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Semiquantitative acid–base analysis in dogs with typical hypoadrenocorticism

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Abstract

Objective: To describe the semiquantitative acid–base status of dogs with untreated naturally occurring typical hypoadrenocorticism and to compare this to the status determined by traditional acid–base analysis.

Design: Retrospective study.

Setting: University teaching hospital.

Animals: Thirty-three dogs with newly diagnosed typical hypoadrenocorticism between 2000 and 2017.

Interventions: None.

Measurements and main results: Dogs were included if they had newly diagnosed hypoadrenocorticism, post-ACTH stimulation serum cortisol concentration <2 μg/dL, and blood collected within 6 hours of presentation for acid–base, electrolyte, and serum biochemical assays. Dogs were excluded if the Na^+:K^+ ratio was ≥28 or the dog had received a mineralocorticoid-containing corticosteroid medication within the preceding month. Traditional acid–base analysis identified normal acid–base status in 1 dog, simple respiratory acid–base abnormalities in 2 of 33 dogs, and simple metabolic acidosis in 14 of 33 dogs. A mixed disorder was most common, noted in 16 of 33 dogs. The semiquantitative approach identified metabolic abnormalities in all cases. All dogs had ≥1 acidifying process, and 29 of 33 had both acidifying and alkalinizing processes. Acidosis attributable to excess free water was present in all dogs, and an acidifying phosphate effect was present in 27 of 33. Hyperlactatemia contributed to the acidosis in 8 of 33 dogs, with a median (range) lactate concentration of 1.5 mmol/L (13.5 mg/dL) (0.3–4.2 mmol/L [2.7–37.8 mg/dL]).

Conclusions: Dogs with untreated Addison's disease have complex acid–base derangements. The semiquantitative approach to acid–base analysis provides greater insight into the underlying mechanisms of metabolic acid–base abnormalities in these dogs, particularly because lactic acidosis appears to be a minor influence in most cases.

Abbreviations: HA, hypoadrenocorticism; SBE, standard base excess

KEYWORDS
Addison's disease, lactate, metabolic acidosis, traditional acid–base analysis

1 | INTRODUCTION

Hypoadrenocorticism (HA), or Addison's disease, is a disease of dogs involving functional failure of the adrenal cortices. Typical HA involves both glucocorticoid and mineralocorticoid insufficiency and can result in acute hypoadrenal crisis with hypovolemia, hyponatremia, hyperkalemia, and metabolic acidosis.[1–4] The metabolic acidosis noted in 40–60%[1,4] of dogs with HA has commonly been attributed to impaired renal hydrogen ion secretion in conjunction with hypovolemia and hypotension resulting in lactic acidosis.[2,5–8] Aldosterone promotes distal nephron hydrogen ion and potassium secretion and, thus, hypoaldosteronism results in type 4 renal tubular acidosis with metabolic acidosis and hyperkalemia.[9–11] Concurrently, hyperkalemia impairs synthesis and excretion of ammonium ions, which further exacerbates the metabolic acidosis.[11,12] Dogs can present in acute hypoadrenal crisis due to hypocortisolemia impairing maintenance of vascular tone and hypoaldosteronism, resulting in failure to maintain normovolemia.[13,14] Hypotension or hypovolemia results in decreased oxygen delivery, onset of anaerobic metabolism, and development of lactic acidosis, which further compounds the metabolic derangement.[15]

The significance of the contribution of lactic acidosis to the metabolic acidosis noted in dogs with HA remains unclear, because 1 study noted a median lactate value within the reference interval.[4] In addition, there are other plausible effects likely contributing to the metabolic acidosis in dogs with HA. Hyperphosphatemia, an acidifying effect,[16] has been documented in nearly 70%[1] of dogs with HA and has been attributed to reduced glomerular filtration rate.[1,14] Hyponatremia, as a marker of increased free water, is another acidifying effect (dilutional acidosis)[17] and has been documented in 81% of dogs with typical HA.[1] The metabolic acidosis in dogs with HA is therefore likely multifactorial and warrants further investigation.

