Original Research Article

Evaluation of pKa as a cause of discordance between calculated and measured bicarbonate in arterial and venous blood

Shanmugapriya Chandrasekaran[1], Poonguzhali Gopinath[2*]

[1]Associate Professor, Department of Biochemistry, Government Medical College, Omandurar Govt. Estate, Chennai, Tamil Nadu, India
[2]Associate Professor, Department of Biochemistry, Government Villupuram Medical College and Hospital, Villupuram, Tamil Nadu, India
[*]Corresponding author email: **poonguzhalig@gmail.com**

International Archives of Integrated Medicine, Vol. 6, Issue 3, March, 2019.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 22-02-2019 **Accepted on:** 27-02-2019
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Shanmugapriya Chandrasekaran, Poonguzhali Gopinath. Evaluation of pKa as a cause of discordance between calculated and measured bicarbonate in arterial and venous blood. IAIM, 2019; 6(3): 127-131.

Abstract

Background: The measurement of bicarbonate level in blood is extremely common and often provides vitally important data used in the care of critically ill patients. The bicarbonate level in blood can be directly measured or derived from calculations using the Henderson-Hasselbalch equation; mostly adopted by the blood gas analyzers. Arterial blood gas (ABG) analysis is commonly performed for clinical evaluation, but the procedure has certain limitations in the form of reduced patient acceptability (because the procedure can be painful) and the potential to cause complications such as arterial injury, thrombosis with distal ischemia, hemorrhage, aneurysm formation, median nerve damage and, rarely, reflex sympathetic dystrophy.

The aim of the study: If there is discordance between arterial and venous blood gas parameters including pH, pCO_2, bicarbonate, Sodium, Potassium, chloride and discordance between measured and calculated bicarbonate in both arterial and venous blood samples.

Materials and methods: Comparison study involving 250 patients for whom clinical Judgment was made that arterial blood sample is needed for assessment of acid-base status. Both arterial and venous blood samples were collected using heparinized autosampler syringes PICO 50 as close in time as possible and were analyzed in Arterial Blood Gas analyzer ABL 80 flex.

Results: There was a statistically significant difference between arterial and venous pO_2 (126$\pm$48.5 vs 62$\pm$30.5, p= 0.001) and SO_2 (95% vs 68%, p=0.03).

Conclusion: According to the study results traditionally measured venous bicarbonate can be a

convenient substitute for calculated arterial bicarbonate in critically ill ICU patients. However, more accurate assessments will require ABG for additional parameters. Besides, the present study design did not involve the collection of data on patient demographics, the severity of illness, and a requirement for inotropic support or prognosis.

Key words

Arterial Blood Gas, Measured Bicarbonate, Calculated Bicarbonate, Henderson Hasselbach Equation.

Introduction

Arterial Blood Gas analysis (ABG) is crucial is managing metabolic and respiratory acid-base disorders and in assessing oxygenation in critically ill patients. The three parameters essential for such decisions are pH, the partial pressure of carbon dioxide pCO_2 and Bicarbonate concentration [HCO_3^-]. The Bicarbonate value obtained in an arterial blood gas analyzer is a calculated parameter [1]. The calculation is based on the fact that the major form of transport of carbon dioxide in the blood is in the form of bicarbonate [2].

According to Henderson – Hasselbach equation [1],

$$pH = pKa + \log \frac{[Base]}{[Acid]}$$

In the equilibrium reaction of carbon dioxide, carbon dioxide is the acid and bicarbonate is the base. pKa of carbonic acid is 6.1. Hence the Henderson Hasselbach equation is modified as,

$$pH = 6.1 + \log \frac{[HCO_3^-]}{[CO_2]}$$

As carbon dioxide concentration is proportionate to the partial pressure of carbon dioxide by a proportionality constant, solubility coefficients [3],

$$[CO_2] = s \times pCO_2$$

The solubility coefficient of carbon dioxide or Bunsen coefficient is approximately 0.03 mmol/L per mmHg at 37^{o}C. On further simplification of equation 1, we get a formula to calculate bicarbonate concentration.

