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Traditional and Quantitative Assessment of Acid-Base and Shock Variables in Horses with Atypical Myopathy

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Background: Descriptions of acid-base disturbances in atypical myopathy (AM) are limited.

Objectives: Describe and compare traditional and quantitative acid-base abnormalities and cardiovascular shock status in horses with AM at admission.

Animals: 34 horses with AM, 15 healthy controls.

Methods: Retrospective case-control study. Records were searched for shock variables (packed cell volume [PCV], blood urea nitrogen [BUN], heart and respiratory rate) and acid-base variables (venous blood gas analysis, electrolytes, total protein, lactate) on admission. Base excess (BE) of free water (BEfw), chloride (BEcl), total protein (BEtp), and unidentified anions (BEua), anion gap (AG), measured strong ion difference (SIDm), and concentration of total nonvolatile weak acids ([Atot]) were calculated. Acid-base classifications, using simplified strong ion model and traditional approach, and shock grades were assigned. A 2-sample Wilcoxon rank-sum test and Bonferroni correction compared variables in AM cases versus control horses. Significance was $P < .05/16$ for acid-base and $P < .05/5$ for shock variables.

Results: Tachycardia, tachypnea, and normal to increased PCV and BUN were common in AM cases. Respiratory, metabolic acid-base alterations, or both were mainly caused by respiratory alkalosis, lactic acidosis, and SIDm alkalosis, alone or in combination. Evaluated variables (except pH, potassium concentration, total protein, and related calculations) were significantly different ($P < .001$) between AM cases and control horses. The strong ion model provided a more accurate assessment than the traditional approach and identified mixed derangements.

Conclusions and clinical importance: Acid-base derangements should be evaluated in horses with AM and this preferably with the strong ion model.

Key words: Acid-base balance; Electrolytes; Equine; Neuromuscular disorders; Shock.

Atypical myopathy (AM) is an acute myopathy occurring in grazing horses, considered an emerging condition in Europe,[1] but also described in the USA.[2,3] In other acute rhabdomyolytic conditions in horses, acid-base and electrolyte disturbances have been described.[4,5] Theoretically, AM-affected horses might also develop acid-base imbalances because of muscle dysfunction (a "multiple acyl-CoA dehydrogenase deficiency or MADD" like defect[6] and decreased activities of mitochondrial complexes[7]), muscle destruction,[8] and cardiovascular and respiratory compromise.[1,9,10] A better understanding of acid-base disturbances in AM could assist clinicians with supportive treatment. However, limited data on acid-base variables in horses with AM are available.[9,11]

The acid-base status of horses can be assessed with different methods. The traditional approach is based on the Henderson-Hasselbalch equation, and focuses on dependent variables (pH, bicarbonate).[12] The quantitative approach of Stewart's strong ion model provides more insight into the pathophysiology of acid-base derangements accounting for the effects of electrolytes,

Abbreviations:

AG	anion gap
AM	atypical myopathy
AMP	adenosine monophosphate
A_{tot}	total plasma concentration of nonvolatile weak buffers
BE	base excess
BEcl	base excess attributable to chloride
BEfw	base excess attributable to free water
BEtp	base excess attributable to total protein
BEua	base excess attributable to unidentified anions
BUN	blood urea nitrogen
C cases	confirmed cases
Cl^-	chloride
HCO_3^-	bicarbonate
HP cases	cases with a high probability of having AM
K^+	potassium
MADD	multiple acyl-CoA dehydrogenase deficiency
Na^+	sodium
pCO_2	partial pressure of carbondioxide
SD	standard deviation
SIDm	measured strong ion difference
TP	total protein

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unidentified anions (including lactate), and nonvolatile weak buffers on acid-base status, and uses independent variables. Several variants of this quantitative approach have been developed for use in horses.[13,14] We hypothesize that complex acid-base derangements occur frequently in cases of AM; therefore, a quantitative approach will be more useful to recognize derangements than the traditional approach.

The objectives of this retrospective study are to 1) describe the acid-base and cardiovascular shock status of horses suffering from AM on admission, and 2) compare the strong ion model to the traditional approach to assess acid-base status.

