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Acid-base disorder analysis during diabetic ketoacidosis using the Stewart approach — a case report

Jakub Szrama, Piotr Smuszkiewicz

Department of Anaesthesiology, Intensive Therapy and Pain Management, University Hospital no. 2 in Poznań, Poland

Abstract

This case report presents a 49 year-old female with type 1 diabetes admitted to the intensive care unit with acute respiratory failure and severe diabetic ketoacidosis with an initial measurement of blood glucose level of 1,200 mg L^{-1}, pH 6.78, serum HCO_3^- 3.2 mmoL L^{-1} and BE –31.2 mmoL L^{-1}. Analysis of the blood gasometric parameters with the Stewart approach and the traditional Henderson-Hasselbalch concept enabled the discovery of metabolic acidosis caused by unidentified anions (mainly ketons). A treatment protocol with intensive fluid management with 0.9% NaCl, intensive intravenous insulin therapy, and potassium supplementation was administered. Analysis of the gasometric parameters after 12 hours of treatment according to the Stewart approach compared to the Henderson-Hasselbalch concept disclosed that metabolic acidosis caused by the unidentified anions has resolved almost completely and been replaced by metabolic hyperchloremic acidosis. The hyperchloremic acidosis was caused by the intensive fluid resuscitation with 0.9% NaCl, which contains a high chloride load, exceeding the chloride levels observed in human serum. Fluid management with balanced fluids other than saline was continued, together with intravenous insulin infusion, potassium supplementation, and 5% glucose administration. Analysis of this case study revealed the advantages of the Stewart approach to acid base abnormalities compared to the traditional Henderson-Hasselbalch concept. The Stewart approach allows the diagnosis of the exact causes of severe life-threatening metabolic acidosis and the appropriate modification of the therapeutic mangement of patients with diabetic ketoacidosis.

Key words: diabetic ketoacidosis, acid-base status, disorders; acid-base status, Stewart approach

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Diabetic ketoacidosis (DKA) is an acute type 1 diabetes mellitus complication and is associated with a 5% mortality rate. Its major causes include bacterial infections, acute coronary syndrome, insulin omissions and inadequate insulin doses [1]. DKA diagnoses are based on high glycaemia, arterial blood acid-base balance analyses (pH, HCO_3^- concentration and base excess — BE), the presence of ketone bodies in the urine and plasma, as well as serum effective osmolality and anion gap (AG) calculations. DKA treatment involves intensive fluid therapy with 0,9% NaCl, intravenous insulin therapy and an electrolyte abnormalities correction [1].

The aim of the present study was to analyse the acid--base balance in a female intensive care unit patient treated for DKA using the Stewart physicochemical method.

CASE REPORT

A 49-year-old female patient diagnosed with arterial hypertension and type 1 diabetes mellitus was admitted to the Department of Cardiology with suspected acute coronary syndrome. ECG recordings showed negative T waves in the III and aVF leads and an elevated ST segment in the V1, V2 and V3 leads. The baseline cardiac troponin level was within the reference values; therefore, the decision was made to postpone coronarography and determine the troponin concentration after 6 hours. Because the patient's consciousness state deteriorated and respiratory disorders developed, the patient was assessed by an anaesthesiologist and qualified for ICU treatment.

On ICU admission, the patient was under sedation and was being mechanically ventilated. Additionally, her circula-

tion was inefficient and was being supported with catecholamine infusion. Moreover, her heart rate was 90 min^{-1}, her arterial pressure was 160/90 mm Hg, and her blood glucose concentration was 1200 mg dL^{-1}.

The results of the first arterial blood acid-base balance and other relevant parameter determinations are presented in Table 1. During hyperglycemia extracellular fluid osmolality increases (glucose poorly permeates the cell membranes in the absence of insulin) and water is shifted from the intracellular to the extracellular space. This leads to a sodium concentration decrease that is proportional to the extracellular fluid dilution. The glycaemia-corrected sodium concentration was calculated according to the formula Na_{corr} = Naact (1.6 × ((Glc*– 100)/100)). Based on this calculation, the patient's Na_{corr} was 139.6 mmoL L^{-1}.

A hyperglycaemic coma and ketoacidosis were diagnosed, and the treatment was instituted according to the following recommended strategy: intensive fluid therapy with 0.9% NaCl, intensive insulin therapy and potassium supplementation.

