Polish Journal of Veterinary Sciences Vol. 15, No. 1 (2012), 119-124

DOI 10.2478/v10181-011-0122-8

Original article

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

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Abstract

Classically, the acid-base balance (ABB) is described by the Henderson-Hasselbach equation, where the blood pH is a result of a metabolic components – the HCO_3^- concentration and a respiratory component – pCO_2. The Stewart model assumes that the proper understanding of the organisms ABB is based on an analysis of: pCO_2, Strong Ion difference (SID) – the difference strong cation and anion concentrations in the blood serum, and the Acid total (Atot) – the total concentration of nonvolatile weak acids. Right sided heart failure in dogs causes serious haemodynamic disorders in the form of peripheral stasis leading to formation of transudates in body cavities, which in turn causes ABB respiratory and metabolic disorders. The study was aimed at analysing the ABB parameters with the use of the classic method and the Stewart model in dogs with the right sided heart failure and a comparison of both methods for the purpose of their diagnostic and therapeutic utility. The study was conducted on 10 dogs with diagnosed right sided heart failure. Arterial and venous blood was drawn from the animals. Analysis of pH, pCO_2 and HCO_3^- was performed from samples of arterial blood. Concentrations of Na^+, K^+, Cl^-, $P_{inorganic}$, albumins and lactate were determined from venous blood samples and values of Strong Ion difference of Na^+, K^+ and Cl^- (SID_3), Strong Ion difference of Na^+, K^+, Cl^- and lactate (SID_4), Atot, Strong Ion difference effective (SIDe) and Strong Ion Gap (SIG_4) were calculated. The conclusions are as follows: 1) diagnosis of ABB disorders on the basis of the Stewart model showed metabolic alkalosis in all dogs examined, 2) in cases of circulatory system diseases, methodology based on the Stewart model should be applied for ABB disorder diagnosis, 3) if a diagnosis of ABB disorders is necessary, determination of pH, pCO_2 and HCO_3^- as well as concentrations of albumins and $P_{inorganic}$ should be determined on a routine basis, 4) for ABB disorder diagnosis, the classic model should be used only when the concentrations of albumins and $P_{inorganic}$ are normal.

Key words: acid-base balance, Stewart model, dogs

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Research supported by the Ministry of Science and Higher Education in Poland in the years 2008-2011 (Project No. N N308 187735)

Introduction

Classically, the acid-base balance (ABB) is described by the Henderson-Hasselbach equation, where the blood pH is the resultant of the metabolic component expressed by the bicarbonate (HCO_3^-) concentration and the respiratory component or the pressure of carbon dioxide (pCO_2) by carbonic acid anhydride (Di Bartola 2006a):

$$pH = 6.11 + \log \frac{[HCO_3^-]}{pCO_2}$$

Changes of the blood pH caused by an original increase or decrease in the partial pressure of CO_2 (pCO_2) are called respiratory acidosis or alkalosis, respectively. If, despite the change of pCO_2, pH is within the norm, it is called compensated respiratory acidosis or alkalosis. In the case of respiratory acidosis, the organism, aiming at pH normalization, stimulates kidneys to regenerate HCO_3^- and expell H^+. In the case of alkalosis compensation, kidneys increase the discharge of HCO_3^- (Constable 2000, Di Bartola 2006a, Morris and Low 2008). Metabolic acidosis or alkalosis is characterized by an original decrease or increase in the HCO_3^- concentration in blood. If, despite the change of the HCO_3^- value, blood pH remains normal, the disorder is compensated. As a result of metabolic acidosis compensation, an increased respiratory action and a decrease in pCO_2 occur, which cause the blood pH to normalize. In the course of the metabolic alkalosis, a decrease in the respiratory action occurs leading to an increase in pCO_2 and blood pH compensation (Di Bartola 2006a, Morris and Low 2008). The compensation phenomenon, its clinical significance, changes of pCO_2 and HCO_3^- which accompany the compensation, and the problem of mixed disorders in dogs have been described in detail (Sławuta et al. 2010).

