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# Arterial blood acid-base and electrolyte values in dogs: conventional and "strong ion" approach

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ABSTRACT

Arterial blood gas analysis is an essential part of diagnosing and managing an animal's oxygenation and acid-base status. The aim of this study was to establish reference intervals for acid-base values and blood gases in clinically healthy dogs of different ages and sex using Stat Profile Critical Care Xpress (CCX), and to provide an insight into the most appropriate approach to analyze complex acid-base abnormalities. Whole-blood arterial samples were obtained from 40 clinically healthy adult dogs of various breeds. Parameters of quantitative acid-base analysis (SID<sub>CLIN</sub>, SID<sub>APP</sub> SID<sub>EFF</sub>, SIG) were calculated using the Stewart-Figge approach. Reference ranges were: pH 7.37 - 7.44, pCO<sub>2</sub> 22.62 - 34.52 mmHg, pO<sub>2</sub>91.35 - 106.05 mmHg, A 106.33 - 120.12 mmHg, a/A 0.80 - 0.90 mmHg, AaDO<sub>2</sub>-0.72 - 32.90 mmHg, HCO<sub>3</sub> 14.06 - 22.10 mmol/L, BEecf -12. 05 - 1. 61 mmol/L, BEb -9.7 - 0.46 mmol/L, SIO<sub>2</sub>LIN 27.94 - 31.41 mmol/L, SID<sub>APP</sub> 26.00 - 31.60 mmol/L, SID<sub>EFF</sub> 29.27 - 36.21 mmol/L, SIG 2.32 - 7.46 mmol/L. Reference values obtained on the CCX analyzer provide valuable baseline information for assessing new acid-base parameters and for interlaboratory comparisons. Differences compared with previously published reference values may be attributed largely to differences in methodology and sampling. The acid-base values determined in this study may be considered to be reference data for health control and disease diagnosis.

Key words: acid-base values, electrolyte, dog, strong ion difference

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## Introduction

Knowledge of normal acid-base and electrolyte values are important for health monitoring, for appropriate diagnosis and treatment of disease, and for nutritional studies (BOUDA et al., 2009). Arterial blood gas analysis is an essential part of diagnosing and managing an animal's oxygenation and acid-base status. Acid-base balance is critical for maintaining the narrow pH range required to maintain various enzyme systems optimally in the body. Acute changes in blood pH induce powerful regulatory effects at the level of the cell, organ and organism (KELLUM, 2000). Thus, the evaluation of acid base status provides important data, especially in relation to the urinary, respiratory, digestive and endocrine systems (BOUDA and JAGOS, 1991).

The measurement of acid-base and electrolyte values is a complex matter and requires high quality instrumentation. A number of portable systems have been developed for point-of-care testing in human medicine, and these systems have proved suitable for veterinary practices, providing quality results at relatively low cost, without specialized knowledge of laboratory techniques. Rapid technological progress in point of care testing has allowed the measurement of multiple analytes in whole blood samples (FLEGAR-MEŠTRIĆ and PERKOV, 2006). In clinical practice, most veterinary clinics already use automatic analyzers for substrate, enzyme and ion measurements, but lack equipment for blood-gas and pH determination (VERWAERDE et al., 2002; SLAWUTA et al., 2010). Convenient assessment for accurate blood-gas and pH measurement as a way of evaluating ventilation and acid-base status is required in modern clinical veterinary practice.

The traditional approach used to evaluate the acid-base status of blood is focused on pH, partial pressure of carbon dioxide (pCO<sub>2</sub>) and bicarbonate (HCO<sub>3</sub><sup>-</sup>), as described by the Henderson-Hasselbalch equation (CARLSON, 1997). However, this traditional approach is an oversimplification of a complex system. According to the Stewart concept, plasma pH results from the degree of plasma water dissociation, which is determined by 3 independent variables: 1) a strong ion difference (SID) which is the difference between all the strong plasma cations and anions; 2) the quantity of plasma weak acids ( $A_{TOT}$ ); 3) the partial pressure of carbon dioxide pCO<sub>2</sub> (STEWART, 1983; RUSSEL et al., 1996; CONSTABLE, 1999). The strong ion approach is mechanistic and, despite its apparent complexity, permits us to understand precisely the mechanisms of acid-base disorders (QUINTARD et al., 2007). A recent study in humans reported that the Stewart approach identified more acid-base disturbances in intensive care unit patients than the conventional approach (BONIATTI et al., 2009). The new approach should therefore be valuable in a clinical setting and in research studies investigating acid-base balance.

Acid-base parameters are rarely analyzed in animals in veterinary practice, although these parameters show a marked change in 30 % of the cases (SŁAWUTA et al., 2010). Acid-base abnormalities are frequently present in a sick dog (CONSTABLE and STÄMPFLI, 2005).