To establish the microbiological diagnosis, blood, urine, cerebrospinal fluid and bronchoalveaolar lavage (BAL) specimens were cultured, and empiric antibiotic therapy was introduced (amoxicillin with clavulanic acid, clarithromycin and metronidazole).

Mechanical lung ventilation, catecholamine infusion, fluid therapy and potassium supplementation were continued. Additionally, glycaemia testing, electrolyte level determinations and arterial blood gasometries were also performed every hour. The results after 12 hours of treatment are presented in Table 2. Because the acid-base balance parameters improved and glycaemia normalised on the following day, solutions other than the 0.9% NaCl fluid were administered. Furthermore, the intravenous insulin therapy, potassium supplementation and 5% glucose solution infusions were continued. On day 3, Gram(+) cocci were found in the blood and BAL cultures, C-reactive protein (CRP level) increased to 365.8 mg dL^{-1}, the procalcitonine (PCT) concentration was 30.5 µg L^{-1} so linezolid was empirically instituted. The patient's general condition and circulatory efficiency improved, and the laboratory and gasometric parameters normalised.

Ultimately, staphylococcus aureus, which was susceptible to methicillin, was observed in the blood and BAL cultures; therefore, the antibiotic therapy was modified to include cloxacillin in accordance with an antibiogram. On day 7, the endotracheal tube was removed, and on day 9, the patient was transferred to the Diabetology department.

*Glc — blood glucose concentration

DISCUSSION

Acid-base disorders are common in ICU patients and contribute to increased mortality and morbidity [2, 3]. Acid-base disorder diagnoses are most commonly based on the traditional Henderson-Hasselbalch (H-H) approach, which takes into account SBE and bicarbonate concentrations but enables the detection of only one type of disorders (e.g., respiratory or metabolic) [3, 4]. The advantage of this method is that it can be used widely and easily in everyday clinical conditions. In cases of simple acid-base disorders, this method is sufficient; however, its usefulness in ICU patients is limited as it provides little information regarding the severity and causes of the disorders [5].

Furthermore, the H-H method oversimplifies complex acid-base disorders, such as the coexistence of several types of metabolic acidosis or of metabolic acidosis and alkalosis. To complement the H-H approach, the anion gap (AG),

Table 1. The baseline selected laboratory parameter values

pH 6.78	Na 122 mmoL L^{-1}	CRP 90.4 mg dL^{-1}
$PaCO_2$ 22.6 mm Hg	Na_{corr} 139.6 mmoL L^{-1}	WBC 20.5 G L^{-1}
HCO_3^- 3.2 mmoL L^{-1}	K 7 mmoL L^{-1}	creatinine 2.89 mg dL^{-1}
BE –31.2 mmoL L^{-1}	Cl 100 mmoL L^{-1}	albumins 35.6 g L^{-1}
PaO_2 171 mm Hg	AG 25.8 mmoL L^{-1}	PCT 19.15 µg L^{-1}
O_2sat 98.2%	lactates 2.0 mmoL L^{-1}	

PaO_2 — partial oxygen pressure; the remaining abbreviations are explained in the text

Table2. The results after 12 hours of treatment

pH 7.11	Na 138 mmoL L^{-1}	glucose 242 mg dL^{-1}
$PaCO_2$ 32.5 mm Hg	Na_{corr} 140.3 mmoL L^{-1}	albumins 28.4 g L^{-1}
HCO_3^- 11.4 mmoL L^{-1}	K 5.4 mmoL L^{-1}	
BE –17.6 mmoL L^{-1}	Cl 120 mmoL L^{-1}	
PaO_2 78.7 mm Hg	AG 12 mmoL L^{-1}	
O_2sat 96.9%	lactates 0.8 mmoL L^{-1}	

PaO_2 — partial oxygen pressure; the remaining abbreviations are explained in the text

i.e., the differences in Na, K, Cl and HCO_3 concentrations, or the anion gap corrected for albumins (AG_{corr}) is calculated, which enables more precise interpretations of complex acid-base disorders.

An alternative approach to acid-base derangements is the physicochemical model designed by Peter Stewart in 1981 [6, 7]. This model includes three independent variables that affect the hydrogen ion concentration and pH. The variables are 1) the strong ion difference (SID), i.e., the difference between the totally dissociated cation and anion concentrations, mainly Na and Cl; 2) the total weak acid concentrations, which are predominantly phosphates and albumins; and 3) $PaCO_2$ [8].Understanding the Stewart method is contingent upon realising that these three variables are relevant for the acid-base balance and that the H^+ and HCO_3^- concentrations are dependent variables. This approach employs mathematical formulae to allow for inclusion of such variables as Na, Cl, and albumin concentrations, as well as the presence of lactates and other unidentified anions (XA^-) [9–11]. Several studies have demonstrated that the use of the Stewart method for acid-base disorder evaluations is superior to the classic H-H interpretation [4, 5, 12, 13].