Advanced acid–base analysis can aid in identification of underlying metabolic disorders and, by guiding treatment of acid–base derangements,[18] may improve outcomes. However, advanced acid–base analysis techniques can be burdensome to perform in practice. The 2 methods of acid–base analysis commonly utilized in clinical practice include the traditional and semiquantitative approaches. Criticisms of the traditional approach include its inability to detect complex metabolic acid–base disturbances and the consequent lack of specific guidance on appropriate management of patient metabolic status.[19–22] The semiquantitative approach to acid–base analysis may provide greater insight into the underlying mechanisms of metabolic acid–base disturbances by allowing calculation of the effects of 5 different acid–base processes on standard base excess (SBE). These processes are evaluated through the measurement of changes in serum free water (marked by serum sodium concentration), chloride, albumin, phosphate, and plasma lactate concentrations.[23] Identification of meaningful contributors to patient acid–base status allows for informed fluid therapy selection to curtail and hasten resolution of acid–base derangements.

The primary objective of this study was to characterize the semiquantitative acid–base status of dogs with naturally occurring typical HA. We hypothesized that dogs with naturally occurring HA would have complex metabolic processes contributing to acidosis resulting from acidifying free water, phosphate, and lactate effects.

2 | MATERIALS AND METHODS

The electronic medical records database of the University of California, Davis, William R. Pritchard Veterinary Medical Teaching Hospital was searched for dogs with a clinical diagnosis of "Addison's disease" or "Hypoadrenocorticism" between January 2000 and December 2017 that also had a serum cortisol concentration measured. The inclusion criteria included a new diagnosis of typical HA and post-ACTH stimulation serum cortisol <2 μg/dL.[13] Cases were excluded if the Na^+:K^+ ratio was ≥28,[13] a diagnosis had been made prior to presentation, the medical record indicated that the dog had received mineralocorticoid-containing medication within 30 days of presentation, there was no acid–base and electrolyte or chemistry panel drawn within 6 hours of presentation, or if the HA was iatrogenic. Information from medical records was recorded on a standardized data collection sheet.

Demographic data including age, sex, reproductive status, weight, and breed were recorded. The medical records were searched for the following complaints based on previously noted association with canine HA in the veterinary resources: weakness, lethargy, vomiting, decreased appetite, diarrhea, weight loss, trembling, polyuria/polydipsia, collapse, and seizures.[8,13,14] Physical examination findings including vital parameters as well as the presence of abdominal pain, obtundation, bradycardia, hypovolemic shock, hypothermia, and varying degrees of dehydration were documented.[7,13,14]

Clinicopathologic data collected included the results of a serum biochemistry panel within 6 hours of presentation as documented in the medical record and a contemporaneous venous acid–base and electrolyte panel. At our institution, heparinized blood samples are measured for acid–base parameters, electrolyte concentrations, and glucose and plasma lactate concentrations immediately after sample collection using a point-of-care blood gas analyzer.[*,†,‡] Blood samples for serum biochemistry panels are collected into sterile glass tubes containing no anticoagulant and are submitted to the diagnostic laboratory for analysis using an automated biochemistry analyzer[§,**] within 12 hours of sample collection. It is hospital protocol that samples collected while the diagnostic laboratory is closed are centrifuged immediately and the serum refrigerated at 4°C pending laboratory

TABLE 1 Formulas for semiquantitative acid–base analysis[19]

Parameter	Formula
Free water effect	0.25 × (measured [Na^+] – mid-normal [Na^+])
Corrected chloride	Measured [Cl^-] X (mid-normal [Na^+]/measured [Na^+])
Chloride effect	Mid-normal [Cl^-] – corrected [Cl^-]
Phosphate effect	0.58 × (mid-normal [phosphorus] – measured [phosphorus])
Albumin effect	3.7 × (mid-normal [albumin] – measured [albumin])
Lactate effect	−1 × measured [lactate]
Sum of effects	Sum = Free water effect + chloride effect + phosphate effect + albumin effect + lactate effect
Unmeasured anion (XA) effect	XA = Base excess – sum of effects

Note. Mid-normal values were determined as the central value of the reference interval. Albumin, g/dL; phosphorus, mg/dL; electrolytes and lactate, mmol/L.

submission. Serum sodium and potassium concentrations from the serum biochemistry panel were utilized to calculate the Na^+:K^+ ratio. Serum electrolytes (Na^+ and Cl^-), minerals (phosphorous), and proteins (albumin) required for semiquantitative analysis were obtained for the serum biochemistry panel, with the plasma lactate concentration taken from the point-of-care acid–base and electrolyte panel. The blood gas, acid–base, and electrolyte panel values (pH, HCO_3^-, $PvCO_2$, SBE, Na^+, Cl^-, and K^+) were used for the traditional acid–base analysis and calculation of the anion gap.