The aim of this study was to establish reference intervals for acid-base values and blood gases in clinically healthy dogs of different ages and seks, using multiprofile analyzer Stat Profile Critical Care Xpress ("CCX", Nova Biomedical, Waltham, Ma, USA), and to discuss the most appropriate approach to analyzing complex acid-base abnormalities.

## Materials and methods

Whole-blood arterial samples were obtained from 40 clinically healthy adult, unsedated dogs of various breeds (Rottweiler, German Shepherd, Golden Retriever, Belgian Shepherd, Yugoslavian Shepherd Sharplaninac), aged from 6 month to 8 years, including 17 males and 23 females, kept under the same conditions on a dog farm. Samples were collected from the femoral artery in anaerobical conditions, into a commercial preheparinized syringe. After collection, the syringe was closed with a stop cock and inserted into a mixture of ice and water until analysis. Samples were analyzed within two hours of blood sampling. All the tested dogs were clinically examined and venepunctured from the v. cephalica antebrachii for hematology and biochemical profile, which contributes to verification of their health status. The study protocol was approved by the Ethical Committee of the Faculty of Veterinary Medicine, University of Zagreb, Croatia.

A blood gas analyzer, Stat Profile Critical Care Xpress (CCX, Nova Biomedical, Waltham, Ma, USA) multiprofile analyzer, with the application of biosensor-based methods, was used to determine the following parameters: pH; pCO<sub>2</sub>-partial pressure of carbon dioxide, mmHg; pO<sub>2</sub>-partial pressure of oxygen, mmHg; PCV-packed cell volume, L/L; Hb-hemoglobin, g/L; A-alveolar oxygen, mmHg; a/A-arterial alveolar oxygen tension ratio; AaDO<sub>2</sub>-arterial alveolar oxygen tension gradient, mmHg; HCO<sub>2</sub>bicarbonate level, mmol/L; BEecf-base excess of extracellular fluid, mmol/L; BEb-base excess of the blood, mmol/L; SO2-oxygen saturation, % ; Ri-respiratory index; SBCstandard bicarbonate concentration, mmol/L; TCO2-total carbon dioxide, mmol/L; pO2/ FIO<sub>2</sub>-partial pressure of oxygen and fraction of inspired oxygen ratio, mmHg; lactate, mmol/L; CaO<sub>2</sub>-arterial oxygen content, mL O<sub>2</sub>/dl; CcO<sub>2</sub>-capillary oxigen content, mL O<sub>2</sub>/dl; Na<sup>+</sup>-sodium, mmol/L; K<sup>+</sup>-potassium, mmol/L; Cl<sup>-</sup>-chloride, mmol/L; Ca<sup>2+</sup>-ionized calcium, mmol/L; Mg<sup>2+</sup>-ionized magnesium, mmol/L; AG-anion gap; Ca<sup>2+</sup>/Mg<sup>2+</sup>-calcium/ magnesium ratio. The anion gap was calculated as a difference between the concentration of Na<sup>+</sup> and K<sup>+</sup> and the concentration of Cl<sup>-</sup> and HCO<sub>2</sub><sup>-</sup>. Protein, albumin and inorganic phosphate concentrations were determined by spectrophotometry, using a biochemical analyzer Olympus AU 600 (Olympus Diagnostica GMBH, Hamburg, Germany). The instruments were maintained, calibrated and operated according to the manufacturer's specifications. All samples were analyzed by same person, after thorough sample mixing.

Using the Stewart-Figge approach, the parameters of quantitative acid-base analysis were calculated (FIGGE et al., 1992; MATOUSEK et al., 2011). The apparent strong ion difference ( $SID_{APP}$ ) was calculated as the difference between the sum of the strong cations and the sum of the strong anions:

 $SID_{APP}(mmol/L) = [Na^+] + [K^+] + 2[Mg^{2+}] + 2[Ca^{2+}] - [Cl^-] - [lactate]$ 

Albuminate (albumin<sup>-</sup>) and ionized inorganic phosphate ( $P_i^-$ ) were calculated from the measured values of albumin,  $PO_4^-$  and pH:

 $[albumin^{-}] (mmol/L) = [albumin] x (0,123 x pH - 0,631)$ 

 $[P_i]$  (mmol/L) =  $[PO_4]$  x (0,309 x pH - 0,469)

The effective strong ion difference was calculated as:

 $SID_{EFF} (mmol/L) = [HCO_3^-] + [albumin^-] + [P_i^-]$ 

The difference between the calculated  $SID_{APP}$  and  $SID_{EFF}$  constitutes a strong ion gap (SIG):

SIG (mmol/L) =  $SID_{APP} - SID_{EFF}$ 

The strong ion difference SID was also calculated by the clinical approach (SID<sub>CLIN</sub>) and corresponded to the difference between Na<sup>+</sup> and Cl<sup>-</sup> (WHITEHAIR et al., 1995; NAGAOKA et al., 2010).

