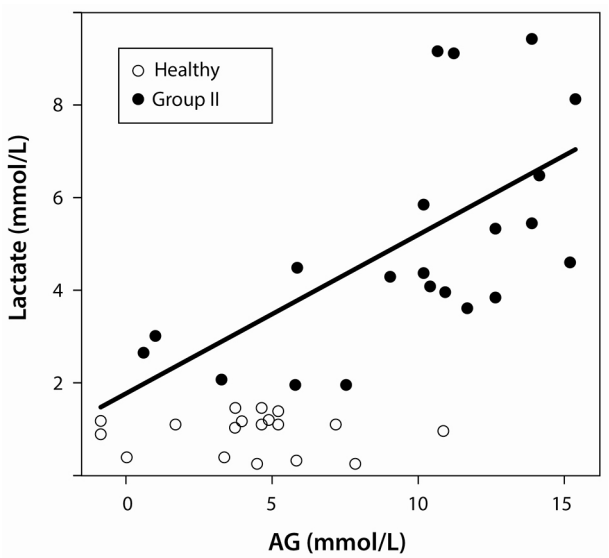

Figure 1. Relationship between the anion gap (AG) and serum lactate with the least squares line for group II (calves with diarrhea). y = 0.34 x +1.25, r = 0.684, n = 20, P < 0.01.

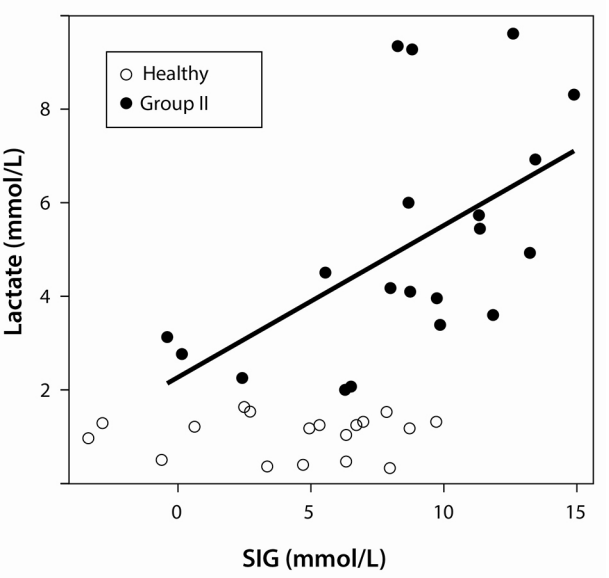

Figure 2. Relationship between SIG and serum lactate with the least squares line for group II (calves with diarrhea). y = 0.32 x +2.29, r = 0.561, n = 20, P < 0.01.

4. Discussion

The analysis of gasometrical and biochemical parameters in the blood is an important tool in evaluating acid–base disturbances. Metabolic acidosis is diagnosed based on decreases in pH, blood bicarbonate, and base excess, which are accompanied by an increased anion gap. Blood electrolytes and serum organic acids may be helpful in diagnosing the type of acidosis (4,8,9). One of them is lactic acidosis. This specific type of acidosis is associated with high lactate concentrations found in the blood (6,9).

The analysis based on the classic model of blood pH and other acid–base balance parameters of calves with diarrhea indicated a mild metabolic acidosis (3,14,15). This type of disorder was considered due to a reduction in pH (reference value: 7.32–7.44) and a negative value of BE (1,16). Our results correspond to commonly reported findings of decreased HCO^-_3 and chloride, and increased potassium. However, the concentrations of $HCO3^-$ and BE indicated the beginning of a compensation process. The calves with diarrhea (group II) presented with significantly lower concentrations of chloride than the controls. Contrary to the calves from group II, in acute diarrhea hyponatremia (Na^+ is usually below reference value: 132–152 mmol/L) and hyperchloremia or normochloremia (reference value: 97–111 mmol/L) are observed (12,16). However, previous studies documented a decrease in plasma Cl^- concentrations of diarrheic calves (17), especially in animals with severe diarrhea (18). The etiology of hypochloremia observed in our calves might be heterogeneous, i.e. resulting from many alimentary disorders, abomasal atony, vomiting, or lack of chloride reabsorption in the distal segment of the alimentary tract (19). The decrease in Cl^- concentration may also represent a compensatory mechanism for prolonged acidosis associated with high concentrations of organic anions, like elevated levels of lactate (20,21).