Materials and Methods

Cases and Study Design

Thirty-four horses with AM during the period 2006–2010 with a venous blood gas analysis performed on admission were included in this retrospective multicenter study. Cases were either admitted to the equine clinic of Liege University, Belgium (n = 21), the equine clinic of Giessen University, Germany (n = 6), the equine clinic of Ghent University, Belgium (n = 5), or Rossdales and Partners, Newmarket, UK (n = 2). Horses were confirmed (C cases) or strongly suspected of having AM (highly probable - HP cases) as defined in previous studies.[1,15,16] In addition, frozen serum of 3 horses was available and retrospective acylcarnitine analysis allowed identification of the typical MADD-like biochemical defect.[6]

Fifteen research horses from Liege University, considered healthy based on history and clinical examination, were used as control group.The signalment of affected horses and control horses is presented in Table 1.

Collection of Data and Samples, and Sample Analysis

Heart and respiratory rates, rectal temperature, venous pH, partial pressure of carbon dioxide (pCO_2), bicarbonate (HCO_3^-; calculated using the blood gas machine[a,b,c]), base excess (BE; calculated using the blood gas machine), packed cell volume (PCV), blood urea nitrogen (BUN), total protein (TP), and plasma concentrations of sodium (Na^+), chloride (Cl^-), potassium (K^+), and L-lactate on admission were retrieved. A previously reported shock grading system[17] was modified such that lactate concentration (for use as independent variable) and blood pressure (unavailable) were excluded. The shock variables (heart and respiratory rates, PCV, and BUN) recorded on admission were used to attribute a shock grade of 1–4 (Table 2).

Table 1. Signalment of horses with atypical myopathy and of control horses.

	AM Horses (n = 34)	Control Horses (n = 15)
Female	22	10
Gelding	7	3
Stallion	5	2
Pony	7	0
Saddle horse	24	15
Draught horse	3	0
Age (years; mean ± SD)	4.6 ± 4.7 range 1.5 months–17 years	12.5 ± 6.8 range 2–25 years

AM, atypical myopathy; SD, standard deviation; n, number of horses.

In all cases, blood had been collected from the jugular vein on admission. Blood gas analysis was performed directly using an automated blood gas analyzer on blood collected anaerobically in heparinized tubes or syringes. Because of controversy over the need for temperature correction with opponents[18] pointing out that there is no logical or scientific basis for the assumption that temperature-corrected values are better than values obtained at 37°C,[18,19] venous blood gas analyses were not corrected for rectal body temperature.

Blood collected in EDTA tubes was used for PCV measurements using centrifugation of capillary tubes or using automated analyzers,[d,e] Plasma TP was measured using refractometer or using an automated analyzer.[f,g,h] Automatic analyzers measured plasma lactate concentration,[b,i,j] BUN,[b,f,g,h] and concentration of electrolytes.[a,b,c,h]

Calculation of Variables and Classification of Acid-Base Disturbances

The acid-base disturbances were classified following 3 different approaches. First, with use of the traditional approach based on the Henderson-Hasselbalch equation[12] horses were diagnosed with the following imbalances:

- Metabolic acidosis when HCO_3^-, BE, or both were below the reference range
- Metabolic alkalosis when HCO^-_3, BE, or both were above the reference range
- Respiratory acidosis when pCO_2 level was above the reference range
- Respiratory alkalosis when pCO_2 level was below the reference range.

To provide more insight in the cause of acid-base imbalances, taking into account effects of electrolytes, unidentified anions (including lactate) and nonvolatile weak buffers on acid-base status, the quantitative approach of Stewart's strong ion model simplified by Constable was used.[14] Therefore the following variables were calculated:

- Measured strong ion difference (SIDm)

Several equations exist for SIDm, in- or excluding unidentified anions or lactate,[14] but for this study, it was chosen to evaluate

Table 2. The shock grading system adapted from Grulke et al[17] that was used to attribute a shock grade to each horse with atypical myopathy.

	Shock Grade			
Shock Variables	I	II	III	IV
Heart rate (bpm)	<60	60–80	80–100	>100
Respiratory rate (rpm)	<25	25–35	35–45	>45
PCV (%)	<45	45–55	55–65	>65
BUN (mmol/L)	<14	14–20	20–25	>25

PCV, packed cell volume; BUN, blood urea nitrogen.

