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Original article

Use of elements of the Stewart model (Strong Ion Approach) – SID_3, SID_4, Atot/A^-, SID_e and SIG for the diagnostics of respiratory acidosis in brachycephalic dogs

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Abstract

Buffer systems of blood and tissues, which have the ability to bind with and give up hydrogen ions, participate in maintaining the acid-base balance (ABB) of the organism. According to the classic model, the system of carbonic acid and bicarbonates, where the first component serves the role of an acid and the second a base, determines plasma pH. The so-called Stewart model, which assumes that ions in blood serum can be separated into completely dissociated – nonbuffer and not dissociated – buffer ions which may give up or accept H+ions, also describes the ABB of the organism. The goal of the study was to find out whether, during respiratory acidosis, the values of SID_3, SID_4, Atot/A^-, SID_e and SIG change. The study was carried out on 60 adult dogs of the boxer breed (32 males and 28 females) in which, on the basis of an arterial blood test, respiratory acidosis was found. A strong overgrowth of the soft palate tissue requiring a surgical correction was the cause of the ABB disorder. Prior to surgery and on the 14th day after the surgery, venous and arterial blood was drawn from each dog. ABB parameters were determined in the arterial blood sample: the blood pH, pCO_2 and HCO_3^-. In the venous blood, concentration of Na^+, K^+, Cl^-, lactate$^-$, albumins, and $P_{inorganic}$ was determined. On the basis of the obtained data, the values of SID_3, SID_4, SID_e, A^- and SIG, before and after the surgery, were calculated. In spite of the fact that the average concentration of ions, albumins, $P_{inorganic}$ and lactate in the blood serum of dogs before and after the surgical procedure was similar and within the physiological norms, the values of SID_3, SID_e and SIG, calculated on the basis of the former, displayed statistically significant differences. Conclusion: On the basis of the results obtained, it can be stated that the values of SID_3, SID_e and SIG change during respiratory acidosis and may be helpful in the diagnostics of ABB disorders in brachycephalic dogs.

Key words: acid-base balance, the Stewart model, brachycephalic syndrome

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Introduction

Buffer systems of blood and tissues, which have the ability to bind with and release hydrogen ions participate in maintaining the acid-base balance (ABB) of the organism. Thanks to these properties, the addition of an acid (or a substance that gives up H^+ ions) or a base (or a substance that binds with H^+ ions) to these systems changes their pH value only to a small extent. According to the classic model, the system of carbonic acid and bicarbonates, where the first component serves the role of an acid and the second a base, is the basic system which determines plasma pH. Disorders of the functioning of this buffer cause systemic types of ABB disorders – acidosis and alkalosis (Balakrishnan et al. 2007, Sławuta et al. 2010). The rules of interpretation of the disorders were described in detail on the basis of the Henderson- Hasselbach (HH) equation, their type, compensation, and clinical significance (Constable 2000, Di Bartola 2006a, Morris and Low 2008, Sławuta et al. 2010). Apart from the HH equation, the ABB of the organism is also described by the Stewart model (Stewart 1978, 1983). According to this theory, which is 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, whereas the buffer ions (or the weak ions) are not fully dissociated and may give up or accept H^+ ions or, according to the Bronsted theory, fulfil the function of an acid or a base (Corey 2005). The following cations: Na^+, K^+, Ca^{2+}, and Mg^{2+} and anions: Cl^-, lactate, β-hydroxybutrate, acetoacetate, and SO_4^- are counted as the most important strong ions (Constable 2003), whereas the weak ions are mainly proteins and phosphates (Figge et al. 1991, 1998, Constable 2003). In practical terms, the Stewart model assumes that proper insight into the ABB of the organism is given by an analysis of: the values of pCO_2 (relationships are identical with the ones in the classic method), the difference of concentrations of strong cations and anions in the blood serum – SID (strong ion difference), and the total concentration of nonvolatile weak acids – Atot/A^- (Stewart 1978, 1983, Constable 2000). Changes in SID occur mainly in connection with the change of concentration of Na^+ and Cl^- (Boyle and Baldwin 2002, Rehm et al. 2004), whereas the value of Atot/A^- consists mainly of proteins and phosphates, which, practically, means that an increase in the total protein concentration causes a decrease in the pH (Figge et al. 1998, Constable 2003). The notion of an apparent strong ion gap – SIG also derives from the Stewart model. Unlike the classic anion gap (AG), whose diagnostic significance has already been described in detail (Sławuta et al. 2015), the concentration of albumins and phosphates is included in the calculation of SIG, thus, its diagnostic value is greater compared to the anion gap (Kellum 1995, Wooten 2004). In addition, the numerical value of SIG is influenced by the following, which are not determined on a routine basis: lactate, ketoanions, β-hydroxybutate, acetoacetate, sulphates and anions associated with uraemia. SIG is, in a sense, a developed concept of a modified anion gap (AG_m) applied in the diagnostics of ABB disorders in people and animals (Oh 2010, Sławuta et al 2015). Some authors (Fencl et al. 2000, Hooper et al. 2014a) treat the completion of the Stewart theory with an analysis of changes in the concentrations of: Cl^-, albumins, phosphorus and lactate as the third model that describes the ABB of the organism, known as the semiquantitive approach. The differences between SIG, AG and AG_m, calculation methods and their practical application in dogs have been described in detail (Sławuta et al. 2015).