The levels of lactate in healthy animals were consistent with typical values for calves, which vary between 0.5 and 2.0 mmol/L (5). The mean concentration of lactate in the group with prolonged diarrhea (5.49 mmol/L) was typical for advance lactic acidosis (>4.0 mmol/L) (5,6,21). However, the lactate concentration measured using a nonstereospecific assay could not explain whether the examined calves had elevated blood concentrations of L-lactate or/and D-lactate (10).

Anion gap values obtained for the control group were consistent with AG values in the literature (9,10,16,19). The calves with diarrhea presented significantly higher anion gaps than the controls. Elevated anion gap acidosis in calves with alimentary disorders generally was due to overproduction of organic acids. The most common anions found in such cases were lactate and keto acids (5,6,10). The results of our study indicate that AG correlated with lactate concentrations in serum only in the group of calves with diarrhea. This finding was consistent with a previous finding that DL-lactate was significantly correlated with AG in diarrheic neonatal calves (10). This association was not observed in the group of healthy calves. A study by Ewaschuk et al. (10) indicated that AG significantly correlated with D-lactate, while another study (9) showed a correlation with serum L-lactate concentrations.

The analysis based on the strong ion model of animals from group II revealed elevated values of SID_3 and SID_7, accompanied by a decrease in A_{Tot} and SID_{Eff}. These findings correspond to a compensated acid–base disorder with a shift towards the alkaline side. Elevated SID parameters indicated a strong anion alkalosis, partly caused by lower concentrations of chloride. SID alkalosis was observed in some calves with diarrhea by Gomez et al. (3), assuming the values 38–46 mmol/L provided by Constable (12) as normal values for calves. Moreover, in group II, SID_3 was higher than in the control group. This finding confirmed the significant influence of lactate concentration on the strong ion difference (3,12). Decreased A_{Tot} indicated a nonvolatile buffer ion alkalosis, most probably due to decreases in plasma concentrations of phosphate and albumin (12). Elevated SIG points to a difference between the sum of all strong cation concentrations and the sum of all measured anion concentrations (chloride, lactate, albumins, phosphate, and HCO_3^-), resulting from the presence of elevated concentrations of unmeasured strong ions, such as fatty acids, keto acids, and sulfate (20,22,23). SIG estimated for healthy calves by Constable is from 3 to –3 mmol/L (3,12). The described disturbance in the strong ion approach was contrary to a previous finding in calves with diarrhea, where A_{Tot} was elevated, while SIG was significantly lower than the reference value (3). Our study showed that the parameters of the strong ion approach (SID and SIG) correlated with concentrations of lactate similarly to AG. Moreover, the observed negative correlation between A_{Tot}, SID_{Eff}, and lactate indicated a compensation of lactic acidosis, by decreases in nonvolatile buffers and bicarbonate concentrations. However, the described associations were observed only in diarrheic calves. These results indicated that in lactic acidosis there were specific disturbances with increased concentrations of unmeasured strong ions detected by the calculation of the SIG. The classic model in this case was useful for describing and classifying acid–base disorders, whereas the strong ion approach (SID, A_{Tot}, and SIG) was more useful for quantifying and explaining these disorders.

Acidosis in calves with diarrhea is due predominantly to a strong ion acidosis in response to hyponatremia accompanied by normochloremia or hyperchloremia (3,4,12). Therefore, a highly effective SID solution (sodium bicarbonate) is used to correct this acid–base disturbance, the strong ion acidosis (decrease of SID). Our data suggest that the presented cases of diarrhea can be treated with an isotonic solution of NaCl, except for treatment of calves with hyperkalemia. In the case of lactic acidosis, the liver metabolizes the circulating lactate (21).

In conclusion, the characterization of acid–base disturbances in cases of lactic acidosis in prolonged diarrhea showed that the classic model has some limitations. Using the strong ion approach, we found the presence of more than one acid–base disturbance and increased concentrations of unmeasured strong ions detected by the calculation of the SIG.

Acknowledgment

This study was performed within the research project No. N N308 575439 funded by the Polish Ministry of Science and Higher Education.

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