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Utility of Partitioning of Standard Base Excess in Euglycemic Diabetic Ketoacidosis with Hyperchloremic Acidosis

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Euglycemic diabetic ketoacidosis (EDKA) can be difficult to recognize during surgery, particularly when the anion gap (AG) is within the normal range. A 73-year-old female patient with type 2 diabetes mellitus underwent surgical adhesiolysis and enterostomy for intestinal obstruction. The patient showed a normal serum glucose level and hyperchloremic acidosis but had an accumulation of unmeasured anions (UA) detected by partitioning of the standard base excess (SBE). This prompted testing for serum ketones, which confirmed the presence of EDKA during surgery. The calculation of the hyperchloremic base deficit as a percentage of the total acidifying base deficit revealed a significant contribution of hyperchloremic acidosis to the severity of mixed metabolic acidosis. The AG approach can misdiagnose high AG metabolic acidosis (HAGMA) with hyperchloremic acidosis as hyperchloremic acidosis only. Partitioning of the SBE can be useful for detecting UA when both HAGMA and hyperchloremic acidosis are present, and it may help determine the necessity of treating hyperchloremia during EDKA.

Keywords: Anion gap, Diabetic ketoacidosis, Hyperchloremia, Metabolic acidosis, Standard base excess

Introduction

Euglycemic diabetic ketoacidosis (EDKA) is characterized by normal glucose level (< 200 mg/dL), metabolic acidosis (pH < 7.3 and serum bicarbonate < 18 mM/L), and ketonemia [1]. EDKA is often discovered incidentally during surgery due to unexplained metabolic acidosis in patients with risk factors. Changes in acid-base status may prompt the evaluation for EDKA. To diagnose EDKA, arterial blood gas analysis (ABG) for high anion gap metabolic acidosis (HAGMA) and serum glucose and ketone testing are essential in diabetic patients [2].

However, the traditional anion gap (AG) approach may be unsuitable for complex acid-base disorders. An alternative assessment of acid-base disorders is a mathematical model based on the physicochemical principles described by Stewart [3]. However, the Stewart approach is a complex method for clinical use. Thus, several studies [4,5] have attempted to simplify the Stewart approach to acid-base physiology and combine it with the base excess approach. Story et al. [6] described the simplified Fencl-Stewart approach for the partitioning of the standard base excess (SBE). This approach uses four equations to estimate the base excess effects of the important components: the strong ion difference (sodium and chloride), the total weak acid concentration (albumin) and unmeasured ions. Therefore, this approach allows the components of acid-base disorders to be quantified individually, providing a better understanding of the pathogenesis.

We present a case of a patient with type 2 diabetes who was diagnosed with

EDKA, even though the AG approach failed to identify HAGMA during surgery. The patient exhibited normal AG metabolic acidosis according to ABG. However, subsequent partitioning of the SBE revealed the presence of unmeasured anions (UA) and a significant contribution of hyperchloremia to the total acidifying base deficit. We will explore the limitations of the AG approach and the advantages of SBE partitioning in the context of the diagnosis of HAGMA with hyperchloremic acidosis and the administration of bicarbonate therapy. Written informed consent has been obtained from the patient for the publication of this paper.

Case report

A 73-year-old female with a height of 141 cm and a weight of 64 kg underwent surgical adhesiolysis and enterostomy for intestinal obstruction. Her comorbidities included type 2 diabetes mellitus and dyslipidemia diagnosed 15 years prior, treated with metformin, linagliptin, glimepiride, and rosuvastatin. She visited the emergency room five days ago due to vomiting and abdominal pain, and an abdominal computed tomography scan revealed that she had a small bowel obstruction. Laboratory tests after admission were as follows. Blood tests showed hemoglobin of 11.5 g/dL, hemoglobin A1c of 7.5%, sodium of 136 mM/L, potassium of 4.4 mM/L, chloride of 106 mM/L, glucose of 309 mg/dL, albumin of 3.98 g/dL, bicarbonate of 18.5 mM/L, and lactate of 3.4 mM/L. The urine test results revealed that glucose was 3+, and protein and ketone were negative. She was hospitalized for intravenous fluid resuscitation and nasogastric decompression. Her home medications for diabetes mellitus were discontinued and sliding scale insulin was ordered, resulting in finger stick blood glucose (FSBG) levels decreasing to 104-152 mg/dL. The results of her laboratory tests measured the day before surgery were as follows. Blood tests showed hemoglobin of 10.1 g/dL, sodium of 134 mM/L, potassium of 3.4 mM/L, chloride of 102 mM/L, glucose of 104 mg/dl and albumin of 3.53 g/dL. The urine test revealed that glucose was 1+, protein was weakly positive, and ketone was negative. Other laboratory findings, including renal and hepatic functions, were unremarkable. She did not receive insulin and glucose overnight. The FSBG revealed 84 mg/dL on the morning of the surgery, and the infusion of regular insulin and dextrose solution was not given with concern of intraoperative hypoglycemia.

