Misdiagnosis of high anion gap acidosis owing to instrument error of a device

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Abstract

The anion gap (AG) is a tool to diagnose metabolic acid–base disorders in the physiological approach to acid–base assessment. It is used to detect high AG acidosis, a type of metabolic acidosis caused by serum concentration increase in usually unmeasured anions; AG larger than the reference for it indicates the presence of high AG acidosis. This report presents a case of hyperlactatemia which was not detected as high AG acidosis possibly because of instrument error of a device in measurement of serum sodium and chloride concentrations. The case indicates that the error will make AG unable to detect high AG acidosis of any cause. Hence, upon suspicion of high AG acidosis caused by measurable anions such as lactate and ketones, it is recommended to measure their serum concentration.

Keywords Acid–base · Anion gap · Electrolyte · Instrument error · Metabolic acidosis · Usually unmeasured anions

Introduction

The physiological approach is one of the three major methods to assess acid–base disorders [1, 2]. In the approach, the anion gap (AG), which is obtained using concentration of sodium (Na), chloride (Cl), and bicarbonate (HCO_3) in mmol/L, is used to assess metabolic acid–base disorders. It is used to detect high AG acidosis, a type of metabolic acidosis caused by increase in concentration of usually unmeasured anions, which increases AG; AG larger than the reference for it indicates the presence of high AG acidosis.

Decrease in serum concentration of albumin (Alb) decreases AG. Hence, it has been recommended to adjust AG by Alb. Generally, AG is adjusted by adding 2.5 for every 1 g/dL decrease in Alb from 4 and calculated by an equation [3–5]

$$\text{AG} = \text{Na} - \text{Cl} - \text{HCO}_3 + 2.5x(4 - \text{Alb}) \quad (1)$$

It has also been recommended to adjust the reference for AG individually in each facility since a baseline AG differs individually [2, 6]. However, instrument error in measurement of Na and Cl has not been considered in the clinical practice [1, 2]. This report presented a case of hyperlactatemia which was not detected as high AG acidosis possibly owing to the error of a device.

Case report

A 73-year-old female visited the emergency department of our hospital because of dizziness. A venous blood gas analysis by the GEM-premier-4000 (Instrumentation Laboratory Company, MA, USA) found pH 7.33 with pO_2 35 mm Hg, pCO_2 45 mm Hg, HCO_3 23.7 mmol/L, Na 136 mmol/L, Cl 103 mmol/L, and lactate concentration 3.3 mmol/L (Table 1). The findings indicated the presence of lactic acidosis, a type of high AG acidosis. However, a simultaneous serum chemistry measurement by the TBA-c8000 (Cannon Medical Systems, Tochigi, Japan) found Alb 3.3 g/dL, and the AG calculated from the Na and Cl of the GEM-premier-4000 did not indicate the presence of high AG acidosis; the AG calculated by Eq. 1 was 11.05, which is within the generally-used reference range for AG [2]. In contrast, the TBA-c8000 presented Na 140 mmol/L and Cl 100 mmol/L, and the AG calculated from them indicated the presence of

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Table 1 Blood gas and serum chemistry analyses

	Blood gas	Serum chemistry
pH	7.33	
pO ₂ (mm Hg)	35	
pCO ₂ (mm Hg)	45	
HCO ₃ (mmol/L)	23.7	
Lac (mmol/L)	3.3	
Na 136 (mmol/L)	136	140
Cl 103 (mmol/L)	103	100
Alb (g/dL)		3.3
Alb-adjusted AG	11.05	18.05

AG anion gap, Alb albumin concentration, Na sodium concentration, Cl chloride concentration, HCO₃ bicarbonate concentration, Lac lactate concentration

high AG acidosis; the AG calculated by Eq. 1 was 18.05 (Table 1).

Discussion

This report presented a clinical case where instrument error of a device in Na and Cl measurement caused misdiagnosis of metabolic acidosis; AG obtained by a device could not detect the existing high AG acidosis of hyperlactatemia. The finding indicates that the error will make AG unable to detect high AG acidosis of any cause.

Difference in measured electrolyte values by device and inappropriateness of AG to screen lactic acidosis was reported previously [2, 6, 7]. In these reports, the difference was attributed to difference in sample preparation such as the elapsed time and the syringes and tubes used in sample collection. However, as we have revealed previously, instrument error of a device will also make AG differ even in Na and Cl measurements for an identical sample with an identical device [8]. Thus, the error should be considered in the clinical practice.

The error could be attributed to difference in sample dilution. Generally, serum chemistry analyzers measure Na and Cl in automatically diluted samples, while blood gas analyzers measure them without sample dilution before measurement. The difference in sample dilution could make Na and Cl differ by device; dilution of the sample components other than Na and Cl will influence the measurement of Na and Cl differently by the rate of dilution. Adjustment of the reference for AG individually in each device in each facility might enable AG to detect high AG acidosis [2, 6]. However, we observed large fluctuations in Na and Cl by instrument error of the GEM-premier-4000 even in the measurement of an identical sample [8]. Thus, the adjustment will not enable

AG of the GEM-premier-4000 to detect high AG acidosis constantly.

We have warned that large fluctuations in Na and Cl by instrument error of the GEM-premier-4000 could influence AG significantly to cause misdiagnosis in acid–base assessment [8]. In our analysis, the error of the TBA-c8000 was smaller than that of the GEM-premier-4000. However, both the devices used the ion-selective-electrode method, a widely-used electrolyte-measuring method, to measure Na and Cl [9]. Thus, difference in their quality control systems would have caused the difference between them [10]. As well as these devices, the commercially available devices generally use the ion-selective-electrode method to measure Na and Cl. Therefore, the magnitude of fluctuations in Na and Cl by instrument error will depend on the quality control system of a device, and suitability of Na and Cl for AG needs to be examined in each device.

Inappropriate maintenance of the GEM-premier-4000 could have increased fluctuations in its measurements of Na and Cl. However, both the devices used in the present report were managed and calibrated appropriately in a core laboratory of the hospital. Although it was possible that only the GEM-premier-4000 device used in the present report malfunctioned, the device did not present any alerts. Therefore, malfunction and mis-calibration of the device would not have caused the fluctuations in Na and Cl measurements.

Conclusion

Instrumental error of a device, which depends on its quality control system, will make the AG obtained by it unsuitable to detect high AG acidosis of any cause. It is recommended to examine suitability for AG in each device. Rather, upon suspicion of high AG acidosis caused by measurable anions such as lactate and ketones, it is recommended to measure their serum concentration.

Compliance with ethical standards

Conflict of interest The authors have no conflict of interests to declare.

Ethical approval This report does not contain any studies with human participants or animals performed by any of the authors. The case is reported with waiving of the informed consent under the proviso that all identifying information was removed from the text.

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