In brachycephalic dogs, respiratory acidosis often occurs, which is caused as a result of permanently disturbed elimination of CO_2 – carbonic acid anhydride. Some anatomic obstacles in the upper airways of dogs make it impossible for air to flow freely (Sławuta et al. 2011, Hoareau et al. 2012).

According to the Stewart theory, the values of SID_3, SID_4, Atot/A^-, SID_e and SIG should change only when metabolic disorders of the acid-base balance are compensated for. However, the authors of this study, taking into account the results obtained earlier (Sławuta et al. 2015), assumed that if respiratory acidosis is of the systemic type then the concentration of ions which buffer the ABB disorders on an intracellular and pericellular level should also change. Thus, the goal of the study was to find out whether, in the course of respiratory acidosis, the values of SID_3, SID_4, Atot/A^-, SID_e and SIG change.

Materials and Methods

This study was carried out on 60 adult dogs of boxer breed (32 males and 28 females) in which, on the basis of the results of arterial blood testing, respiratory acidosis was found. A strong overgrowth of the soft palate tissue requiring a surgical correction was the cause of the ABB disorder diagnosed in endoscopic examination. Prior to surgery and on the 14th day after the surgery, arterial and venous blood was drawn from each dog. While planning the study, it was assumed that by the 14th day after surgery, the surgical wound healing process, swelling of the operated area and the influence of the drugs used during the surgery

Table 1. Effect of soft palate correction procedure on ABB parameters – mean values and standard deviation n=60.

Before procedure (37°C)			After procedure (14 th day after procedure, 37°C)		
pH	PCO_2 mmHg	HCO_3^- mmol/l	pH	pCO_2 mmHg	HCO_3^- mmol/l
7.41*	44.03*	25.80	7.43*	32.21*	22.011
±0.03	±3.42	±1.00	±0.01	±1.51	±1.31

Explanations: * – p≤0.01

Table 2. Concentration of ions, albumins, $P_{inorganic}$ and lactate in blood serum before and after soft palate correction procedure – mean values and standard deviation n= 60.

Before procedure (37°C)						After procedure (14 th day after procedure, 37°C)					
Na^+ mmol/l	K^+ mmol/l	Cl^- mmol/l	Alb g/l	Pi mmol/l	Lact mmol/l	Na^+ mmol/l	K^+ mmol/l	Cl^- mmol/l	Alb g/l	Pi mmol/l	Lact mmol/l
148.51	4.69	112.76	36.18	1.38	1.85	141.05	4.45	104.12	32.73	1.82	2.31
±1.30	±0.28	±1.90	±1.09	±0.20	±0.20	±1.13	±0.27	±1.50	±0.93	±0.15	±0.36

Table 3. Values of SID_3, SID_4, SID_e and SIG calculated before and after soft palate correction procedure – mean values and standard deviation, n=60.

Before procedure					After procedure (14 th day after procedure)				
SID_3	SID_4	$Atot/A^-$	SID_e	SIG	SID_3	SID_4	$Atot/A^-$	SID_e	SIG
40.46*	38.61	12.65	27.27**	11.36**	41.37*	39.05	12.06	34.61**	4.44**
1.91	1.92	0.57	2.48	1.36	1.63	1.71	0.38	1.28	1.86