The Stewart model assumes that the proper insight into the organism ABB is given by an analysis of: pCO_2 (dependencies identical with those described for the classic method), SID (Strong Ion difference) – the difference in serum concentrations of strong cations and anions and the so-called Acid total – the total concentration of nonvolatile weak acids (Atot; the abbreviation A^- is used in some elaborations) (Stewart 1978, Stewart 1983). According to this theory called the Strong Ion approach, the ions in the blood serum can be divided into two groups – nonbuffer ions and buffer ions. The first group, which is also called strong ions, is fully dissociated and does not produce the buffering effect. The following cations are counted as the most important strong ions: Na^+, K^+, Ca^{2+}, Mg^{2+} and anions: Cl^-, lactate, β–hydroxybutrate, acetoacetate, and SO_4^- (Constable 2003). The changes of SID occur mainly in connection with the change of the Na^+ and Cl^- concentrations. Atot is a total of the buffer ions derived from plasma weak acids. The level of Atot consists mainly of proteins and phosphates, which practically means that an increase in the total protein concentration causes a decrease in the pH (Constable 2003). A decrease in SID, which occurs most often as a result of a decrease in the Na^+ concentration or an increase in Cl^-, causes the formation of strong ion (metabolic, hyperchloremic) acidosis, whereas an increase in SID is caused most often by an increase in Na^+ or a decrease in Cl^- and causes strong ion (metabolic) alkalosis (Boyle and Baldwin 2002, Rehm et al. 2004). With a change of the Atot concentration resulting from an increase in albumin, globulin and phosphate concentrations, nonvolatile buffer ion acidosis occurs. On the other hand, alkalosis is caused by a decrease in the nonvolatile buffer concentration, especially albumins, therefore it is sometimes called hypoalbuminemia. The notion of a strong ion gap (SIG) is derived from the Stewart model. This is an apparent difference between all unmeasured strong cations and all unmeasured strong anions. It differs from the anion gap connected with the classic model ($AG = [Na^+ + K^+] - [Cl^- + HCO_3^-]$) in that the albumin and phosphate concentrations are included in its calculation (Wooten 2004).

Right sided heart failure in dogs is caused the most often by: secondary right ventricular and atrial overload, as a result of the respiratory tract diseases, pulmonary artery stenosis or pulmonary hypertension (Glińska et al. 2006). It causes serious haemodynamic disorders in the form of peripheral stasis leading to transudates in body cavities, stasis oedema of parenchymatous organs and their functional impairment (Lambert et al. 1991), in connection with which respiratory and metabolic disorders may occur. Due to the accumulation of fluids in body cavities, administration of diuretics is one of the major elements of a therapy, which can lead to further complications in the form of loss of ions.

The aim of the presented paper is to shoe the analysis of ABB parameters in dogs with right sided heart failure with the use of the classic method and the Stewart model and comparison of both methods for the purpose of their diagnostic and therapeutic utility.

Materials and Methods

The study was carried out on 10 dogs of different breeds and sex, 6 to 9 years old with right sided heart failure diagnosed on the basis of clinical symptoms and signs (mixed dyspnoea, ascites, a drop in physical activity, anorexia) and echocardiographic examination (Aloka Prosound SSD 4000 SV with 5/7.5 MHz

probe) from the standard projections on the right and left side of the chest. All dogs examined were receiving a loop diuretic (Furosemid) as a part of treatment. Arterial and venous blood was drawn from each animal. One ml of full blood was drawn from the femoral artery into a heparinized syringe equipped with a needle with an internal diameter of 0.7 mm and the blood was passed on to the analytical laboratory immediately after its drawing. The following acid-base balance (ABB) parameters were determined in the arterial blood by means of the Osmetech OPTI CCA Blood Gas Analyser: pH, partial pressure of CO_2 (pCO_2), and concentration of bicarbonates (HCO_3^-). Six ml of full blood was drawn from the cephalic vein with a needle with an internal diameter of 0.8 mm into the test-tube. By means of Konelab prime 30i, venous blood concentrations of Na^+, K^+, Cl^-, $P_{inorganic}$, albumins and lactate were determined, as well as the alanine aminotransferase (ALAT) and aspartate aminotransferase (ASPAT) liver enzymes activity and the concentration of urea and creatinine. In all the animals, puncture of the abdominal cavity was performed. The animals were laid on the right or left side. Only in dogs with severe dyspnea this procedure was performed in the standing position. Abdominal skin was shaved to a minimum area of 25 cm^2 (5 x 5 cm), covering the navel in the center and disinfected twice with a solution of iodine. Puncture was performed in the white line 2-6 cm from the navel at the caudal direction. During the puncture, 5 ml of fluid was collected into the tubes with sylikon balls. The contents of albumins and Cl^- in the fluid drawn from the abdominal cavity were determined. The parameters that characterize the Stewart model were calculated according to the following formulas:

$SID_3 = (Na^+) + (K^+) – (Cl^-)$ (Siegling-Vlitakisi et al. 2007),

$SID_4 = [(Na^+) + (K^+)] – [(Cl^-) + (lactate^-)]$ (Siegling-Vlitakisi et al. 2007),

$Atot = [albumin \times (0.123 \times pH - 0.631)] + [P_{inorganic} \times (0.309 \times pH – 0.469)]$ (Rehm et al. 2004)

SIDe (SIDeffective) = (Atot) + (HCO_3^-) (Corey 2005).