The case described illustrates the use of Stewart approach and its superiority over the traditional H-H model. Thanks to the Stewart method, all severe metabolic acidosis sources were determined, and the therapeutic process was suitably modified. Our type 1 diabetes mellitus patient was admitted because of severe ketone acidosis, which developed due to sepsis. Analysis of the first gasometry, according to the H-H model, revealed severe metabolic acidosis with elevated AG caused by the presence of ketone bodies. However, calculating the anion gap is essential, considering the sodium concentration corrected for hyperglycaemia and AG_{corr} according to the formula $AG_{corr} = AG + (42 - alb_{act}$ g $L^{-1})/4$. The calculations are as follows:

$$AG = Na_{corr} + K - Cl - HCO_3^- =$$
$$= 139.6 + 7 - 100 - 3.2 = 43.4 \text{ mmoL } L^{-1}$$

$$AG_{corr} = 43.4 + (42 - 35.6)/4 = 44.5 \text{ mmoL } L^{-1}.$$

The anion gap from the first gasometry was 25.8 mmoL L^{-1}, which demonstrates how carefully raw laboratory results should be interpreted, as they do not consider the certain pathophysiological changes that result from hyperglycaemia and hyperalbuminaemia.

The same gasometry analysed with the Stewart method provided more precise acid-base disorder characteristics in our patient. There are simple "bedside" formulae that enable rapid gasometric metabolic disturbance analysis and use the four elements that affect the acid-base balance mentioned earlier, i.e., Na, Cl, albumin and the presence of unidentified XA^- ion concentrations (including lactates, ketoacids and others). Gasometric SBE is always a de facto net value and a result of all disturbances, while each component (Na, Cl, XA^- and albumin) contributes its "own" BE value. Thus, the gasometric SBE should be equal to the sum of all components:

$$SBE_{lab} = BE_{NaCl} + BE_{alb} + BE_{XA^-}$$

In this equation, SBE_{lab} is the gasometric SBE value, and BE_{NaCl}, BE_{alb}, BE_{XA^-} are the BE values resulting from changes in the Na and Cl, albumin and XA^- concentrations, respectively. After transformation, the BE, induced by the presence of XA^-, is calculated according to the formula

$$BE_{XA^-} = SBE - BE_{NaCl} - BE_{albumin}$$

Additionally, each BE value can be calculated using the simple formulae

$$BE_{NaCl} = Na - Cl - 38$$

and

$$BE_{albumin} = (42 - \text{albumins g } L^{-1})/4$$

By replacing the suitable parameter values from the first gasometry, the calculations are as follows (with Na_{corr} taken into account):

$$BE_{NaCl} = 139.6 - 100 - 38 = +1.6$$

and

$$BE_{albumin} = (42 - 35.6)/4 = +1.6$$

Hence,

$$BE_{XA^-} = -31.2 - 1.6 - 1.6 = -34.4$$

The calculations show that the 31.2 gasometric SBE value reflects metabolic acidosis resulting from the presence of unidentified XA^- anions ($BE_{XA^-} = -34.4$ mEq L^{-1} [predominantly ketone bodies]), slight metabolic alkalosis resulting from the abnormal Na/Cl ratio ($BE_{NaCl} = +1.6$ mEq L^{-1}) and slight metabolic alkalosis resulting from slight hypoalbuminaemia ($BE_{alb} = +1.6$). Moreover, both the H-H and Stewart method scan identified respiratory alkalosis ($pCO_2 = 22.6$ mm Hg). Analysis of the first gasometry points mainly to significant metabolic acidosis caused by the presence of ketone bodies. In this case, the classic H-H approach and the Stewart method are to a great extent similar, except that the latter method identified two other coexisting disorders (alkalosis resulting from the Na/Cl ratio and alkalosis associated with hypoalbuminemia); however, these disorders are of no clinical importance.