$$\mathbf{HCO_3^- = 0.03 \times pCO_2 \text{ Antilog } (pH - pK')}$$

However, this calculation is based on the assumption that both pKa (6.1) and solubility coefficient (0.03) are constants value, which is not true. pKa of bicarbonate is increased in acidic pH and is decreased in alkalotic pH [4]. pKa is also affected by temperature variations [5]. These variations are observed more in acutely ill patients, as they present with extremes of pH and temperature [6]. Solubility coefficient is also affected by pH and ionizing strength of blood. This might result in underestimation and overestimation of Bicarbonate concentration in extremes of pH which may mislead us in both diagnosing the primary acid-base disorder and analyzing the magnitude of compensation. Bicarbonate concentration, on the other hand, can be measured directly in both arterial and venous blood with acceptable discordance by enzymatic method. This measurement is not affected by changes in pH. In addition, direct measurement of Bicarbonate by enzymatic method measures total carbon dioxide (TCO_2) or the potential bicarbonate [7]. Total Carbon dioxide is a sum of dissolved carbon dioxide, bicarbonate, carbonic acid, carbonate, and carbamates. Knowledge of total carbon dioxide is essential in deciding the requirement and dosage of bicarbonate therapy in acidosis. However, measured bicarbonate is affected by the presence of organic acids like acetylsalicylic acid, valproic acid, benzoic acid. All these acids cause an overestimation of measured bicarbonate [8]. Calculated Bicarbonate [HCO_3^-] obtained in Arterial-Blood-Gas (ABG) analyzer is affected by pH and ionizing strength of blood. Direct measurement of Bicarbonate, which measures total carbon dioxide (TCO_2) is not affected by these changes and is essential in deciding on bicarbonate therapy. Hence, a discordance between measured and calculated bicarbonate is expected [9].

Materials and methods

The study was conducted in the year 2017 in Omandurar Govt. Estate, Chennai. Totally 250 patients for whom clinical Judgement was made that arterial blood sample was needed for assessment of acid-base status. Both arterial and venous blood samples were collected using heparinized autosampler syringes PICO 50 as close in time as possible and were analyzed in Arterial Blood Gas analyzer ABL 80 flex. The plasma from both arterial and venous blood samples was separated by centrifugation at 37°C and was utilized to measure bicarbonate by the enzymatic method developed by Forrester, et al. [6]. The method was based on phosphoenolpyruvate method. We used a fully automated clinical chemistry analyzer for this purpose.

Results

There was no statistically significant difference between arterial and venous pH (7.382±0.436 vs 7.367±0.456, p= 0.31), pCO_2 (39.3±14.32 vs 41.9±16.11, p=0.23), calculated HCO_3^- (22.91±7.93vs 24.15±8.21, p=0.24), measured bicarbonate (24.82±8.15vs25.63±9.21, p=0.43), anion gap (11.21±3.74 vs 10.78±4.89, p=0.22). There was a statistically significant difference between arterial and venous pO_2 (126±48.5 vs 62±30.5, p= 0.001) and SO_2 (95% vs 68%, p=0.03). Bland Altman analysis revealed narrow limits of agreement when arterial and venous pH, pCO_2, calculated Bicarbonate, measured bicarbonate and anion gap values (0.04 to 0.11, -0.3 to -3.4, -1.1 to -3.8, -2.1 to -4.4, 2.1 to -1.1 respectively). Bland Altman analysis revealed narrow limits of agreement when arterial and venous pH, pCO_2, calculated Bicarbonate, measured bicarbonate and anion gap values (0.04 to 0.11, -0.3 to -3.4, -1.1 to -3.8, -2.1 to -4.4, 2.1 to -1.1 respectively). On Bland Altman analysis, poor agreement in PO_2 and SO_2 measurements between arterial and venous samples were observed. 95% limits of agreement for PO_2 and SO_2 include 145.3 to 32.9 and 33 to 12. There was a statistically significant difference when arterial measured and calculated bicarbonate values were compared (24.82±8.15 vs 22.91±7.93. There was a weak correlation between pH and bias in TCO_2 and [HCO_3^-] in arterial (r=0.576, p=0.01) and venous samples (r=0.532, p=0.01) as per **Table – 1**.

Table - 1: Comparison of various parameters in arterial and venous blood samples.

Sr. No.	Parameter	Arterial Value		Venous Value		P Value
		Mean	**SD**	**Mean**	**SD**	
1	pH	7.382	0.218	7.367	0.228	0.31
2	pCO_2	39.3	7.16	41.9	8.06	0.23
3	Calculated Bicarbonate	22.91	3.97	24.15	4.11	0.24
4	Measured Bicarbonate	24.82	4.08	25.63	4.61	0.43
5	Anion Gap	11.21	1.87	10.78	2.49	0.22
6	PO_2	126	24.25	62	15.25	<0.001