Note: For each individual horse, a shock grade is determined for each variable (heart rate, respiratory rate, PCV, and BUN). A global shock grade for the horse is then attributed based on the most common or mean shock grade of the 4 variables. If 1 variable is missing, the shock grade for the horse is attributed according the other 3 variables.

lactate separately and to use the following formula for SIDm[14]: SIDm = $(Na^+ + K^+) - Cl^-$.

Lactate was evaluated using lactate measurements and estimated by calculation of the anion gap (AG).[13,20,21]

- AG was calculated with the following formula[22]: AG = $(Na^+ + K^+) - (Cl^- + HCO_3^-)$
- Total plasma concentration of nonvolatile weak buffers (A_{tot}) was calculated with the following formula[14]: $A_{tot} = 2.24 \times TP$ (g/dL)

The more accurate formula for A_{tot}, which considers the concentration of albumin, globulin, and phosphate,[14] could not be used as this data was unavailable in the majority of the cases. With use of this quantitative approach, horses were diagnosed with the following acid-base imbalances[14]:

- Metabolic acidosis when lactate, AG and/or A_{tot} values were above the reference range, and/or SIDm below
- Metabolic alkalosis when SIDm was above the reference range, A_{tot} below, or both
- Respiratory acidosis when pCO_2 level was above the reference range
- Respiratory alkalosis when pCO_2 level was below the reference range.

The reference ranges that were used for the acid-base variables are indicated in Table 3.[14,21,23,24] The agreement on presence or absence of metabolic acid-base derangements between the traditional approach and the simplified strong ion model was assessed.

Thirdly, another quantitative approach, Fencl's application of Stewart's principles, was used to estimate the magnitude of the separate components to metabolic acid-base imbalances. This approach was first described in equine medicine by Whitehair et al[13] and has been demonstrated to have clinical utility.[21] The following variables were calculated:

- Base excess attributable to free water (BEfw):
  BEfw = 0.3 (Na^+ measured−Na^+ normal)
  (Na^+ normal = 140 mmol/L)

- Base excess attributable to chloride (BEcl):
  BEcl = Cl^- normal – ((Cl^- measured × Na^+ normal) / Na^+ measured)
  (Na^+ normal = 140mmol/L, Cl^- normal = 105)

- Base excess attributable to total protein (BEtp):
  BEtp = 0.224 × (TP normal – measured TP measured)
  (TP normal = 67 g/L)

- Base excess attributable to unidentified anions (BEua): BEua = BE measured – (BEfw + BEcl + BEtp). The effect of phosphate on BE could not be calculated as data on phosphate concentrations were unavailable.

Statistical Analysis

Data are reported as mean ± standard deviation (SD), range, and, where appropriate, the number of horses out with reference ranges.[14,21,23,24] Acid-base and shock variables in AM cases were compared to those of control horses using a 2-sample Wilcoxon rank-sum (Mann-Whitney) test. A Bonferroni correction for multiple comparisons was applied. Statistical significance was defined as $P < .05/k$, with k being the number of comparisons made. Because of the low overall survival rate, a statistical comparison could not be performed between survivors and nonsurvivors.

Results

Four cases survived AM (2 from Liege University, 1 from Ghent University, and 1 from Rossdales and Partners) and 30 died or were euthanized (survival rate 12%). Cases commonly presented with tachycardia, tachypnea, normal to increased PCV, and BUN on admission. They were hypo- (12 cases), normo- (19 cases), or hyperthermic (3 cases) (37.2 ± 1.1°C, range 34.6–40.5°C). Horses were attributed a shock grade I (n = 10), II (n = 19), or III (n = 5). None of the AM cases were attributed a shock grade of IV. The blood pH was variable (Table 3 and 4). Sodium, chloride, and potassium derangements were common, and although mostly mild, they led in the majority of cases to an increased SIDm. Of the 3 considered electrolytes, acid-base status was mostly affected by chloride. Only 1 horse had a combination of hyponatremia, hypochloremia, and hyperkalemia. All affected horses had a mild-to-severe increase in AG and the majority an increased plasma lactate concentration and decreased BEua. Four horses had mildly elevated AG, but normal lactate concentrations. The majority of horses had normal TP concentrations, A_{tot} and BEtp values, and if deviations occurred they were mild. When hyperproteinemia occurred, it was always together with high PCV; however, not all cases with high PCV had increased TP. BUN often, but not always, paralleled increases in PCV.