$SIG_4 = (SID_4) – (SIDe)$ (Siegling-Vlitakisi et al. 2007),

The analysis of the ABB and its disorders was performed with the use of the classic method – on the basis of the HH equation, including the concentration of HCO_3^- and pCO_2 (Sławuta et al. 2010):

Disorder	pH	Primary change	Compensation
Respiratory acidosis	↓	↑ pCO_2	↑ HCO_3^-
Respiratory alkalosis	↑	↓ pCO_2	↓ HCO_3^-
Metabolic acidosis	↓	↓ HCO_3^-	↓ pCO_2
Metabolic alkalosis	↑	↑ HCO_3^-	↑ pCO_2

and assuming the values: pH-7.35-7.46, pCO_2 – 30.8-42.8 mmHg, HCO_3^- – 18.8 -25.6 mmol/l provided by Di Bartola (2006a) as normal values for dogs, and with the use of the Stewart method – applying the criteria provided by Corey (2005):

Acid-base disturbances	Disease state
Metabolic acidosis	Low SID and high SIG
	Low SID and low SIG
Metabolic alkalosis	Low serum albumin
	High SID

and assuming the values calculated for healthy dogs by Siegling-Vlitakis et al. (2007) as normal values for dogs: SID_3 – 33.10-50.90 mmol/l, SID_4 – 31.80-49.60 mmol/l, SIDe 27.30-37.40 mmol/l, SIG_4 (-)1.90 – (+)18.60 mmol/l, Atot 8.50-13.10 mmol/l

Results

The acid-base balance parameters presented in Table 1 and interpreted according to the classic model indicate compensated respiratory acidosis or compensated metabolic alkalosis in dogs No. 1, 2, 3, 4, 5, 6, 7, and 8: pH normal values in arterial blood, with concurrent pCO_2 and HCO_3^- exceeding the reference

Table 1. Values of the acid-base balance (ABB) parameters determined in arterial blood of ten dogs examined.

Item	pH	pCO_2 mmHg	HCO_3^- mmol/l
1.	7.40	53.00	32.50
2.	7.46	39.00	26.00
3.	7.42	46.00	29.30
4.	7.46	43.00	31.10
5.	7.45	44.00	28.70
6.	7.42	45.00	29.10
7.	7.44	46.00	30.00
8.	7.39	40.00	27.50
9.	7.46	34.00	26.30
10.	7.45	38.00	25.40

The reference values of the basic ABB parameters for dogs*

pH	pCO_2 mmHg	HCO_3^- mmol/l
7.35-7.46	30.8-42.8	18.8-25.6

* DiBartola SP (2006) Introduction to acid – base disorders. In: DiBartola SP (ed) Fluid, electrolyte and acid base disorders in small animal practice. Saunders Elsevier, St Louis, p 240.

Table 2. Concentrations of ions, albumins and lactate determined in blood serum of ten dogs examined.

Item	Na^+ mmol/l	K^+ mmol/l	Cl^- mmol/l	albumins g/l	P_i mmol/l	lactate mmol/l
1.	141.00	5.19	100.50	22.00	1.66	2.89
2.	142.80	4.58	101.90	21.00	1.79	2.26
3.	140.80	4.26	97.80	23.00	2.02	2.14
4.	146.60	4.94	101.70	24.00	1.07	1.43
5.	145.60	4.47	102.00	23.00	1.92	2.00
6.	144.10	4.49	99.80	21.00	1.48	1.98
7.	143.90	4.38	100.10	22.00	1.74	2.11
8.	141.30	4.27	98.70	25.00	1.65	2.61
9.	145.10	4.52	101.00	22.00	1.27	1.92
10.	142.10	4.32	99.10	22.00	1.62	2.69
Average values ±SD	143.33 2.04	4.54 0.30	100.26 1.43	22.50 1.26	1.62 0.28	2.20 0.42
Maximum value	146.60	5.19	102.00	25.00	2.02	2.89
Minimum value	140.80	4.26	97.80	22.00	1.07	1.43

The reference values of the ions, albumins and lactate in blood serum for dogs*

Na^+ mmol/l	K^+ mmol/l	Cl^- mmol/l	albumins g/l	P_i mmol/l	lactate mmol/l
139.10-156.50	4.10-5.40	98.70-115.6	33.00-56.00	1.35-2.87	1.11-3.89

* Winnicka A (1997) Badanie biochemiczne krwi. In: Winnicka A (ed) Wartości referencyjne podstawowych badań laboratoryjnych w weterynarii. Wydawnictwo SGGW, Warszawa, pp 37, 38, 44, 49, 51, 58, 62, 65

Table 3. Parameters that characterize the Stewart model calculated for ten dogs examined.