General anesthesia was induced with propofol 40 mg and rocuronium 50 mg. The patient was intubated, and anesthesia was maintained with sevoflurane, remifentanil, and rocuronium. In addition to standard anesthesia monitoring, which includes pulse oximetry, electrocardiogram, non-invasive blood pressure, capnography, temperature, etc., an arterial line was established for hemodynamic monitoring and blood sampling. The results of ABG with serum glucose and lactate 60 minutes after the initiation of operation were (Table 1).

In a simplified Fencl-Stewart approach for the partitioning of SBE [6,7], we employed the equation

$SBE_{UA} = SBE - SBE_{NaCl} - SBE_{Lactate} - SBE_{Albumin}$, where:
$SBE_{NaCl} = Na^+ - Cl^- - 38$ (mM/L)
$SBE_{Lactate} = 1 - lactate$ (mM/L)
$SBE_{Albumin} = 2.5 \times (4.2 - albumin$ in g/dL)

SBE_{NaCl} indicated hyperchloremic acidosis. The difference between SBE and SBE_{NaCl} suggested that HAGMA might be developing. To confirm this, serum albumin should be measured. However, the actual serum albumin level was not measured during surgery as albumin has a lag time of about 60 min for the identification of the result in our laboratory. Therefore, based on the preoperative level of albumin, it was 'estimated' that the $SBE_{Albumin}$ was $\geq$ +1.7 mM/L, and the SBE_{UA} was $\leq$ -4.4 mM/L, strongly indicating the development of HAGMA. This prompted testing for β-hydroxybutyrate. The measured serum β-hydroxybutyrate was 5.2 mM/L. The corrected AG (AGc) was estimated to be $\geq$ 14.3 mM/L, which is within the normal range of 8 to 16 mM/L.

Next, we estimated the quantitative contribution of hyperchloremia to the total acidifying base deficit, based on the pre-

Table 1. Perioperative laboratory findings

	Intraoperative	PACU	Mid-reference value
pH	7.21	7.33	7.4
pCO_2 (mmHg)	38	34	40
Na^+ (mM/L)	139	141	140
K^+ (mM/L)	3.1	3.0	4.5
Cl^- (mM/L)	111	108	102
Ca^{2+} (mM/L)	1.10	1.11	1.2
HCO_3- (mM/L)	15.4	17.8	24
Glucose (mg/dL)	109	117	87.5
Lactate (mM/L)	0.7	1.1	1
Anion gap (mM/L)	12.6	15.2	12
SBE (mM/L)	-12.4	-8.2	
SBE_{NaCl} (mM/L)	-10	-5	
$SBE_{Lactate}$ (mM/L)	0.3	-0.1	

PACU, post anesthesia care unit; SBE, standard base excess.

vious studies [7,8]. The total acidifying base deficit (by excluding alkalinizing SBE partitions), as proposed in a study [7], was calculated as follows: SBE_{NaCl} + SBE_{UA} = -10 - 4.4 = -14.4 mM/L. Thus, the contribution of hyperchloremia (SBE_{NaCl}) to the total acidifying base deficit (SBE_{NaCl} + SBE_{UA}) was calculated to be 69% (-10/-14.4).