Explanations:
* – p=0.06; ** – p<0.001

would end, and therefore the results obtained would be credible. A sample of arterial blood was drawn using the method described by Sławuta et al. (2015). With the use of an Osmetech OPTI CCA Blood Gas Analyzer unit, the following was determined in the drawn sample of arterial blood: blood pH, HCO_3^-, and pCO_2. The range of values provided for the arterial blood of dogs by Di Bartola (2006), was used as the standard. Hematologic testing of venous blood was carried out, including the following: complete blood count and concentration of Na^+, K^+, Cl^-, lactate$^-$, albumins, and $P_{inorganic}$. On the basis of the data obtained, the values of SID_3, SID_4, SID_e, $Atot/A^-$, and SIG were calculated before and after the surgical procedure, using the equations provided by Siegling-Vlitakis et al. (2007):

Parameter	Formula
SID_3	$([Na^+] + [K^+]) - Cl^-$
SID_4	$([Na^+] + [K^+]) - ([Cl^-] + [lactate^-])$
$Atot/A^-$	(albumin x [0.123 x pH-0.631]) + + ($P_{inorganic}$ x [0.309 x pH – 0.469])
SID_e	$Atot/A^- + HCO_3^-$
SIG	$(SID_4) - (SID_e)$

The results were subject to statistical analysis. The average value, standard deviation, and range of the obtained values were calculated. In order to compare the values of SID_3, SID_4, SID_e, $Atot/A^-$, and SIG obtained before and after the therapy, the paired t-Student test was applied for related variables. The analyses conducted with a significance level of 5% were carried out using the STATISTICA 10 software package manufactured by StatSoft, Inc. The endoscopic examination and the surgical procedure were carried out in general anaesthesia. In premedication, the patients received, intramuscularly, medetomidine at a dose of 30 µg/kg of body mass. After 15 minutes, fentanyl was administered intravenously at a dose of 2 µg/kg of body mass together with atropine at a dose of 40 µg/kg of body mass. The induction was carried out with the use of propophol at a dose of 4 mg/kg of body mass. Doses of medications and the anaesthesia procedure were in accordance with those described by other researchers (Ambros et al. 2008, Covey-Crump and Murison 2008, Enouri et al. 2008, Grint et al. 2010). For the performance of the study, the consent of the Local Ethics Commission II for Animal Experiments in Wrocław, number 07/2008, was received.

Results

According to the interpretation rules of the classic model (De Morais and Di Bartola 1991, Kellum 2000, Di Bartola, 2006, Sławuta et al. 2010), the obtained values of the pH of arterial blood and pCO_2 and HCO_3^- (Table 1) are evidence of compensated respiratory acidosis that occurred prior to the soft palate correction procedure in the examined dogs. On the other hand, on the 14th day after the surgery, the animals examined were free from the acid-base balance disorders. In spite of the fact that the mean concentrations of the studied ions, albumins, $P_{inorganic}$ and lactate in the blood serum of dogs before and after the procedure were similar and within the limits of physiological norms (Table 2), the values of SID_3, SID_e and SIG calculated on the basis of the above-mentioned values showed a statistically significant difference (Table 3).

Discussion

The values of SID_3, SID_4, SID_e, Atot/A^- and SIG calculated on the 14th day after the procedure, when the animals were free of respiratory acidosis, are compatible with the results obtained by other researchers examining healthy dogs (Siegling-Vlitakis et al. 2007, Hopper et al. 2014a, Wagner et al. 2015). In the literature, there is a lack of data regarding SID_3, SID_4, SID_e, Atot/A^- and SIG values through the duration of respiratory acidosis, since researchers concerned with ABB and its disorders believe that Stewart's model and its variant, described as a semiquantitative approach, are tools serving strictly the analysis of metabolic types of disorders. This is due to the views of the model's originator, Peter Stewart, who ascertained that respiratory ABB disorder analysis should be performed as in the classic model, in other words, on the basis of pCO_2 and HCO_3^- concentration, whereas metabolic disorder diagnostics should be based on the analysis of dependency between the passage of ions through cell membranes and the pH change thus created (Stewart 1978, 1983, Corey 2005).

In the results presented by Siegling-Vlitakis et al. (2007), a large difference is visible in the values of SID_3, SID_4, A^-, SID_e and SIG between dogs from the control group and the group of dogs with metabolic ABB disorders. In the presented study, such a tendency is also visible – dog SID_3, SID_e and SIG before and after the procedure displayed statistically significant differences. According to the authors of this study, this confirms the hypothesis of this study that buffer ions react to ABB disorders independently of the type of disorder. From this point of view, a very clear difference between the SID_e value for dogs with respiratory acidosis and dogs free from this disorder is especially important, since its calculation considers practically all buffers deemed to be „strictly metabolic" (Figge et al 1991, 1998, Corey 2005). It is also worthwhile to note that SID_e was significantly different in spite of the Atot/A^- value, which is used in its calculation, being almost identical in dogs before and after the procedure.