2.1 | Acid–base analysis

Bicarbonate concentration and SBE were calculated by the analyzer using the Henderson–Hasselbalch and van Slyke equations, respectively. The value for CO_2 solubility in plasma used by the blood gas machine was 0.03 mmol/L/mm Hg. Calculated acid–base variables were derived from measured acid–base, electrolyte, and metabolite values using previously established equations (Table 1).[19] For the purposes of acid–base calculations, serum phosphate and albumin concentrations were measured in mg/dL and g/dL, respectively, whereas serum electrolyte and plasma lactate concentrations were measured in mmol/L. The metabolic acid–base diagnosis of each dog was determined using the traditional and semiquantitative approaches, as outlined in Table 2.[19] The anion gap reference interval of 11.9–23.5 mmol/L (11.9–23.5 mEq/L) in venous canine blood established by Vanova et al was used for further classification of metabolic acidosis by anion gap.[24] The mid-normal values utilized in the semiquantitative formulae were determined as the central values of the appropriate reference interval for the machine used. Given that local reference intervals for blood gas and acid–base variables were not available for all point-of-care blood gas analyzers used during the study period, comparisons were made to previously published values.[24]

2.2 | Statistical methods

Due to the small number of dogs included in the study, descriptive statistics were used, and all data are presented as median (range).

3 | RESULTS

A total of 33 dogs satisfied all of the study criteria. All 33 dogs survived to discharge with a median duration of hospitalization of 2 days (1–8 days). The median age was 5 years (<1–12), and the median body weight was 26 kg (2.2–66.4). There were 16 neutered males, 2 intact females, and 15 neutered females. Thirty-six percent were mixed breed dogs (n = 12), with 17 pure breeds represented. The most common purebred dogs were Labrador Retrievers (n = 3; 9%), Miniature Pinschers (n = 2; 6%), and German Shorthaired Pointers (n = 2; 6%). Historical complaints included decreased appetite (n = 27; 82%), lethargy (n = 25; 76%), vomiting (n = 20; 60%), diarrhea (n = 11; 33%), weakness (n = 10; 30%), and collapse (n = 10; 30%). Physical examination abnormalities included obtundation (n = 24; 73%), hypothermia (n = 14; 42%), mild to moderate dehydration (n = 12; 36%), and bradycardia (n = 10; 30%). Sixty-four percent of dogs received shock crystalloid fluid resuscitation, and 33% were administered a dextrose bolus during stabilization. Summary acid–base, electrolyte, and lactate values for the whole population are shown in Table 3. Traditional acid–base analysis revealed an abnormality in 32 of 33 cases, with simple respiratory acid–base abnormalities in 2 cases and simple metabolic acidosis present in 14 cases (Table 4). A mixed disorder of metabolic and respiratory acidosis was found in 14 of 33 dogs, and 2 of 33 had metabolic acidosis with respiratory alkalosis. The anion gap could not be calculated in 2 dogs due to missing chloride values on the point-of-care acid–base and electrolyte panel. Of the 31 dogs in which anion gap was calculated, all were found to be within the reference interval.

The semiquantitative approach identified metabolic acid–base abnormalities in all 33 cases. One dog had 1 acidotic process, 11 of 33 had 2 acidotic processes, 18 of 33 had 3 acidotic processes, 1 of 33 had 4 acidotic processes, and 2 of 33 had 5 acidotic processes. Coexisting alkalotic processes were noted in 29 of 33 dogs. The most common abnormalities were dilutional acidosis (33/33), an acidotic phosphate effect (27/33), and increased unmeasured anions (18/33) (Table 5). Lactic acidosis was evident in 8 of 33 dogs, with a median plasma lactate concentration of 1.5 mmol/L (13.5 mg/dL) (0.3–4.2 mmol/L [2.7–37.8 mg/dL]). The most common alkalinizing effect was hypoalbuminemia (21/33), followed by an alkalinizing chloride effect (5/33).

4 | DISCUSSION

This study found that the semiquantitative acid–base approach identified the presence of multifactorial metabolic acid–base abnormalities in dogs with untreated typical HA. The semiquantitative acid–base approach diagnosed coexisting metabolic acidotic and alkalotic processes in many dogs. Although many of the abnormalities identified with the semiquantitative approach were minor, recognition

TABLE 2 Diagnostic criteria for traditional and semiquantitative acid–base analysis[19,24]