To alleviate concurrent hyperchloremic acidosis, we infused 80 mEq of sodium bicarbonate, targeting an increase in serum bicarbonate to 18 mM/L (a criterion for diagnosing EDKA), as calculated by the equation 0.5 × weight × [target serum bicarbonate – present serum bicarbonate] [9]. This resulted in a satisfactory decrease in metabolic acidosis (Table 1) and in the hyperchloremic contribution to the total acidifying base deficit (from 69% to 53%). Following the bicarbonate therapy, the surgery ended, and the patient was extubated and transferred to post anesthesia care unit (PACU). The operative time was 100 minutes, and blood loss was estimated between 100 and 150 mL. Intraoperatively, 600 mL of balanced salt solutions (Hartmann's solution [JW Pharmaceutical] and Plasma Solution-A® [HK innoN]) were administered, with a urine output of 100 mL. The ABG results checked in the PACU are shown in Table 1. Hyperventilation occurred because of metabolic acidosis.

The patient was transferred to the general ward and started on a regular insulin infusion in 5% dextrose. Immediately after arrival on the ward, follow-up serum albumin and β-hydroxybutyrate levels were 2.93 g/dL and 3 mM/L, respectively. The urine test conducted on the next day showed a weak positive for ketones. Despite this finding, the postoperative course was uneventful, and the patient was discharged in good health a week after surgery.

Discussion

The diagnosis of EDKA often begins with the verification of HAGMA. However, when HAGMA and hyperchloremic acidosis occur together, the traditional AG (including AGc) approach may be unreliable [7]. Hyperchloremia can decrease the AG [10], making it insufficient to identify HAGMA, even if the blood ketones are high. In our case, partitioning of SBE was used to avert this problem and was more suitable for identifying HAGMA than the AG approach.

Partitioning of the SBE may also be advantageous in quantifying the contribution of hyperchloremic acidosis to mixed acidosis. SBE_{NaCl} was found to be more reliable for evaluating the effect of chloride on the acid-base status compared to other methods such as SBE_{Cl} [11]. By calculating SBE_{NaCl} and SBE_{UA} (mostly due to ketoacid anions), we were able to quantify the acidifying severity of each partition, including chloride and non-chloride ketoacid anions. This showed a significant contribution of hyperchloremic acidosis to the severity of mixed metabolic acidosis in this patient. The high degree of the hyperchloremic base deficit as a percentage of the total acidifying base deficit may suggest the necessity of treating hyperchloremia to alleviate the severity of acidosis.

There has been considerable debate regarding the pros (even in mild to moderate metabolic acidosis, pH < 7.3 and BE < -4mEq/L) [12,13] and cons [14] of bicarbonate therapy for the treatment of hyperchloremic acidosis. In our opinion, the treatment of hyperchloremic acidosis may have some advantages for the following reasons when hyperchloremic acidosis significantly contributes to the total acidifying base deficit. First, metabolic acidosis may cause discomfort for patients, such as hyperventilation, dyspnea, nausea, vomiting, hypotension, and tachycardia [9]. Bicarbonate therapy may facilitate the resolution of hyperchloremic metabolic acidosis [15]. As a result, bicarbonate infusion during surgery may shorten or alleviate the patient's discomforts after surgery. We believe that hyperventilation would have been more severe after surgery if bicarbonate was not administered during surgery in this patient and waiting for spontaneous resolution may not be reasonable. Second, it has been reported that acid-base status is a factor that determines the severity of DKA [16]. Hyperchloremic acidosis is not usually dangerous, but it increases the severity of metabolic acidosis. In addition, hyperchloremia has been linked to prolonged hospital stay, and reduced kidney function, in DKA [17]. Hyperchloremia can lead to adverse clinical outcomes even in the absence of severe acidosis [15]. Therefore, treating hyperchloremic acidosis may be preferable to not treating it as it could help reduce the severity of mixed acidosis.

Some may argue that using preoperative albumin level would miscalculate SBE_{UA} and hyperchloremic contribution to the total acidifying base deficit because the intraoperative albumin level may differ from the preoperative level. Because it took a long time to obtain results, albumin levels were not measured during surgery, which is a limitation of this study. Due to potential surgery-induced leakage of albumin [18] and fluid therapy, it is more likely that the level decreased rather than increased or remained unchanged. The decrease in serum albumin after surgery in this patient suggests that the albumin level during surgery would have been between the preoperative (3.53 g/dL) and postoperative (2.93 g/dL) levels. This could have decreased the SBE_{UA} (between -4.4 and -5.9 mM/L)

and the contribution of hyperchloremia to the total acidifying base deficit (between 53% and 45%). Therefore, it is necessary to take this into account when calculating partitions of SBE.