Acid-base disturbances classified by the traditional approach and the simplified strong ion model are listed in Table 5. The only 2 cases classified with respiratory acidosis had metabolic acidosis at the same time and were shortly euthanized after arrival. The 2 classification systems showed poor agreement on the presence of acid-base derangements. Nine cases classified as having no derangements according to the traditional approach, had mild lactic acidosis (2 cases), lactic acidosis and SIDm alkalosis (5 cases) and lactic acidosis, A_{tot} acidosis and SIDm alkalosis (1 case) according to the simplified strong ion model. Of the ninth case without acid-base abnormality following the traditional approach, not enough data were available to perform the full quantitative analysis of the simplified strong ion model.

The pCO_2, HCO_3^-, BEfw, BEua, sodium concentration, and chloride concentration were significantly lower in cases compared with controls, and heart rate, respiratory rate, PCV, BUN, lactate concentration, AG, SIDm, and BEcl significantly higher (Table 3 and 4).

The 4 survivors appeared to have a lower BEcl (3.0 ± 0.3 mEq/L versus 8.5 ± 5.4 mEq/L), PCV (38.2 ± 6.6% versus 47.4 ± 7.4%), and BUN (6.2 ± 3.6 mmol/L versus 9.3 ± 3.8 mmol/L) and higher chloride concentration (102 ± 2.8mmol/L versus 94 ± 7.7 mmol/L) compared to nonsurvivors, but the small sample size precluded statistical analysis.

Discussion

This study confirms that horses suffering from AM frequently have acid-base derangements on admission.

Table 3. Acid-base variables from horses with atypical myopathy on admission and from healthy control horses.

		Cases (n=34)					Controls (n=15)		Comparison AM versus Control
Acid-Base Variable	Reference Value[14,21,23,24]	Mean ± SD	Range	n	Number above Reference Range	Number below Reference Range	Mean ± SD	Range	*P* Value (Significance $P < .05/k$; $k = 16$)
pH	7.31–7.45	7.36 ± 0.09	7.14–7.56	34	3	7	7.40 ± 0.02	7.38–7.44	.092
pCO_2 (mmHg)	41–53	40.1 ± 8.0	26.3–62.0	34	2	17	46.1 ± 2.3	42.2–50.2	<.001*
HCO_3^- (mmol/L)	24–30	22.0 ± 4.4	9.5–29.9	34	0	22	28.2 ± 0.98	26.1–30	<.001*
BE total (mEq/L)	−6–+6	−3.1 ± 4.7	−16.7–3.9	34	0	9	2.8 ± 1.1	0.6–4.5	<.001*
Na^+ (mmol/L)	134–144	136.5 ± 6.0	124–148	32	3	9	142.3 ± 2.7	136–147	<.001*
BEfw (mEq/L)	X	−1.1 ± 1.8	−4.8–2.4	32	X	X	0.7 ± 0.8	−1.2–2.1	<.001*
Cl^- (mmol/L)	100–110	94.7 ± 7.7	76–105	27	0	19	106 ± 2.4	100–110	<.001*
BEcl (mEq/L)	X	8.1 ± 5.4	0.3–27.3	27	X	X	0.7 ± 2.3	−3.1–4.2	<.001*
K^+ (mmol/L)	2.5–4.5	4.0 ± 0.5	2.8–5.1	32	3	0	3.8 ± 0.5	2.8–4.6	.235
SIDm (mmol/L)	38–44	46.0 ± 5.0	38.4–65.5	27	18	0	40.1 ± 2.8	34.9–44.2	<.001*
TP (g/L)	60–75	65.6 ± 7.5	43–78	31	3	4	67.6 ± 4.3	60–72	.878
BEtp (mEq/L)	X	0.3 ± 1.7	−2.5–5.4	31	X	X	−0.1 ± 1.0	−1.1–1.6	.878
A_{tot} (mEq/L)	13–17	14.7 ± 1.7	9.6–17.5	31	1	3	15.1 ± 1.0	13.4–16.1	.878
BEua (mEq/L)	X	−10.8 ± 6.1	−23.4–−2.6	26	X	X	1.5 ± 2.8	−4.2–5.2	<.001*
AG (mmol/L)	6–15	24.2 ± 6.1	15.1–38.3	27	27	0	12.0 ± 2.8	6.6–17.3	<.001*
lactate (mmol/L)	<2	6.7 ± 4.4	0.8–18.7	24	19	0	0.8 ± 0.6	LOW–2.2	<.001*