All statistical analyses were performed using a statistical computer application, Statistica 8 (statistical software program Statistica 8 for Windows, StatSoft Inc.). Normality of data distribution was tested using the Kolmogorov-Smirnov test. All data were reported as mean and standard deviation (SD) for parametric variables, or medians for neparametric variables with the corresponding interquartile range, respectively. Reference ranges were calculated as mean  $\pm 2$  SD for parametric variables or as interquartile range for neparametric variables.

## Results

Results obtained from blood analysis on the CCX-analyzer are shown in Table 1, as mean and standard deviation (SD) or median with the corresponding interquartile range. Strong ion approach parameters are given in Table 2, as median and interquartile range.

Reference ranges for all parameters are shown in Table 3.

Parameter	Unit	Valid N	Mean	SD	Median	Lower - Quartile	Upper - Quartile
pН		40			7.41	7.37	7.44
pCO <sub>2</sub>	mmHg	40	28.56	2.97		27.00	30.30
pO <sub>2</sub>	mmHg	40			100.55	91.35	106.05
PCV	L/L	40	39.83	6.48		35.00	44.00
Hb	g/dL	24	12.54	2.03		10.95	13.80
А	mmHg	40	113.23	3.45		111.00	115.45
a/A	mmHg	40			0.90	0.80	0.90
AaDO <sub>2</sub>	mmHg	36	16.09	8.40		7.10	21.05
HCO <sub>3</sub> -	mmol/L	40	18.08	2.01		16.40	19.45
BEecf	mmol/L	40	-6.83	2.61		-8.65	-5.30
BEb	mmol/L	40	-4.62	2.54		-6.25	-3.15
SO <sub>2</sub>	%	24	97.18	1.43		96.30	97.95
Ri		36			0.15	0.10	0.20
SBC	mmol/L	40	20.66	2.04		19.35	21.85
CaO <sub>2</sub>	$ml O_2/dL$	13	21.73	4.02		21.90	23.70
CcO <sub>2</sub>	$ml O_2/dL$	13	21.58	3.99		21.60	23.50
pO <sub>2</sub> /FiO <sub>2</sub>	mmHg	40			482.25	437.00	507.45
Na <sup>+</sup>	mmol/L	40			145.05	125.10	146.10
$K^+$	mmol/L	19	4.19	0.31		4.00	4.30
Cl-	mmol/L	38			114.20	96.60	115.60
Ca <sup>2+</sup>	mmol/L	40			1.22	0.73	1.29
Mg <sup>2+</sup>	mmol/L	38			0.26	0.24	0.34
Lac	mmol/L	32	1.80	0.87		1.15	2.20
TCO <sub>2</sub>	mmol/L	40	18.96	2.05		17.25	20.40
AG	mmol/L	36	12.58	3.55		11.50	15.30
Ca/Mg		35	3.51	0.73		2.80	4.20
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Table 1. Blood acid-base parameters in healthy dog

 $pCO_2$ -partial pressure of carbon dioxide,  $pO_2$ -partial pressure of oxygen, PCV-packed cell volume, Hbhemoglobin, A-alveolar oxygen, a/A-arterial alveolar oxygen tension ratio, AaDO<sub>2</sub>-arterial alveolar oxygen tension gradient, HCO<sub>3</sub>-bicarbonate level, BEecf-base excess of extracellular fluid, BEb-base excess of the blood, SO<sub>2</sub>-oxygen saturation, Ri-respiratory index, SBC-standard bicarbonate concentration, TCO<sub>2</sub>-total carbon dioxide, pO<sub>2</sub>/FIO<sub>2</sub>-partial pressure of oxygen and fraction of inspired oxygen ratio, Lac-lactate, CaO<sub>2</sub>arterial oxygen content, CcO<sub>2</sub>-capillary oxigen content, Na<sup>+</sup>-sodium, K<sup>+</sup>-potassium, Cl<sup>-</sup>-chloride, Ca<sup>2+</sup>-ionized calcium, Mg<sup>2+</sup>-ionized magnesium, AG-anion gap, Ca<sup>2+</sup>/Mg<sup>2+</sup>-calcium/magnesium ratio

Parameter	Unit	Valid N	Median	Lower - Quartile	Upper - Quartile
Protein	g/L	25	67.0	63.0	71.0
Albumin	g/L	25	34.0	32.0	34.0
P <sub>i</sub>	mmol/L	25	1.30	1.20	1.50
[Alb <sup>-</sup> ]	mmol/L	25	9.3	8.92	9.62
[P <sub>i</sub> <sup>-</sup> ]	mmol/L	25	2.36	2.19	2.70
A	mmol/L	25	11.69	11.29	12.06
SID	mmol/L	34	29.26	27.94	31.41
SID	mmol/L	12	30.10	26.00	31.60
SID	mmol/L	25	35.24	29.27	36.21
SIG	mmol/L	5	2.42	2.32	7.46