In summary, partitioning of the SBE can be advantageous for detecting UA and may be used to determine the necessity of intraoperative bicarbonate therapy when HAGMA and hyperchloremic acidosis occurred together. Bicarbonate therapy may potentially reduce the severity of mixed metabolic acidosis and any related symptoms. Treating hyperchloremic acidosis may be better than not treating it to reduce the severity of mixed acidosis.

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Ethics approval

Written informed consent has been obtained from the patient for the publication of this paper. Ethical review and approval of this study was waived.

Conflict of interest

The authors have nothing to disclose.

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References

1. Modi A, Agrawal A, Morgan F. Euglycemic diabetic ketoacidosis: a review. Curr Diabetes Rev. 2017;13:315–21.
2. Nasa P, Chaudhary S, Shrivastava PK, Singh A. Euglycemic diabetic ketoacidosis: a missed diagnosis. World J Diabetes. 2021;12:514–23.
3. Stewart PA. Modern quantitative acid-base chemistry. Can J Physiol Pharmacol. 1983;61:1444–61.
4. Balasubramanyan N, Havens PL, Hoffman GM. Unmeasured anions identified by the Fencl-Stewart method predict mortality better than base excess, anion gap, and lactate in patients in the pediatric intensive care unit. Crit Care Med. 1999;27:1577–81.
5. Fencl V, Jabor A, Kazda A, Figge J. Diagnosis of metabolic acid-base disturbances in critically ill patients. Am J Respir Crit Care Med. 2000;162:2246–51.
6. Story DA, Morimatsu H, Bellomo R. Strong ions, weak acids and base excess: a simplified Fencl-Stewart approach to clinical acid-base disorders. Br J Anaesth. 2004;92:54–60.
7. Dos Passos MG, Blaya LB, Boniatti MM. Comparison of a modified Story approach to traditional evaluation of acid-base disturbances in patients with shock: a cohort study. J Clin Monit Comput. 2022;36:817–22.
8. Taylor D, Durward A, Tibby SM, Thorburn K, Holton F, Johnstone IC, et al. The influence of hyperchloraemia on acid base interpretation in diabetic ketoacidosis. Intensive Care Med. 2006;32:295–301.
9. Seifter J. Acid-base disorders. In: Goldman L, Schafer AI, editors. Goldman-Cecil medicine. 26th ed. Elsevier; 2019. p. 731–43.
10. Kraut JA, Madias NE. Serum anion gap: its uses and limitations in clinical medicine. Clin J Am Soc Nephrol. 2007;2:162–74.
11. Gucyetmez B, Tuzuner F, Atalan HK, Sezerman U, Gucyetmez K, Telci L. Base-excess chloride; the best approach to evaluate the effect of chloride on the acid-base status: a retrospective study. PLoS One. 2021;16:e0250274.
12. Yagi K, Fujii T. Management of acute metabolic acidosis in the ICU: sodium bicarbonate and renal replacement therapy. Crit Care. 2021;25:314.Erratum in: Crit Care. 2024;28:110.
13. Fujii T, Udy AA, Nichol A, Bellomo R, Deane AM, El-Khawas K, et al. Incidence and management of metabolic acidosis with sodium bicarbonate in the ICU: an international observational study. Crit Care. 2021;25:45.
14. Sabatini S, Kurtzman NA. Bicarbonate therapy in severe metabolic acidosis. J Am Soc Nephrol. 2009;20:692–5.
15. Kraut JA, Kurtz I. Treatment of acute non-anion gap metabolic acidosis. Clin Kidney J. 2015;8:93–9.
16. Nyenwe EA, Kitabchi AE. The evolution of diabetic ketoacidosis: an update of its etiology, pathogenesis and management. Metabolism. 2016;65:507–21.
17. Ahmed HM, Elnaby HRH, El Kareem RMA, Hodeib M. The relationship between hyperchloremia and acute kidney injury in pediatric diabetic ketoacidosis and its impact on clinical outcomes. Pediatr Nephrol. 2022;37:1407–13.
18. Norberg Å, Rooyackers O, Segersvärd R, Wernerman J. Leakage of albumin in major abdominal surgery. Crit Care. 2016;20:113.