X, no reference range available; SD, standard deviation; n, number of horses; pCO_2, partial pressure of venous carbon dioxide; HCO_3^-, bicarbonate; BE, base excess; Na^+, sodium; BEfw, base excess attributable to free water; Cl^-, chloride; BEcl, base excess attributable to chloride; K^+, potassium; SIDm, measured strong ion difference; TP, total protein; BEtp, base excess attributable to total protein; A_{tot}, total plasma concentration of nonvolatile weak buffers; BEua, base excess attributable to unidentified anions; AG, anion gap;

*significant difference.

Table 4. Shock variables and shock grades from horses with atypical myopathy on admission and from healthy control horses.

		Cases (n = 34)					Controls (n = 15)		Comparison AM versus Control
Shock Variable	Reference Value	Mean ± SD	Range	n	Number above Reference Range	Number below Reference Range	Mean ± SD	Range	*P* Value (Significance P < .05/*k*; *k* = 5)
HR (bpm)	<45	65 ± 18.5	36–112	34	30	0	36 ± 6.1	28–44	<.001*
RR (rpm)	<25	29.6 ± 12.7	8–62	32	20	0	19.5 ± 4.0	16–24	<.001*
PCV (%)	30–45	46.3 ± 7.8	30–62	34	22	0	35.1 ± 2.3	31–38	<.001*
BUN (mmol/L)	2–8	8.9 ± 3.8	1.9–18.7	27	15	1	4.8 ± 1.1	3.2–6.8	<.001*
Shock grade	1	1.9 ± 0.7	1–3	34	24	0	1 ± 0	1	<.001*

SD, standard deviation; n, number of horses; HR, heart rate, RR, respiratory rate; PCV, packed cell volume; BUN, blood urea nitrogen;

*significant difference.

They are often mixed and therefore not necessarily resulting in altered blood pH (acidemia or alkalemia). Metabolic acidosis in AM is demonstrated to be mainly the result of changes in serum concentrations of lactate and electrolytes (SIDm), as lactic acidosis was the most notable finding followed by SIDm alkalosis, whereas nonvolatile weak buffers (A_{tot}) do not seem to have major impact. Massive cell destruction is known to cause electrolyte abnormalities, more specifically, the combination of hyponatremia, hypochloremia and hyperkalemia, caused by the release of intracellular constituents.[5,20,21,25] Even though expected to occur in AM cases caused by severe rhabdomyolysis, this combination was only encountered in a single case in the current study. In a study on acid-base and electrolyte derangements in horses with exertional myopathy, hypochloremia was the most consistent electrolyte abnormality,[4] as was the case in the current study. Although probably not systematically present in all affected cases, other theoretical causes of electrolyte derangements in AM are 1) electrolyte losses via excessive sweating, saliva, or both[1,9,21,26] and 2) renal dysfunction.[1,27] Increased BUN was indeed reported in several cases in the current study. Further assessment of renal function was not performed. False hyponatremia and -chloremia can also occur in the face of hyperglycemia and hyperlipemia,[28] which are regularly encountered in AM.[9] Unfortunately, phosphate and calcium could not be evaluated in this retrospective

Table 5. Acid-base imbalances identified in 34 horses affected by atypical myopathy (AM) classified with the traditional approach and the simplified strong ion model.