Table 2. Calculated strong ion approach parameters in healthy dogs

 $P_i$ -inorganic phosphate concentration; [Alb<sup>-</sup>]-albuminate; [ $P_i$ <sup>-</sup>]-ionised inorganic phosphate;  $A_{ror}$ -total weak acid concentration; SID<sub>CLIN</sub>-strong ion difference by clinical approach; SID<sub>APP</sub>-apparent strong ion difference; SIG-strong ion gap

Parameter	Unit	Reference range
pН		7.37 - 7.44
pCO <sub>2</sub>	mmHg	22.62 - 34.52
pO <sub>2</sub>	mmHg	91.35 - 106.05
PCV	L/L	26.86 - 52.79
Hb	g/dL	8.46 - 16.61
A	mmHg	106.33 - 120.12
a/A	mmHg	0.80 - 0.90
AaDO <sub>2</sub>	mmHg	- 0.72 - 32.90
HCO <sub>3</sub> <sup>-</sup>	mmol/L	14.06 - 22.10
BEecf	mmol/L	-12. 05 - 1. 61
BEb	mmol/L	-9.7 - 0.46
SO <sub>2</sub>	%	94.31 - 100
Ri		0.10 - 0.20
SBC	mmol/L	16.59 - 24.74
CaO <sub>2</sub>	ml O <sub>2</sub> /dL	13.69 - 29.77
CcO <sub>2</sub>	ml O <sub>2</sub> /dL	13.59 - 29.56
pO <sub>2</sub> /FiO <sub>2</sub>	mmHg	437.00 -507.45
Na <sup>+</sup>	mmol/L	125.10 - 146.10
K <sup>+</sup>	mmol/L	3.57 - 4.81

Table 3. Reference acid-base ranges for clinically healthy dogs

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Parameter	Unit	Reference range
Cl-	mmol/L	96.60 - 115.60
Ca <sup>2+</sup>	mmol/L	0.73 - 1.29
Mg <sup>2+</sup>	mmol/L	0.24 - 0.34
Lac	mmol/L	0.06 - 3.54
TCO <sub>2</sub>	mmol/L	14.87 - 23.06
AG	mmol/L	5.49 - 19.67
Ca/Mg		2.06 - 4.97
A <sub>TOT</sub>	mmol/L	11.29 - 12.06
SID <sub>CLIN</sub>	mmol/L	27.94 - 31.41
SID <sub>APP</sub>	mmol/L	26.00 - 31.60
SID <sub>EFF</sub>	mmol/L	29.27 - 36.21
SIG	mmol/L	2.32 - 7.46

Table 3. Reference acid-base ranges for clinically healthy dogs (continued)

pCO<sub>2</sub>-partial pressure of carbon dioxide, pO<sub>2</sub>-partial pressure of oxygen, PCV-packed cell volume, Hbhemoglobin, A-alveolar oxygen, a/A-arterial alveolar oxygen tension ratio, AaDO<sub>2</sub>-arterial alveolar oxygen tension gradient, HCO<sub>3</sub>-bicarbonate level, BEecf-base excess of extracellular fluid, BEb-base excess of the blood, SO<sub>2</sub>-oxygen saturation, Ri-respiratory index, SBC-standard bicarbonate concentration, TCO<sub>2</sub>-total carbon dioxide, pO<sub>2</sub>/FIO<sub>2</sub>-partial pressure of oxygen and fraction of inspired oxygen ratio, Lac-lactate, CaO<sub>2</sub>arterial oxygen content, CcO<sub>2</sub>-capillary oxigen content, Na<sup>+</sup>-sodium, K<sup>+</sup>-potassium, Cl<sup>-</sup>-chloride, Ca<sup>2+</sup>-ionized calcium, Mg<sup>2+</sup>-ionized magnesium, AG-anion gap, Ca<sup>2+</sup>/Mg<sup>2+</sup>-calcium/magnesium ratio; A<sub>TOT</sub>-total weak acid concentration; SID<sub>CLIN</sub>-strong ion difference by clinical approach; SID<sub>APP</sub>-apparent strong ion difference; SID<sub>EFF</sub>-effective strong ion difference; SIG-strong ion gap.

## Discussion

Acid-base balance is critical for maintaining the narrow pH range required for various enzyme systems to work optimally in the body. Small deviations from normal can produce marked changes in enzyme activity and chemical reactions in the body. The buffer systems that maintain this pH balance are bicarbonate, phosphates and proteins. In addition to buffers, the lungs and kidneys play a major role in acid-base homeostasis (CUNNINGHAM, 2002). Many of the clinical signs observed in animals with acid-base disturbances are the result of the primary disease process, but there are also clinical signs that can develop as a result of the acid-base disturbance itself. Changes in neural function, cardiac output and changes in concentrations of electrolytes may occur as a direct result of acid-base abnormalities.