Traditional acid–base analysis	Semiquantitative acid–base analysis
1. Simple disturbances a. Metabolic acidosis: pH < 7.32, HCO_3^- < 18 mmol/L, $Pvco_2 = 40 - (\Delta HCO_3^- \times 0.7) \pm 3$ ΔHCO_3^- = Mid-normal HCO_3^- [22 mmol/L] – Measured HCO_3^- b. Metabolic alkalosis: pH > 7.43, HCO_3^- > 26 mmol/L, $Pvco_2 = 40 + (\Delta HCO_3^- \times 0.7) \pm 3$ ΔHCO_3^- = Mid-normal HCO_3^- [22 mmol/L] – Measured HCO_3^- c. Respiratory acidosis: pH < 7.32, $Pvco_2$ > 45 mm Hg, $HCO_3^- = 22 + (0.15–0.35 \times \Delta Pco_2) \pm 2$ d. Respiratory alkalosis: pH > 7.43, $Pvco_2$ < 37 mm Hg, $HCO_3^- = 22 - (0.25–0.55 \times \Delta Pvco_2) \pm 2$ $\Delta Pvco_2$ = Mid-normal $Pvco_2$ [41 mm Hg] – Measured $Pvco_2$ 2. Mixed disturbances Response in the secondary system not within predicted range 3. Metabolic acidosis further classified by anion gap: AG = $(Na^+ + K^+) - (HCO_3^- + Cl^-)$ High anion gap metabolic acidosis: AG > 23.5 mmol/L (23.5 mEq/L)	Free water effect: • Dilutional acidosis: Free water effect < −1.25 mmol/L • Contraction alkalosis: Free water effect > 1.0 mmol/L Chloride effect: • Acidosis: Chloride effect < −5.0 mmol/L • Alkalosis: Chloride effect > 5.0 mmol/L Albumin effect: • Acidosis: Albumin effect < −2.0 mmol/L • Alkalosis: Albumin effect > 2.0 mmol/L Phosphorus effect: • Acidosis: Phosphorus effect < −1.0 mmol/L • Alkalosis: Phosphorus effect > 1.0 mmol/L Lactate effect: • Acidosis: Lactate effect < −2.0 mmol/L Unmeasured anions effect: • Unmeasured acids: XA – 0.5 mmol/L • Unmeasured alkalis: XA > 0.5 mmol/L

of these individual processes may enhance understanding of acid–base pathophysiology and help guide treatment.

The study population signalment is well aligned with previous reports,[1,2,4] with young to middle-aged dogs, females, and mixed breed dogs most commonly affected. This study identified the nonspecific complaints typical of hypoadrenal dogs with decreased appetite, lethargy, gastrointestinal disturbance, and weakness noted in expected frequencies.[3,25] The dogs in this study also exhibited the anticipated physical examination abnormalities.[13,14,26] The presentation of acute Addisonian crisis was also represented, with two-thirds of dogs receiving volume resuscitation. The spectrum of presentation severity represented by this patient cohort enhances the generalizability of our acid–base analysis findings.

Metabolic acidosis was more common in this study than previously reported,[1,4] being identified in 90% and 100% of untreated hypoadrenal dogs by traditional and semiquantitative acid–base analysis, respectively. This may be because this is the first study to the authors' knowledge to specifically evaluate the acid–base status of these patients or suggest a greater severity of illness in our study population. Although illness severity scoring was not performed due to the retrospective nature of this study, the incidences of historical complaints and physical examination abnormalities suggest our dogs are similar to previously studied cohorts. Aldosterone is important in renal handling of acid because it promotes renal sodium reabsorption, which increases renal tubular lumen negativity and subsequently promotes hydrogen ion and potassium excretion. In addition, aldosterone directly drives hydrogen ion excretion by increasing the activity of its transporter.[10] The absence of aldosterone will thus lead to reduced hydrogen ion excretion and promote the development of metabolic acidosis (type 4 renal tubular acidosis). Furthermore, hyperkalemia compounds the acidosis through a postulated mechanism of competitive inhibition impairing ammonium recycling.[12] Thus, when utilizing the traditional approach to acid–base analysis, adrenal insufficiency typically results in a normal anion gap metabolic acidosis, as noted in the dogs in this study. Interestingly, hyperlactatemia did not appear to be a major contributor to the metabolic acidosis in the dogs here, as the median plasma lactate concentration was within the reference interval at 1.5 mmol/L (13.5 mg/dL). This finding is supported by another study that also identified a normal plasma lactate concentration in most hypoadrenal dogs.[4]