Notably, in simple acid-base disorder cases (one type of acidosis, such as ketone acidosis) the approaches appear to be comparable, whereas in complex acid-base abnormalities, they are not. This differences is evidenced by the

gasometry analysis performed after 12 hours of treatment and the infusion of 5.5 L of 0.9% NaCl solution. Thus, the individual BE constituents were recalculated as follows:

$$BE_{NaCl} = 140.3 - 120 - 38 = -17.7$$

$$BE_{albumin} = (42 - 28.4)/4 = +3.4$$

$$BE_{XA^-} = -17.6 - (-17.7) - 3.4 = -3.3$$

$$AG_{corr} = 12 + (42 - 28.4)/4 = 15.4$$

Parameter analyses according to the H-H theory still revealed metabolic acidosis, which gradually normalised (AG_{corr} in the upper normal limit) but did not identify the cause of acidosis. The analysed parameters may suggest that the acidosis was still associated with the presence of unidentified XA^- anions (ketones). Such a conclusion would result in the continuation of the treatment undertaken earlier (i.e., the 0.9% NaCl solution fluid therapy), which may have intensified the metabolic acidosis.

Using the Stewart method, we could be sure that after the 12-hour therapy, the metabolic acidosis associated with the presence of XA^-anions (BE_{XA^-}= –3.3)would virtually subside. Additionally, this acidosis was replaced mainly by hyperchloraemic metabolic acidosis with a total laboratory SBE = –17.6. This SBE value indicated slight acidosis resulting from the presence of XA^- (most likely ketone bodies), severe hyperchloraemic acidosis (with a BE_{NaCl} = –17.7) and hypoalbuminaemic alkalosis (with a BE_{alb} = +3.4). Hyperchloraemic acidosis mostly results from intensive 0.9% NaCl fluid therapy, during which the chlorine content fluid markedly exceeds the plasma values. Considering that the gasometry parameters were interpreted in such a way, the fluid therapy was modified, and balanced fluids, plus a 8.4% $NaHCO_3$ solution, were administered to supply Na and to increase the difference between the Na and Cl ions (i.e., to increase the SID difference and to normalise the acid-base balance). Due to the fluid therapy change from the 0.9% NaCl solution to the balanced lower chlorine fluid content, the hyperchloraemic acidosis was abated.

The analyses in our case demonstrate that complex acid-base disorders can be properly interpreted and that the actual gasometry abnormality cause can be found using the Stewart method. Moreover, this approach is relevant for fluid therapy and indicates that the fluids used are likely to affect the gasometry results. The treatment strategy for ketone acidosis involves intravenous insulin therapy, potassium supplementation and intensive fluid therapy during which 5.5–6.2 L of 0.9% NaCl solution is infused over the first 24 h. However, it should be strongly emphasised that the so called "physiological saline" is not actually physiological, as the concentration of Na and Cl equals 154 mmoL L^{-1} (SID = 0), which is far from the physiological plasma Na concentration and even farther from the Cl concentration (SID = 38). The supply of fluids with a high Cl content result in enhanced water dissociation and an increased H^+ ion concentration. To avoid post-infusion acid-base disorders, balanced fluids should be used (i.e., with SID = 24 mEq L^{-1}) [14]. The term "hyperchloraemic acidosis" is not correct for all cases, as the chlorine concentration should always be considered in relation to the sodium concentration. The Na/Cl ratio is more important (norm = 0.75) because this value increases during acidosis. This type of acid-base abnormality should be termed as acidosis with a "low SID". Currently there is no explicit evidence that hyperchloraemic acidosis (i.e., acidosis with a "low SID") increases ICU patient mortality or morbidity. Nevertheless, a certain tendency can be observed, in which this acidosis type adversely affects the functioning of some organs (mostly gastrointestinal organs, kidneys or the clotting system), increases nitrogen oxide synthesis and induces hypotension. These negative effects can result from acidosis per se, hyperchloraemia or both [15].

The analyses presented above demonstrate the superiority of the Stewart method over the traditional H-H model. Thanks to the Stewart approach, all acid-base disorder causes were determined, as were the severe metabolic acidosis sources. Moreover, the therapeutic management was suitably modified. This case provides evidence that fluid therapy during DKA should take into account more widely balanced fluid use (and not "physiological saline") to avoid the development of hyperchloraemic acidosis with low a SID.

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Corresponding author:
Jakub Szrama, MD
Department of Anaesthesiology
Intensive Therapy and Pain Management
University Hospital no. 2
ul. Przybyszewskiego 49, 60–355 Poznań, Poland
tel.: +48 61 869 13 57
fax: +48 61 869 16 85
e-mail: jakub.szrama@gmail.com

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