Discussion

Arterial Blood gas analysis is essential in managing critically ill patients, who often present with extremes of pH and temperature. Many medical decisions are based on the bicarbonate value of the arterial blood gas analysis report [10]. For example, the anion gap calculation, which is essential for identifying the type of metabolic acidosis is dependent on the bicarbonate value. However, the calculated bicarbonate value in an ABG report is found to be affected by many variables. Hence, we proposed that measured bicarbonate in a simultaneously collected venous sample should be included in the panel of blood gas reports [11]. The agreement between arterial and venous pH, pCO, TCO_2 and [HCO_3^-] and discordance between arterial and venous pO2 indicate that venous blood sample would suffice for identifying and managing an acid-base disorder unless oxygen delivery is to be assessed [12]. The wider LOA of both arterial and venous total carbon dioxide or in other words measured bicarbonate and calculated bicarbonate indicate that TCO2 has to be measured to assess the acid-base status [13]. However, the weak correlation between pH and bias between measured and calculated bicarbonate indicate that predicting measured bicarbonate based on pH and calculated bicarbonate values is not possible. At the same time, we should have in mind the possibility of measured bicarbonate getting affected by the presence of organic acids, as organic acids are well-known interferences for measured bicarbonate estimation by enzymatic method [14].

Conclusion

The measurement of bicarbonate level in blood is extremely common and often provides vitally important data used in the care of critically ill patients. The bicarbonate level in blood can be directly measured or derived from calculations using the Henderson-Hasselbalch equation; mostly adopted by the blood gas analyzers [1]. Arterial blood gas (ABG) analysis is commonly performed for clinical evaluation, but the procedure has certain limitations in the form of reduced patient acceptability (because the procedure can be painful) and the potential to cause complications such as arterial injury, thrombosis with distal ischemia.

Acknowledgments

The authors would like to thank the Professors, Associate Professor, and Postgraduate students, Department of Biochemistry, Government Medical College, Omandurar Govt. Estate, Chennai for helping with data collection and analyses.

References

1. Austin WH, Ferrante V, Anderson C. Evaluation of whole blood pK in the acutely ill patient. J Lab Clin Med., 1968; 72: 129-35.
2. De Raedt M, Vandenbergh E, van de Woestijne KP. Direct and indirect determination of partial pressure of CO2 in the arterial blood of patients with respiratory insufficiency. Clin Sci., 1968; 35: 347-52.
3. Henderson LJ. The theory of neutrality regulation in animal regulation in the animal organism. Am J Physiol., 1908; 21: 427-48.
4. Henry's Law: Chemistry, Gas Laws, William Henry (chemist), Partial Pressure, Solubility, Carbonation, Soft Drink, Carbon Dioxide, Atmospheric Pressure, Champagne (wine), Dalton's Law.
5. Holbek CC. The Radiometer ABL300 blood gas analyzer. J Clin Monit., 1989; 5: 4-16.
6. Lolekha PH, Boonlert W, Kost GJ, Vanavanan S, Lolekha S. Comparative study of values of calculated bicarbonate and measured total carbon dioxide content. Point Care, 2003; 2: 135–43.
7. Masters P, Blackburn ME, Henderson MJ, Barrett JF, Dear PR. Determination of plasma bicarbonate of neonates in intensive care. Clin Chem., 1988; 34: 1483–5.
8. Rifai N, Hyde J, Iosefsohn M, Glasgow AM, Soldin SJ. Organic acids interfere in the measurement of carbon dioxide concentration in the Kodak Ektachem 700. Ann Clin Biochem., 1992; 29: 105-8.
9. Rispens P, Dellebarre CW, Eleveld D, Helder W, Zijlstra WG. The apparent first dissociation constant of carbonic acid in plasma between 16 and 42.5°. Clin Chim Acta., 1968; 22: 627-37.
10. Scott MG, Klutts JS. Electrolytes and blood gases. In: Burtis CA, Ashwood ER, Bruns DE, editors. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, 4th edition, Missouri: Saunders; 2006, p. 983–1018.
11. Severinghaus JW, Stupfel M, Bradley AF. Variations of serum carbonic acid

pK with pH and temperature. J Appl Physiol., 1956; 9: 197-200.

12. Story DA, Poustie S, Bellomo R. Comparison of three methods to estimate plasma bicarbonate in critically ill patients: Henderson-Hasselbalch, enzymatic and strong-ion-gap. Anaesth Intensive Care, 2001; 29: 585–90.
13. Story DA, Poustie S. Agreement between two plasma bicarbonate assays in critically ill patients. Anaesth Intensive Care, 2000; 28: 399–402.
14. Ungerer JP, Ungerer MJ, Vermaak WJ. Discordance between measured and calculated total carbon dioxide. Clin Chem., 1990; 36: 2093-6.