Item	SID_3 mmol/l	SID_4 mmol/l	Atot mmol/l	SIDe mmol/l	SIG_4 mmol/l
1.	45.69	42.8	9.15	41.65	1.15
2.	45.48	43.22	9.29	35.29	7.92
3.	47.26	45.12	10.15	39.45	7.81
4.	49.84	48.41	8.83	39.93	8.48
5.	48.07	46.07	10.07	38.77	7.3
6.	48.79	46.81	8.6	37.7	9.11
7.	48.18	46.07	9.43	39.43	6.64
8.	46.87	44.26	9.93	37.43	6.83
9.	48.62	46.70	8.63	34.93	11.77
10.	47.32	44.63	9.08	34.48	10.15
Average values ±SD	47.61 1.37	45.40 1.73	9.31 0.57	37.90 2.38	7.71 2.79
Maximum value	49.84	48.41	10.15	41.65	1.77
Minimum value	45.48	42.80	8.60	34.48	1.15

The reference values that that characterize the Stewart model for dogs*

SID_3 mmol/l	SID_4 mmol/l	Atot mmol/l	SIDe mmol/l	SIG_4 mmol/l
33.10-50.90	31.80-49.60	8.50-13.10	27.30-37.40	(-)1.90 – (+)18.60

* Siegling-Vlitakis C, Kohn B, Kellermeier C, Schmitz R, Hartmann H (2007) Qualification of the Stewart variables for the assessment of the acid-base status in healthy dogs and dogs with different diseases. Berl Munch Tierarztl Wochenschr 120: 148-155.

values (in dog No. 8, the concentration of HCO_3^- was increased and the concentration of pCO_2 was at the upper limit of the normal), whereas dog No. 9 (solely an insignificant increase in the HCO_3^- concentration) and dog No. 10 should be considered as free from ABB disorders. The average values of ions and lactate determined in blood serum (Table 2) were within normal limits as well as liver enzyme activity and the concentration of urea and creatinine. The concentration of albumins was below reference values for dogs (Winnicka 1997). The Stewart model parameters are presented in Table 3. The values of SID_3, SID_4 and SIDe in all animals examined exceeded the average values calculated for healthy dogs, whereas Atot and SIG_4 were within the reference values (Siegling-Vlitakis et al. 2007). According to the interpretation of the Stewart model provided by Corey (2005), a low concentration of albumins and a high value of SID are typical for metabolic alkalosis.

Discussion

While interpreting ABB disorders on the basis of the HH equation, it is essential to consider the compensation mechanisms and specifically to answer the question (which does not normally pose a problem) whether an increase/decrease in pCO_2 or an increase/decrease in HCO_3^- initially occurred, i.e. whether a disorder is of respiratory or metabolic character. In the course of right sided heart failure and development of haemodynamic abnormalities (Lambert et al. 1991, Glińska et al. 2006), it is difficult to determine whether an increase in pCO_2 occurred initially, or whether metabolic alkalosis occurred initially with an increase in HCO_3^- concentration as a results of compensation mechanisms, a loss of Cl^- resulting from diuretic treatment (Di Bartola 2006b), and/or ion loss into peritoneal cavity fluid, or excessive kidney regeneration of HCO_3^-. In both cases, the blood gasometry results will be similar with normal pH and increased pCO_2 and HCO_3^- (Sławuta et al. 2010). It is also difficult to assess clinically whether the observed dyspnoea was initially caused by a compensation of respiratory alkalosis (which is characterised by a decrease in the frequency of breathing mentioned before) or by respiratory tract diseases. In connection with that, it is impossible to confirm whether dogs No. 1 to 8 suffered from compensated respiratory acidosis or compensated metabolic alkalosis, which is important from a diagnostic point of view. This distinction is more important when chosing therapy as respiratory acidosis treatment is aimed of treating the underlying disease (i.e. the one causing dyspnoea) (Di Bartola 2006a, Sławuta et al. 2010), whereas metabolic alkalosis requires KCl administration (Di Bartola 2006b). According to the classic model, which does not take into account an influence of albumins and ions on the blood pH, dogs No. 9 and 10 are free from ABB disorders.