For most acid-base disturbances, the traditional approach to acid-base balance seems certain to prevail. For the clinician, the three variables of greatest use are the pH,  $pCO_2$  and base excess (BEb). Frequently pH,  $pCO_2$ ,  $HCO_3^-$ , BEb and total CO<sub>2</sub> (TCO<sub>2</sub>) as

determined by blood acid-base analyzers and calculated anion gap (AG), are used for the evaluation of acid-base disorders (CARLSON, 1997).

The blood pH of healthy domestic animals is maintained within narrow limits, between 7.35 and 7.45, the pH optimum for most enzymatic reactions. Changes in pH have direct effects on the rates of reaction and many basic biological processes in the organism. Values below 7.0 and above 7.7 are life threatening (BOUDA and JAGOS, 1991; CARLSON, 1997). Data obtained for pH (7.37 - 7.44) in this study was similar to those obtained by other authors (ILKIW et al., 1991; AGUILERA-TEJERO et al., 1997).

In the interpretation of the acid-base component of blood gas results, the pH represents the overall change,  $pCO_2$  the respiratory component and BEb the metabolic component. The mean value for  $pCO_2$  (28.57 mmHg) was considerably lower than those found by other authors: 36.8 mmHg and 33.9 mmHg, respectively (ILKIW et al, 1991; SIMEONOVA, 2003). These results could be due to transportation or due to the slight hyperventilation of the animals during sampling.

The  $pO_2$  is an index of the oxygenating efficiency of the lungs (HASKINS, 2004). The median value for  $pO_2$  (100.55 mmHg) was similar to values found by ILKIW et al. (1991) (102.1 mmHg).

The mean value for HCO<sub>3</sub><sup>-</sup>(18.08 mmol/L) was similar or slightly lower than that found by other authors: 21.4 mmol/L, 20.5 mmol/L, 17.78 mmol/L, respectively (ILKIW et al., 1991; AGUILERA-TEJERO et al., 1997; SIMEONOVA, 2003). The bicarbonate concentration may be used as a screening parameter of a non-respiratory acid-base disturbance when respiratory disturbances are taken into account (SIGGAARD-ANDERSEN and FOGH-ANDERSEN, 1995). The mean value for SBC (20.66 mmol/L) was lower than values found by ILKIW et al. (1991) (22.4 mmol/L) and higher than those obtained by SIMEONOVA (2003) (17.8 mmol/L).

Clinically, the BEb represents the amount of acid per unit volume that must be added to achieve a normal pH. A positive BE indicates alkalosis, whereas a negative BE indicates acidosis. The mean value for BEb (-4.62 mmol/L) was lower than values found by ILKIW et al. (1991) (-1.8 mmol/L) and AGUILERA-TEJERO et al. (1997) (-2.78 mmol/L). Low values could be due to the lactate production of red blood cells during transport. The diagnostic use and prognostic value of BEb is well documented. Changes in BEb have proved to be the best predictor of blood volume changes in a canine hemorrhagic shock model (WAISMAN et al., 1993). Older references for the anion gap reported a range of 12 to 24 mmol/L (MADIAS et al., 1984) and recent studies (CONSTABLE and STÄMPFI, 2005) a mean of 18.8 mmol/L, which is higher than our mean value (12.58 mmol/L).

The mean value for  $TCO_2$  (18.96 mmol/L) was similar to findings by SIMEONOVA (2003) and lower than results by ILKIW et al. (1991) (22.4 mmol/L). The A-aDO<sub>2</sub> parameter indicates the efficiency of the oxygen exchange process in the alveolar-capillary unit,

so it is a useful parameter for respiratory syndromes, lung tumors or cardiac illnesses (KOGAN et al., 2008; SINGH et al., 2010). We determined a mean value of 16.09 mmHg. The  $pO_2/FiO_2$  ratio is a method for expressing lung oxygenating efficiency when the patient is breathing an enriched oxygen mixture. In normal lungs, the  $pO_2/FiO_2$  is around 500 mmHg (HASKINS, 2004). Our median was 482 mmHg, which is in agreement with previous findings. Calculating this parameter is useful during general anesthesia and is grossly dependent on the  $pO_2$ .

Blood lactate analysis is clinically valuable in predicting prognosis and survival, evaluating tissue perfusion and treatment response in human and veterinary critical care settings. Lactate is the most accurate blood indicator of acute hypoperfusion and the only plasma marker for tissue hypoxia (ROCKTAESCHEL et al., 2003). We determined a mean value for lactate of 1.80 mmol/L.

According to Stewart's theory, changes in blood pH are regulated by three independent variables: the SID (difference between fully dissociated anions and cations);  $pCO_2$  and the total weak acid concentration  $A_{TOT}$  (consisting mainly of albumin and phosphate) (STEWART, 1983; RUSSEL et al., 1996; CONSTABLE, 1999).