Current studies concerned with the utilisation of buffer ion concentration changes in the diagnostics of ABB disorders are limited to metabolic disorder types (Russel et al. 1996, Mc Cullough and Constable 2003, Corey 2005, Constable and Stampfli 2005, Siegling-Vlitakis et al. 2007, Hopper et al. 2014a,b). Correy (2005) developed rules of interpretation and diagnostics of metabolic acidosis and alkalosis on the basis of changes of SID and SIG values, albumin concentration and their mutual relationships. Hopper et al. (2014 a,b) found, upon analysis of metabolic ABB disorders in dogs and cats, a minor diagnostic and clinical usefulness of the classic model in the event that the studied animals have other than the physiological albumin and/or phosphorus concentrations, hence confirming Constable's (2000) suggestion.

The results obtained in the present study confirm Sławuta et al. (2015) earlier suggestion that regulation of the acid-base balance throughout the change of pCO_2 and HCO_3^- or concentration of buffer ions is part of the same process which ensures homeostasis of the organism. Currently, respiratory acidosis therapy practically comes down to treatment of the basic disease causing CO_2 retention. The authors of this study consider that a possibility for the practical application of the Stewart model in the diagnostics and therapy of the ABB disorders of respiratory type can complete a currently applied therapy with supplementation of ion concentrations or, alternatively dilution of their surplus with the use of nonelectrolyte fluids. This however, it would require further clinical research. The answer to the question whether there is a relationship this between the concentration of bicarbonates (HCO_3^-) and buffer ions during respiratory acidosis and what type of relationship this is also requires further research. The obtained results show a clear, although not statistically significant, increase in HCO_3^- concentration in dogs with respiratory acidosis. According to the interpretation rules of the classic model, this is obviously the result of compensation of the increase in partial pressure of CO_2 (pCO_2), whereas in this buffer system, HCO_3^- serves the role of a base (De Morais and Di Bartola 1991, Kellum 2000, Di Bartola 2006, Sławuta et al. 2010). However, it is not known whether, during respiratory acidosis, there is a dependency between the change of SID_3, SID_e and SIG concentrations and the HCO_3^- concentration and if, in this case as well, HCO_3^- accepts protons. The authors of this study have attempted to answer this question. It seems that such a relationship ought to exist since, as mentioned before, the SID_e value in dogs with respiratory acidosis differed significantly from the same value in dogs free from this disorder and, as it results from the equation intended for SID_e calculation, the value combines the concentration of ions and HCO_3^-.

Conclusions

The Stewart model, in practice, is used for differentiation of acid-base balance disorders in the case when interpretation according to the classic method, which does not include the influence of plasma proteins and phosphates on the blood pH, raises doubts. All clinical situations which require this have been described in detail (Sławuta et al. 2015). It is known that they are metabolic disorders but, on the basis of the results obtained, it may be stated that the values of SID_3, SID_e and SIG may also be useful in the diagnostics of respiratory acidosis in brachycephalic dogs.

References

Ambros B, Duke-Novakovski T, Pasloske KS (**2008**) Comparison of the anesthetic efficacy and cardiopulmonary effects of continuous rate infusions of alfaxalone-2-hydroxypropyl-beta-cyclodextrin and propofol in dogs. Am J Vet Res 69: 1391-1398.

Balakrishnan S, Gopalakrishnan M, Alagesan M, Prakash ES (**2007**) What is the ultimate goal in acid-base regulation? Adv Physiol Educ 31: 51-54.

Boyle M, Baldwin I (**2002**) Introduction to an alternate view of acid/base balance: the strong ion difference or Stewart approach. Aust Crit Care 15: 14-20.

Constable PD (**2000**) Clinical assessment of acid-base status: comparison of the Henderson-Hasselbalch and strong ion approaches. Vet Clin Pathol 29: 115-128.

Constable PD (**2003**) Hyperchloremic acidosis: the classic example of strong ion acidosis. Anesth Analg 96: 919-922.

Constable PD, Stampfli HR (**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.

Corey HE (**2005**) Bench-to-bedside review: Fundamental principles of acid-base physiology. Crit Care 9: 184-192.

Covey-Crump GL, Murison PJ (**2008**) Fentanyl or midazolam for co-induction of anaesthesia with propofol in dogs. Vet Anaesth Analg 35: 463-472.

De Morais HS, Di Bartola SP (**1991**) Ventilatory and metabolic compensation in dogs with acid-base disturbances. J Vet Emerg Crit Care 1: 39-49.