An analysis of ion concentrations in blood serum does not provide an answer regarding the character of the disorder. An observed low concentration of chlorides – 100.26 mmol/l (the norm range is: 98.7 – 115.6 mmol/l; Winnicka 1997) is typical for respiratory acidosis as the kidney compensation of this disorder is associated with an increase in the HCO_3^- synthesis during the amoniagenesis process, and the NH_4 created is discharged together with Cl^- ions (Wall 2001). However, this can also result from a loss of Cl ions with urine as a result of diuretic therapy, which is, in turn, a typical cause of metabolic alkalosis in dogs and cats (Di Bartola 2006b). The loss of Cl^- may also be connected with passing of these ions into the fluid in body cavities – the concentration of Cl^- in the peritoneal cavity fluid of the examined dogs amounted, on average, to 103.9 mmol/l ±4.48. A low concentration of blood serum albumins also resulted from their movement into the peritoneal cavity fluid, where their concentration was an average of 19.00 g/l ± 1.72.

The average correct values of SID_3, SID_4 and SIDe for dogs were provided by Siegling-Vlitakis et al. (2007), and they are 42.00 mmol/l, 40.70 mmol/l and 32.40 mmol/l, respectively. Values obtained in this study were higher (Table 3). Special attention should be drawn to the value of SIDe (SIDeffective = Atot + HCO_3^-). According to the formulas provided by Rehm et al. (2004) and Corey (2005) this value takes into account practically all plasma buffers, including albumins, $P_{inorganic}$ and HCO_3^- – most significant in clinical practice. The upper normal limit of 37.40 mmol/l was determined by Siegling-Vlitakis et al. (2007), whereas in this study, the average SIDe value was 37.90 mmol/l, and the lowest obtained value was 34.48 mmol/l, thus it was higher than the average values provided by the above-mentioned authors. According to the interpretation of the Stewart theory provided by Corey (2005), the diagnostics of the presented cases does not raise any doubts: a low concentration of albumins and increased concentrations of SID prove a metabolic alkalosis. A metabolic alkalosis is also present in dogs No. 9 and 10, as evidenced by low albumins levels (equalled 22.00 g/l in both cases) and high SID_3, SID_4 and SIDe.

The use of H-H equation for ABB interpretation is still widely used in diagnostics because of its simplicity and the fact that virtually all laboratory equipment used for gasometry examinations measure pH, pCO_2 and HCO_3^- (and many other parameters) without calculating SID, Atot and SIG values. From the

clinical point of view, the classic method has some limitations as it does not take into account an influence of plasma proteins and inorganic phosphate on the blood pH. Therefore, it should not be applied in the course of those diseases which cause a decrease in the production of albumins and albuminuria (e.g.: hepatic or renal failure) (Constable 2000). At present, there is a discussion, which also concerns veterinary medicine, about which diagnostic method for ABB disorders is the proper one (Russel et al. 1996, Constable 2000, McCullough and Constable 2003, Constable and Stämpfli 2005, Siegling-Vlitakis et al. 2007). The Stewart model, or the Strong Ion approach, requires theoretical preparation, yet there are still too few elaborations on its interpretation in veterinary medicine (Elkhair et al. 2009, Elkhair and Hartmann 2010) and the use in dogs and cats (Russel et al. 1996, Mc Cullough and Constable 2003, Constable and Stämpfli 2005). In practice, only the study of Siegling-Vlitakis et al. (2007) shows a successful comparison of both methods from a clinical point of view. The authors provided the values of SID, SIG and Atot, and their ranges in 58 healthy and 3 ill dogs (septic shock, acute renal failure, hypovolaemic shock in the course of gastric volvulus) together with a clear descriptions of their calculation methods.

In the light of the results obtained, the following conclusions can be drawn:

1) diagnosis of ABB disorders on the basis of the Stewart model showed metabolic alkalosis in all dogs examined

2) ABB disorders in cardiovascular system diseases should be estimated by means of methodology based on the Stewart model, because it is more accurate and indicates additional possibilities of the therapy (e.g.: KCl supplementation)

3) if ABB disorder diagnostics is necessary the concentration of albumins and $P_{inorganic}$ ought to be determined on a routine basis, additionally to usually measured pH, pCO_2 and HCO_3^-

4) according to Constabl's suggestion (2000), in case of ABB disorder diagnostics, the classic model should be used only when the concentrations of albumins and $P_{inorganic}$ are within normal limits.

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