Our results suggest that the metabolic acidosis in acutely ill Addisonian dogs is primarily due to the free water effect (hyponatremia). This dilutional acidosis is multifactorial, with adrenal insufficiency resulting in hyponatremia via impaired renal sodium resorption, gastrointestinal losses leading to decreased effective circulating volume and stimulation of antidiuretic hormone release and thirst, and loss of the inhibitory effect of cortisol on antidiuretic hormone release.[10] Hyperphosphatemia was the other major contributor to the metabolic acidosis of these dogs and is likely attributable to hypovolemia-induced prerenal azotemia and retention of acidic compounds such as phosphates.[9] Most dogs had a small amount of unmeasured anions contributing to the metabolic acidosis that may be other retained uremic acids such as sulfates, urate, and hippurate.[27] Hypoalbuminemia was the predominant alkalinizing effect. Several mechanisms have been proposed for this abnormality in dogs with HA, including anorexia, gastrointestinal hemorrhage, decreased hepatic albumin synthesis, protein-losing enteropathy, and inflammation.[14,28]

The acid–base status of dogs with HA is clinically relevant for informed therapeutic decision-making, particularly pertaining to fluid selection. The cornerstone of initial management of hypoadrenal crisis is adequate and appropriate IV fluid therapy. The metabolic acidosis in HA is generally corrected with fluid resuscitation,[13,14,29] which restores circulating volume and renal perfusion and thus resolves lactic acidosis and prerenal azotemia. Traditionally, 0.9% NaCl has been recommended as the fluid of choice in acute hypoadrenal crisis as it provides sodium ions and volume repletion but does not exacerbate hyperkalemia.[5,8,30–32] However, there are no studies supporting this recommendation, and severe neurological complications including osmotic demyelination syndrome have been documented in hypoadrenal dogs with too rapid correction of hyponatremia.[33,34] Moreover,

TABLE 3 Venous acid–base, electrolyte, and lactate values in 33 dogs with untreated typical hypoadrenocorticism measured within 6 hours of hospital presentation

Parameter	Median (range), Conventional units	Median (range), SI units
Sodium	129 (115–139) mEql/L	129 (115–139) mmol/L
Potassium	7.1 (4.9–9.6) mEq/L	7.1 (4.9–9.6) mmol/L
Chloride	98 (82–115) mEq/L	98 (82–115) mmol/L
Chloride corrected	112.4 (102.2–122.5) mEq/L	112.4 (102.2–122.5) mmol/L
Albumin	2.9 (1.5–4.2) g/dL	29 (15–42) g/L
Phosphorus	7.6 (2.1–13.7) mg/dL	2.5 (0.7–4.4) mmol/L
pH	7.281 (7.127–7.507)	7.281 (7.127–7.507)
$Pvco_2$	35.3 (23.4–51.6) mm Hg	35.3 (23.4–51.6) mm Hg
Bicarbonate	16.5 (10.8–23.9) mEq/L	16.5 (10.8–23.9) mmol/L
Base excess	−9.2 (−15.8 to −1.6) mEq/L	−9.2 (−15.8 to −1.6) mmol/L
Lactate	13.5 (2.7–37.8) mg/dL	1.5 (0.3–4.2) mmol/L
Anion gap[a]	13.9 (1.3–22) mEq/L	13.9 (1.3–22) mmol/L
Free water effect	N/A	−4.8 (−8.6 to −2.0) mmol/L
Chloride effect	N/A	−1.3 (−10.5 to 9.8) mmol/L
Albumin effect	N/A	2.6 (−2.2 to 8.9) mmol/L
Phosphorus effect	N/A	−1.7 (−5.7 to 1.0) mmol/L
Lactate effect	N/A	−1.5 (−4.2 to −0.3) mmol/L
Sum of effects	N/A	−7.2 (−13.9 to 2.9) mmol/L
XA	N/A	−0.8 (−11.4 to 5.8) mmol/L

Abbreviation: XA, unmeasured anions.
[a]Anion gap evaluated in 31 dogs.

any isotonic crystalloid fluid will help restore effective circulating volume, dilute hyperkalemia, and increase renal perfusion and thus enhance renal potassium and acid excretion.[23] In addition, balanced isotonic crystalloid fluids contain buffers that promote resolution of metabolic acidosis. Administration of 0.9% saline is considered an acidifying fluid due to the lack of buffers and the impact of a large chloride load on renal handling of bicarbonate.[35] A balanced isotonic crystalloid solution that contains a buffer and more physiological sodium and chloride concentrations may therefore be a more ideal choice in these dogs to avoid overly rapid changes in plasma sodium concentration, an acidifying chloride effect, hyperchloremia-induced renal vasoconstriction, and decline in glomerular filtration rate.[22,36,37] Although the optimal fluid for dogs with HA is unknown, the findings of the current investigation suggest that further study is warranted to determine whether the historical recommendation for 0.9% NaCl is appropriate.