	Acid-Base Imbalance	n	N	%
Traditional approach	No imbalance	9	34	26
	Metabolic acidosis	6	34	18
	Metabolic alkalosis	0	34	0
	Respiratory acidosis	0	34	0
	Respiratory alkalosis	3	34	9
	Metabolic acidosis + respiratory alkalosis	14	34	41
	Metabolic acidosis + respiratory acidosis	2	34	6
Simplified strong ion model	Incomplete data for this quantitative approach	8*	34	24
	No imbalance	0	26	0
	Lactic acidosis	4	26	15
	Lactic acidosis + SIDm alkalosis	8	26	31
	Lactic acidosis + SIDm alkalosis + A_{tot} alkalosis	1	26	4
	Lactic acidosis + SIDm alkalosis + A_{tot} alkalosis + respiratory alkalosis	1	26	4
	Lactic acidosis + SIDm alkalosis + respiratory alkalosis	4	26	15
	Lactic acidosis + SIDm alkalosis + respiratory acidosis	2	26	8
	Lactic acidosis + SIDm alkalosis + A_{tot} acidosis	1	26	4
	Lactic acidosis + A_{tot} alkalosis	1	26	4
	Lactic acidosis + respiratory alkalosis	4	26	15

N, number of total response for each category; n, number of positive response for each category; SIDm, measured strong ion difference; A_{tot}, total plasma concentration of nonvolatile weak buffers.

*For the horses without a complete quantitative analysis because of lacking data, still 1 or several individual parts of the analysis were assessed, and at least 1 single abnormality in each horse was identified (mostly respiratory alkalosis or lactic acidosis or both). Therefore these horses are not classified as having no abnormalities.

study. Nevertheless, hypocalcemia occurs commonly in AM[9,29] and it should be recognized that hyperphosphatemia can occur after rhabdomyolysis[5] and has been demonstrated in some cases of AM.[9,29–31] Hyperphosphatemia can also contribute to metabolic acidosis.

TP, BEtp, and A_{tot} were demonstrated by the current study to have few effects on acid-base status in AM, but A_{tot} could be underestimated mainly by the effect of hyperphosphatemia. The authors also recognize that TP measurement using refractometer, as used on some of the studied horses, is less precise than the use of automatic analyzers and refractometric results might be falsely increased by hyperglycemia and hyperlipemia.[32]

Lactate concentrations, as well as its estimates AG and BEua, were abnormal in most AM cases. Lactate is typically produced in conditions with tissue hypoxia and cell lysis,[21] which might occur in AM caused by cardiac pathology,[10] cardiovascular shock, hypoventilation,[1,9] and inadequate mitochondrial oxygen utilization in muscles related to MADD[6] and lowered activity of mitochondrial complexes.[7] However, in 4 horses mildly elevated AG was identified with normal lactate concentrations. This difference might indicate hyperproteinemia[13] or increases in other unidentified anions than lactate. As TP was noted to be normal in these 4 cases, it might relate to increases in acyl-carnitines, glycine conjugates, organic acids, and ketone bodies in plasma. Organic acids in plasma are, although, not consistently elevated in AM[6] and the production of ketone bodies is unlikely, however, not excluded in horses.[33]

Both respiratory acidosis and respiratory alkalosis were documented in the current study. Respiratory acidosis can be explained by dyspnea and hypoventilation that is secondary to damage of respiratory muscles as frequently detected at postmortem.[8] Unexpectedly, respiratory acidosis only occurred in 2 horses (together with metabolic acidosis). However, these data were recorded on admission and AM cases often have declining respiratory function, with increasing dyspnea, decreasing arterial oxygen tension,[9] and increasing arterial carbon dioxide tension (personal observation). Both horses with respiratory acidosis in this study were euthanized very shortly after arrival, suggesting respiratory acidosis as poor prognostic factor. Respiratory alkalosis was more commonly observed in this study, and most likely relates to hyperventilation caused by pain or distress, and compensation for metabolic acidosis and anaerobic metabolism.

The survival rate of this study (12%) is lower than in other recent studies (25–26%).[1,15] This is explained by the fact that this study has a different study population, only including referral cases. A previously reported larger epidemiologic study on AM-affected horses identified remaining standing, normothermia normal mucous membranes and fecal output as prognostic indicators associated with survival.[16] Prognosis was considered poor when horses are recumbent, or show sweating, anorexia, dyspnea, tachypnea, tachycardia, or both.[16] Complementary to this, the current study suggests that nonsurvivors have a higher BEcl, PCV, and BUN and lower chloride concentration on admission and that respiratory acidosis is an indicator of poor prognosis. However, as the case numbers of this study were limited, with only very few survivors, a statistical prognostic assessment could not be performed.