The major strong ions in plasma are sodium and chloride. The difference between Na<sup>+</sup> and Cl<sup>-</sup> represents the clinical SID. It could be a very practical parameter, because it is easy to calculate and may be used as an estimation of SID (WHITEHAIR et al., 1995; NAGAOKA et al., 2010). We found the reference range for SID<sub>CLIN</sub> to be 27.94 - 31.41 mmol/L, with a median of 29.26 mmol/L. In humans, SID<sub>CLIN</sub> has been shown to be an accurate tool for chloride-associated acidosis recognition in dysnatremic patients (NAGAOKA et al., 2010), while in veterinary medicine there are no data about this parameter.

Changes in SID result from either a relative or an absolute change in strong ion concentrations. An increase in SID, which indicates a net increase in cations, results in metabolic alkalosis. A decrease in SID, which indicates a net increase in anions, results in metabolic acidosis (FIDKOWSKI and HELSTROM, 2009). This approach separates the net metabolic abnormality into components, and allows easy detection of mixed metabolic acid-base abnormalities.

We established the reference range for SID<sub>APP</sub> as 26.00 - 31.60 mmol/L, with a median of 30.10 mmol/L; and for SID<sub>EFF</sub> 29.27 - 36.21 mmol/L, with a median of 35.24 mmol/L. These findings are in agreement with those obtained by CONSTABLE and STÄMPFLI (2005) (27 mmol/L), but are lower or in the lower reference range of other findings (AQUILERA-TEJERO et al., 1997; SIEGLING-VLITAKIS et al., 2007).

The A<sub>TOT</sub> range of 11.29 - 12.06 mmol/L was similar to that found by SIEGLING-VLITAKIS et al. (2007) (8.5-13.1 mmol/L) but was in the lower reference range compared to results by CONSTABLE and STÄMPFLI (2005) ( $17.4 \pm 8.6$  mM).

The Stewart model provides the concept of strong ions gap (SIG), which is the apparent difference between concentrations of all strong cations and all strong anions. Its diagnostic value is greater than AG, because it includes concentrations of albumin and phosphate. The median value for SIG was 2.42 mmol/L. The SIG has not been adequately tested in dogs and data are inconsistent. Our data are within the reference range for SIG (-1.90 - 18.60 mmol/L) found by SIEGLING-VLITAKIS et al. (2007) in healthy dogs. Mixed metabolic disorders are reported when SIG is less than -5 mmol/L (DE MORAIS and CONSTABLE, 2006). AQUILERA-TEJERO et al. (1997) found a mean of 9.5 mmol/L, while in dogs with right sided heart failure, the reported values were from 1.15 to 11.77 mmol/L (SŁAWUTA and GLIŃSKA-SUCHOCKA, 2012).

The electrolyte status is a description of the most important electrolytes. We established a reference range for Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, Ca<sup>2+</sup>, Mg<sup>2+</sup> and Ca<sup>2+</sup>/Mg<sup>2+</sup> ratio. Absolute changes in strong ions will also alter SID.

Determination of acid-base values (pH,  $pCO_2$ ,  $HCO_3^-$ , BE,  $TCO_2$ ), electrolyte levels (Na<sup>+</sup>, K<sup>+</sup>, Cl) and AG allows for the evaluation of most acid-base disorders (CARLSON, 1997). However, it gives an inadequate pathophysiological analysis, which may lead to a false diagnosis, especially with complex acid-base imbalances. A mixed acid-base disorder should be suspected when inappropriate compensation for the primary disorder is demonstrated. The strong ion approach works well clinically and is recommended for use whenever serum total protein, albumin and phosphate concentrations are markedly abnormal (CONSTABLE, 1999). If the laboratory is not equipped with an acid-base analyzer, the determination of AG, TCO<sub>2</sub> and SID can be used for evaluation of metabolic acid-base disorders (RUSSEL et al., 1996; CONSTABLE, 1999).

The reference values for 31 variables obtained in this study could be useful to clinicians and researchers for better interpretation of acid-base, blood gas and electrolyte disturbances in dogs. Reference values obtained on the Stat Profile Critical Care Xpress (CCX) analyzer provide valuable baseline information for assessing new acid-base parameters and for interlaboratory comparisons. Differences compared with previously published reference values can be attributed largely to differences in methodology and possibly to the effect of excitement and transportation. The usefulness of this diagnostic tool is dependent on the ability to interpret the results correctly. The proper application of the concepts of acid-base balance will help the veterinarian not only to follow the progress of a disorder, but also to evaluate the efficacy of care being provided. The strong ion approach provides the clinician with an improved understanding of complex acid-base and electrolyte disorders. The acid-base values determined in this study may be considered reference data for health control and disease diagnosis.