Di Bartola 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, pp 229-251.

Enouri SS, Kerr CL, McDonell WN, Dyson DH (**2008**) Cardiopulmonary effects of anesthetic induction with thiopental, propofol, or a combination of ketamine hydrochloride and diazepam in dogs sedated with a combination of medetomidine and hydromorphone. Am J Vet Res 69: 586-595.

Fencl V, Jabor A, Kazda A, Figge J (**2000**) Diagnosis of metabolic acid-base disturbances in critically ill patients. Am J Respir Crit Care Med 162: 2246-2251.

Figge J, Jabor A, Kazda A, Fencl V (**1998**) Anion gap and hypoalbuminemia. Crit Care Med 26: 1807-1810.

Figge J, Rossing TH, Fencl V (**1991**) The role of serum proteins in acid-base equilibria. J Lab Clin Med 117: 453-467.

Grint NJ, Alderson B, Dugdale AH (**2010**) A comparison of acepromazine-buprenorphine and medetomidine-buprenorphine for preanesthetic medication of dogs. J Am Vet Med Assoc 237: 1431-1437.

Hoareau GL, Jourdan G, Mellema M, Verwaerde P (**2012**) Evaluation of arterial blood gases and arterial blood pressures in brachycephalic dogs. J Vet Intern Med 26: 897-904.

Hopper K, Epstein SE, Kass PH, Mellema MS (**2014a**) Evaluation of acid-base disorders in dogs and cats presenting to an emergency room. Part 1: comparison of three methods of acid-base analysis. J Vet Emerg Crit Care (San Antonio) 24: 493-501.

Hopper K, Epstein SE, Kass PH, Mellema MS (**2014b**) Evaluation of acid-base disorders in dogs and cats presenting to an emergency room. Part 2: comparison of anion gap, strong ion gap, and semiquantitative analysis. J Vet Emerg Crit Care (San Antonio) 24: 502-508.

Kellum JA (**2000**) Determinants of blood pH in health and disease. Crit Care 4: 6-14.

Kellum JA, Kramer DJ, Pinsky MR (**1995**) Strong ion gap: a methodology for exploring unexplained anions. J Crit Care 10: 51-55.

McCullough SM, Constable PD (**2003**) Calculation of the total plasma concentration of nonvolatile weak acids and the effective dissociation constant of nonvolatile buffers in plasma for use in the strong ion approach to acid-base balance in cats. Am J Vet Res 64: 1047-1051.

Morris CG, Low J (**2008**) Metabolic acidosis in the critically ill: part 1. Classification and pathophysiology. Anaesthesia 63: 294-301.

Oh YK (**2010**) Acid-base disorders in ICU patients. Electrolyte Blood Press 8: 66-71.

Rehm M, Conzen PF, Peter K, Finsterer U (**2004**) The Stewart model. „Modern" approach to the interpretation of the acid-base metabolism. Anaesthesist 53: 347-357.

Russell KE, Hansen BD, Stevens JB (**1996**) Strong ion difference approach to acid-base imbalances with clinical applications to dogs and cats. Vet Clin North Am Small Anim Pract 26: 1185-1201.

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.

Sławuta P, Glińska-Suchocka K, Cekiera A (**2015**) The use of elements of the Stewart model (Strong Ion Approach) for the diagnostics of respiratory acidosis on the basis of the calculation of a value of a modified anion gap (AG_m) in brachycephalic dogs. Pol J Vet Sci 18: 217-222.

Sławuta P, Nicpoń J, Domańska S (**2011**) Influence of the wing-of-the-nostrils correction procedure on the change of the acid-base balance parameters and oxygen concentration in the arterial blood in French bulldogs. Pol J Vet Sci 14: 77-80.

Sławuta P, Nicpoń J, Skrzypczak P (**2010**) Contemporary approach to acid-base balance and its disorders in dogs and cats Pol J Vet Sci 13: 561-567.

Stewart PA (**1978**) Independent and dependent variables of acid -base control. Respir Physiol 33: 9-26.

Stewart PA (**1983**) Modern quantitative acid-base chemistry. Can J Physiol Pharmacol 61: 1444-1461.

Wagner J, Rieker T, Siegling-Vlitakis C (**2015**) Blood gas analysis in dogs in veterinary practice. A review. Tierarztl Prax Ausg K Kleintiere Heimtiere 43: 260-272.

Wooten EW (**2004**) Science review: quantitative acid-base physiology using the Stewart model. Crit Care 8: 448-452.