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$_4$, 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$_4$, A$^-$ 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$_4$ 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, Slawuta 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, Slawuta 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, fulfill the function of an acid or a base (Corey 2005). The following cations: Na⁺, K⁺, Ca²⁺, and Mg²⁺ and anions: Cl⁻, lactate, β-hydroxybutrate, acetoacetate, and SO₄²⁻ 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 pCO₂ (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 non-volatile 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 (Slawuta 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 (AGm) applied in the diagnostics of ABB disorders in people and animals (Oh 2010, Slawuta 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 semiquantitative approach. The differences between SIG, AG and AGm calculation methods and their practical application in dogs have been described in detail (Slawuta et al. 2015).

In brachycephalic dogs, respiratory acidosis often occurs, which is caused as a result of permanently disturbed elimination of CO₂ – carbonic acid anhydride. Some anatomic obstacles in the upper airways of dogs make it impossible for air to flow freely (Slawuta et al. 2011, Hoareau et al. 2012).

According to the Stewart theory, the values of SIDe, SIDₐ, Atot/A’; SIDₐ 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 (Slawuta 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 SIDe, SID₂, Atot/A’, SIDₐ 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 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.

<table>
<thead>
<tr>
<th></th>
<th>Before procedure (37°C)</th>
<th>After procedure (14th day after procedure, 37°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.41* ±0.03</td>
<td>7.43* ±0.01</td>
</tr>
<tr>
<td>PCO₂ mmHg</td>
<td>44.03* ±3.42</td>
<td>32.21* ±1.51</td>
</tr>
<tr>
<td>HCO₃⁻ mmol/l</td>
<td>25.80 ±1.00</td>
<td>22.01 ±1.31</td>
</tr>
</tbody>
</table>

Explanations: * – p ≤ 0.01

Table 2. Concentration of ions, albumins, Pₐₙ₉ᵢ₉ᵢ₉₉ and lactate in blood serum before and after soft palate correction procedure – mean values and standard deviation n = 60.

<table>
<thead>
<tr>
<th></th>
<th>Before procedure (37°C)</th>
<th>After procedure (14th day after procedure, 37°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ mmol/l</td>
<td>148.51 ±1.30</td>
<td>141.05 ±1.13</td>
</tr>
<tr>
<td>K⁺ mmol/l</td>
<td>4.69 ±0.28</td>
<td>4.45 ±0.20</td>
</tr>
<tr>
<td>Cl⁻ mmol/l</td>
<td>112.76 ±1.90</td>
<td>104.12 ±1.50</td>
</tr>
<tr>
<td>Alb g/l</td>
<td>36.18 ±1.09</td>
<td>32.73 ±1.50</td>
</tr>
<tr>
<td>Pi mmol/l</td>
<td>1.38 ±0.20</td>
<td>1.82 ±0.93</td>
</tr>
<tr>
<td>Lact mmol/l</td>
<td>1.85 ±0.20</td>
<td>2.31 ±0.36</td>
</tr>
</tbody>
</table>

Table 3. Values of SID₃, SID₄, SIDₑ, and SIG calculated before and after soft palate correction procedure – mean values and standard deviation, n=60.

<table>
<thead>
<tr>
<th></th>
<th>Before procedure</th>
<th>After procedure (14th day after procedure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SID₃</td>
<td>40.46*</td>
<td>41.37*</td>
</tr>
<tr>
<td>SID₄</td>
<td>38.61</td>
<td>39.05</td>
</tr>
<tr>
<td>Atot/A⁻</td>
<td>12.65</td>
<td>12.06</td>
</tr>
<tr>
<td>SIDₑ</td>
<td>27.27**</td>
<td>34.61**</td>
</tr>
<tr>
<td>SIG</td>
<td>11.36**</td>
<td>4.44**</td>
</tr>
<tr>
<td>SID₃</td>
<td>1.91</td>
<td>1.92</td>
</tr>
<tr>
<td>SID₄</td>
<td>0.57</td>
<td>0.57</td>
</tr>
<tr>
<td>Atot/A⁻</td>
<td>2.48</td>
<td>2.48</td>
</tr>
<tr>
<td>SIG</td>
<td>1.36</td>
<td>1.36</td>
</tr>
</tbody>
</table>

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

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 SID₃, SID₄, SIDₑ, 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 propofol 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 Wroclaw, 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, Slawuta 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 14\(^{th}\) 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\(_{\text{Horgan}}\) 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\(_4\), Atot/A\(^-\) 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 14\(^{th}\) 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\(_3\) 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, McCullough 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 Slawuta 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, Slawuta 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 (Slawuta 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


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