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## References

- AGUILERA-TEJERO, E., H. FERNANDEZ, J. C. ESTEPA, R. MAYER-VALOR, M. RODRIGUEZ (1997): Arterial blood gases and acid-base balance in geriatric dogs. Res. Vet. Sci. 63, 253-256.
- BONIATTI, M. M., P. R. CARDOSO, R. K. CASTILHO, S. R. VIEIRA (2009): Acid-base disorders evaluation in critically ill patients: we can improve our diagnostic ability. Intensive Care Med. 35, 1377-1382.
- BOUDA, J., P. JAGOS (1991): Disorders in the acid-base balance. In: Metabolic disorders and their prevention in farm animals. (Vrzgula, L., Ed.) Elsevier, Amsterdam. pp. 248-268.
- BOUDA, J., L. NÚÑEZ-OCHOA, E. ÁVILA-GONZÁLEZ, J. DOUBEK, B. FUENTE-MARTINEZ, J. AGUILAR-BOBADILLA (2009): Blood acid-base and plasma electrolyte values in healthy ostriches: The effect of age and sex. Res. Vet. Sci. 87, 26-28.
- CARLSON, G. P. (1997): Fluid, electrolyte and acid-base balance. In: Clinical Biochemistry of Domestic Animals. (Kaneko, J. J., J. W. Harvey, M. L. Bruss, Eds.) Academic Press, San Diego, fifth ed. pp. 485-516.
- CONSTABLE, P. D. (1999): Clinical assessment of acid-base status. Strong ion difference theory. Vet. Clin. North. Am. Food. Anim. Pract. 15, 447-471.
- CONSTABLE, P. D., H. R. STÄMPFLI (2005): Experimental determination of net protein charge and A(tot) and K(a) of nonvolatile buffers in canine plasma. J. Vet. Intern. Med. 19, 507-514.
- CUNNINGHAM, J. G. (2002): Textbook of Veterinary Physiology. 3<sup>rd</sup> ed., W. B. Saunders Company, Philadelphia. pp. 459-466.
- DE MORAIS, H. A., P. D. CONSTABLE (2006): Strong ion approach to acid-base disorders. In: Fluid, Electrolyte and Acid-Base Disorders in Small Animal Practice. (DiBartola, S.P., Ed.) 3<sup>rd</sup> ed., Saunders Elsevier, St. Louis. pp. 310-321.
- FIDKOWSKI, C., J. HELSTROM (2009): Diagnosing metabolic acidosis in the critically ill: bridging the anion gap, Stewart, and base excess methods. Can. J. Anaesth. 56, 247-256.
- FIGGE, J., T. MYDOCH, V. FENCL (1992): Serum proteins and acid-base equilibria: a follow-up. J. Lab. Clin. Med. 120, 713-719.
- FLEGAR-MEŠTRIĆ, Z., S. PERKOV (2006): Comparability of point-of-care whole-blood electrolyte and substrate testing using a Stat Profile Critical Care Xpress analyzer and standard laboratory methods. Clin. Chem. Lab. Med. 44, 898-903.
- HASKINS, S. C. (2004): Interpretation of blood gas measurements. In: Textbook of respiratory disease in dogs and cats. (King, L. G., Ed.) Elsevier Health Sciences, St. Louis. pp. 181-190.

- ILKIW, J. E., R. J. ROSE, I. C. A. MARTIN (1991): A comparison of simultaneously collected arterial, mixed venous, jugular venous and cephalic venous blood samples in the assessment of blood gas and acid base status in dogs. J. Vet. Intern. Med. 5, 294-298.
- KELLUM, J. A. (2000): Determinants of blood pH in health and disease. Crit. Care 4, 6-14.
- KOGAN, D. A., L. R. JOHNSON, K. E. JANDREY, R. E. POLLARD (2008): Clinical, clinicopathologic, and radiographic findings in dogs with aspiration pneumonia: 88 cases (2004-2006). J. Am. Vet. Med. Assoc. 233, 1742-1727.
- MADIAS, N. E., W. H. BOSSERT, H. J. ADROGUE (1984): Ventilatory response to chronic metabolic acidosis and alkalosis in the dog. J. Appl. Physiol. 56, 1640-1646.
- MATOUSEK, S., J. HANDY, S. E. REES (2011): Acid-base chemistry of plasma: consolidation of the traditional and modern approaches from a mathematical and clinical perspective. J. Clin. Monitor. Comp. 25, 57-70.
- NAGAOKA, D., A. P. NASSAR JUNIOR, A. T. MACIEL, L. U. TANIGUCHI, D. T. NORITOMI, L. C. AZEVEDO, L. M. NETO, M. PARK (2010): The use of sodium-chloride difference and chloride-sodium ratio as strong ion difference surrogates in the evaluation of metabolic acidosis in critically ill patients. J. Crit. Care 25, 525-531.
- QUINTARD, H., S. HUBERT, C. ICHAI (2007): What is the contribution of Stewart's concept in acid-base disorders analysis? [In French.] Ann. Fr. Anesth. Reanim. 26, 115-128.
- ROCKTAESCHEL, J., H. MORIMATSU, S. UCHINO, R. BELLOMO (2003): Unmeasured anions in critically ill patients: can they predict mortality? Crit. Care Med. 31, 2131-2136.
- RUSSELL, K. E., B. D. HANSEN, J. B. STEVENS (1996): Strong ion difference approach to acidbase imbalances with clinical application to dogs and cats. Vet. Clin. North. Am. Small. Anim. Pract. 26, 1185-2001.
- SIEGLING-VLITAKIS, C., B. KOHN, C. KELLERMEIER, R. SCHMITZ, H. HARTMANN (2007): Qualification of the Stewart variables for the assessment of the acid-base status in healthy dogs and dogs with different diseases. [In German.] Berl. Münch. Tierärztl. Wochenschr. 120, 148-155.
- SIGGAARD-ANDERSEN, O., N. FOGH-ANDERSEN (1995): Base excess or buffer base (strong ion difference) as measure of a non-respiratory acid-base disturbance. Acta Anaesthesiol. Scand. Suppl. 107, 123-128.
- SIMEONOVA, G. (2003): Acid-base status and blood gas analysis in three different anaesthesia schemes in dogs. Turk. J. Vet. Anim. Sci. 28, 769-774.
- SINGH, A. J., V. BRONSHTEIN, M. KHASHU, K. LEE, J. E. POTTS, J. FRIEL, P. CHESSEX (2010): Vitamin A is systemically bioavailable after intratracheal administration with surfactant in an animal model of newborn respiratory distress. Pediatr. Res. 67, 619-623.
- SŁAWUTA, P., J. NICPOŃ, P. SKRZYPCZAK (2010): Contemporary approach to acid-base balance and its disorders in dogs and cats. Pol. J. Vet. Sci. 13, 561-567.
- SŁAWUTA, P., K. GLIŃSKA-SUCHOCKA (2012): Comparison of the utility of the classic model (the Henderson-Hasselbach equation) and the Stewart model (Strong Ion Approach) for the