The current study demonstrated that BUN was frequently increased on admission in accordance to previous studies,[9,29,30] and suggested it to be higher in nonsurvivors. Also, the presence of renal casts on histology is consistent in AM.[8] Even though only few cases seem to suffer from clinical renal dysfunction,[1] these findings highlight the need for renal monitoring and support in AM patients. It can be suggested that BUN increases as a result of renal damage caused by myoglobinuria.[25,34] However, full renal assessment of the described cases was not available and increased BUN might also be a consequence of dehydration (prerenal azotemia), protein catabolism for gluconeogenesis or deamination of adenosine monophosphate (AMP). Indeed, the current study shows that PCV was frequently increased (hemoconcentration). The possibility of protein catabolism is supported by the finding that a reduced amount of muscle protein was found in another study on AM[7]; increased uric acid excretion in urine suggests that deamination of AMP occurs.[7] It remains, however, unclear if these 2 mechanisms of BUN production would lead to significant rises in serum BUN levels. Other indicators for renal dysfunction, such as creatinine and urine analysis, would be needed to evaluate the significance of elevated BUN, but were unfortunately unavailable in this retrospective study for the majority of the cases.

Previous reports on several equine conditions have demonstrated that quantitative acid-base analysis provides more insight in acid-base pathophysiology and allows diagnosis of mixed metabolic disturbances.[13,23,24] In the same line, the current study points out the importance of using quantitative acid-base analysis over the traditional approach in AM affected horses, especially, because mixed disturbances occurred frequently. Quantitative acid-base assessment allows better identification of disturbances, which is needed to efficiently correct them.

This study is limited by restricted availability of blood biochemistry because of its retrospective nature, the small number of cases, and few survivors. Although AM has been more common in Europe in the past years,[1] it remains a rare condition and thus difficult to generate large and complete data sets. Nevertheless, these data remain important for a better understanding of the condition and help clinicians to adapt treatment for horses suffering from AM. A further limitation is that samples were analyzed in different clinics using different techniques. Small disagreements between data from different clinics might therefore have occurred. Nevertheless, small discrepancies in analysis methods are most likely overshadowed by the importance of the observed derangements in AM cases and the highly significant statistical differences shown by this study between AM cases and controls. In addition, other

studies on acid-base derangements in horses have shown variables of normal healthy horses to be overall pretty consistent with reference values obtained from literature.[13,23,24] This was also the case for our control group, therefore, suggesting that reference ranges from literature can be used without major problems instead of laboratory specific reference ranges. In addition, the variables of the controls cases were measured using the same methods of analyses as the majority of the AM-affected cases.

In conclusion, this study shows that the majority of horses suffering from AM have respiratory or metabolic acid-base alterations or both and that they are better recognized by quantitative than traditional acid-base analysis. In AM patients, alterations are mainly the result of respiratory alkalosis, lactic acidosis, SIDm alkalosis, or both. This study has provided novel insight into the complexity of acid-base derangements in horses affected by AM. Additional research is required to determine the prognostic value of acid-base assessment in overall survival of AM-affected horses.

Footnotes

[a] AVL OMNI Modular system, Roche Diagnostics, Rotkreuz, Switzerland
[b] Roche OMNI S 6, Roche, Mannheim, Germany
[c] IDEXX vet stat, IDEXX Laboratories B.V., Hoofddorp, The Netherlands
[d] Adiva120, Siemens, UK
[e] Haematokrit 24, Hettich Zentrifugen, Tuttlingen, Germany
[f] Spotchem, A. Menarini diagnostics, Zaventem, Belgium
[g] Ilab 600, Instrumentation Laboratory, Cheshire, UK
[h] Fujyfilm Dri-Chem 3500-I, Fujy, Tokyo, Japan
[b] Roche OMNI S 6, Roche
[i] Accutrend Plus, Roche
[j] Accusport, Boehringer Mannheim, Brussels, Belgium

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