TABLE 4 Traditional acid–base diagnosis of 33 dogs with untreated typical hypoadrenocorticism within 6 hours of hospital presentation based on venous blood gas evaluation

Acid–base diagnosis	N (%)
Normal acid–base balance	1 (3)
Simple disorders	
Respiratory acidosis	1 (3)
Respiratory alkalosis	1 (3)
Metabolic acidosis	14/33 (42)
Metabolic acidosis with normal anion gap	12/31 (39)
Metabolic acidosis with elevated anion gap	0
Metabolic alkalosis	0
Mixed disorders	
Metabolic acidosis and respiratory acidosis	14/33 (42)
Normal anion gap	14/31 (45)
Elevated anion gap	0
Metabolic acidosis and respiratory alkalosis	2/33 (6)
Normal anion gap	2/31 (7)
Elevated anion gap	0
Metabolic alkalosis and respiratory alkalosis	0
Metabolic alkalosis and respiratory acidosis	0

Note. Anion gap was calculated in only 31 dogs.

TABLE 5 Semiquantitative approach acid–base diagnosis of 33 dogs with untreated typical hypoadrenocorticism within 6 hours of hospital presentation based on venous blood gas and biochemical evaluation

Metabolic acid–base diagnosis	N (%)
One or more acidotic processes	33 (100)
One or more alkalotic processes	29 (88)
Both alkalotic and acidotic processes	29 (88)
Dilutional acidosis	33 (100)
Acidotic chloride effect	5 (15)
Alkalotic chloride effect	5 (15)
Acidotic albumin effect	1 (3)
Alkalotic albumin effect	21 (64)
Acidotic phosphate effect	27 (82)
Lactic acidosis	8 (24)
Unmeasured anions	18 (55)
Unmeasured cations	10 (30)

This study has several limitations. For accuracy, evaluation of all required parameters on the same blood sample would be ideal. It is standard practice in our hospital to draw serum, EDTA whole blood, and heparinized blood samples simultaneously during placement of the IV catheter, so it is unlikely that there is a significant time discrepancy between point-of-care acid–base, electrolyte and lactate analysis, and reference laboratory evaluation of the serum biochemistry panel. In this study, we allowed a 6-hour time interval

between presentation to the hospital and blood gas and biochemistry sample collection, so we cannot rule out the possibility that fluid and other therapies given during a period prior to sample collection may have influenced the results or led to discordant findings within patient results. However, once again, as the majority of samples were drawn simultaneously, this effect is unlikely to meaningfully change the conclusions made. Another limitation is the small number of dogs included in this study; a larger study population should be evaluated to confirm these findings. As previously mentioned, the multiple analyzers utilized and externally determined reference intervals may have affected the accuracy of these results. Similarly, the acid–base analyzers and the equations they utilize are designed for human patients, and this may result in a small and unavoidable source of error during extrapolation to canine patients. In addition, the study was performed in a tertiary referral institution, so the nature of the population with HA included may not be representative of the general practice clinical situation.

In conclusion, this study demonstrates that dogs with untreated typical HA have complex acid–base derangements. The semiquantitative approach to acid–base analysis, in comparison to the traditional approach, provides greater insight into the underlying mechanisms of metabolic acid–base abnormalities in these dogs, particularly because lactic acidosis appears to be only a minor influence in most cases. These results suggest that dogs with Addison's disease may benefit from fluid resuscitation using balanced isotonic electrolyte solutions that contain a buffer and have lower sodium and chloride concentrations than the traditionally recommended 0.9% NaCl.

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ENDNOTES

* ABL 705, Radiometer Medical A/S, Copenhagen, Denmark.
† ABL 800, Radiometer Medical A/S, Copenhagen, Denmark.
‡ ABL 815, Radiometer Medical A/S, Copenhagen, Denmark.
§ Chemistry analyzer, Hitachi 917, Roche Diagnostics, Indianapolis, IN.
** Chemistry analyzer, Hitachi c501, Roche Diagnostics, Indianapolis, IN.

CONFLICT OF INTERESTS

Dr Burkitt-Creedon is an Associate Editor for the Journal. Dr Steven Epstein is an Assistant Editor for the Journal. However, both contributed only as authors and were not involved in the review or editorial processes for this manuscript.

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