diagnostics of acid-base balance disorders in dogs with right sided heart failure. Pol. J. Vet. Sci. 15, 119-124.

- STEWART, P. A. (1983): Modern quantitative acid-base chemistry. Can. J. Physiol. Pharmacol. 61, 1444-1461.
- VERWAERDE, P., C. MALET, M. LAGENTE, F. DE LA FARGE, J. P. BRAUN (2002): The accuracy of the i-STAT portable analyser for measuring blood gases and pH in whole-blood samples from dogs. Res. Vet. Sci. 73, 71-75.
- WAISMAN, Y., P. Q. EICHACKER, S. M. BANKS, W. D. HOFFMAN, T. J. MaCVITTIE, C. NATANSON (1993): Acute hemorrhage in dogs: Construction and validation of models to quantify blood loss. J. Appl. Physiol. 74, 510-519.
- WHITEHAIR, K. J., S. C. HASKINS, J. G. WHITEHAIR, P. J. PASCOE (1995): Clinical applications of quantitative acid-base chemistry. J. Vet. Intern. Med. 9, 1-11.

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SAŽETAK

Analiza plinova u arterijskoj krvi ključni je dio dijagnostike i praćenja oksigenacije organizma te acidobazičnog statusa. Svrha ovog istraživanja bila je utvrditi referentne vrijednosti za acidobazne pokazatelje i plinove u krvi klinički zdravih pasa različitog spola i dobi pomoću analizatora Stat Profile Critical Care Xpress (CCX) i omogućiti uvid u najprikladniji način analiziranja kompleksnih acidobaznih poremećaja. Arterijski uzorci pune krvi uzeti su od 40 klinički zdravih odraslih pasa različitih pasmina. Pokazatelji kvantitativnoga acidobaznog statusa (SID<sub>CLIN</sub>, SID<sub>APP</sub>, SID<sub>EFF</sub>, SIG) izračunani su Stewart-Figge-ovim pristupom. Referentni rasponi bili su: pH 7,37-7,44, pCO<sub>2</sub>22,62-34,52 mm Hg, pO<sub>2</sub>91,35-106,05 mm Hg, A 106,33-120,12 mm Hg, a/A 0,80-0,90 mm Hg, AaDO<sub>2</sub>-0,72-32,90 mm Hg, HCO<sub>3</sub>-14,06-22,10 mmol/L, BEecf -12,05-1,61 mmol/L, BE -9,7-0,46 mmol/L, SID<sub>CLIN</sub> 27,94-31,41 mmol/L, SID<sub>APP</sub> 26,00-31,60 mmol/L, SID<sub>EFF</sub> 29,27-36,21 mmol/L, SIG 2,32-7,46 mmol/L. Referentne vrijednosti dobivene na analizatoru CCX pružaju vrijedne informacije za postavljanje novih acidobaznih pokazatelja i za njihovu usporedbu između laboratorija. Razlike u odnosu na prethodno objavljene referentne vrijednosti acidobaznih pokazatelja iz ovog istraživanja mogu se smatrati referentnim vrijednostima za kontrolu zdravlja i dijagnostiku bolesti.

Ključne riječi: acidobazni pokazatelji, elektroliti, pas, jaki ioni