Application of Boston Compensation Rules in the Development of a Stepwise Approach for Novel Diagnostic Arterial Blood Gas Interpretation Method

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Received on: 17 August 2023; *Accepted on:* 13 September 2023; *Published on:* 30 September 2023

Ab s t rac t

Background: Arterial blood gas (ABG) interpretation plays an indispensable role in health care. The total changes in hydrogen ion concentration or actual pH are due to both the changes in respiratory and non-respiratory (metabolic) components affecting the hydrogen ion concentration or pH in the acid–base homeostasis. Using this concept, an innovative ABG interpretation method was developed and published by the current author. The aim of this study is to apply the compensation rules and to develop a stepwise approach in this novel method to interpret various acid–base disorders.

Methods: The total change in pH (ΔpH), non-respiratory hydrogen ion concentration (NRH⁺), changes in non-respiratory pH (ΔNRpH), and respiratory change in pH (ΔRpH) were calculated for 232 ABG samples. The expected pCO₂ (Exp pCO₂) or expected bicarbonate (Exp HCO₃⁻) values were calculated using the compensation rules and compared with their actual given values.

Results: Few acid–base disorder cases were shown as examples comparing the physiological, standard base excess (Std BE) and parameters such as ΔpH, ΔRpH, and ΔNRpH values of novel ABG interpretation method which change in different acid–base disorders.

Conclusion: The stepwise approach in this novel method appears to be much user-friendly providing interpretation of various acid–base disorders easily and quickly.

Clinical significance: This innovative method may help to overcome the challenging task of ABG interpretation.

Keywords: Compensation rules, Novel arterial blood gas interpretation, Stepwise approach.

Indian Journal of Critical Care Medicine (2023): 10.5005/jp-journals-10071-24552

HIGHLIGHTS

The novel acid–base balance theory may help to view the problems in acid–base homeostasis from a different perspective but with a holistic approach. A stepwise approach using this novel diagnostic ABG interpretation method appears to be much more user-friendly providing interpretation of various acid–base disorders easily and quickly.

INTRODUCTION

Arterial blood gas (ABG) interpretation plays an indispensable role in emergency medicine and intensive care patients yet its interpretation is challenging.¹ Bicarbonate is highly influenced by $pCO₂$ values and it is rectified by standard bicarbonate (Std $HCO₃$) which is the plasma bicarbonate concentration from blood equilibrated with pCO₂ of 40 mm Hg.^{[2–](#page-6-1)[5](#page-6-2)} The hydrogen ion concentration calculated using Std HCO₃ is known as the nonrespiratory hydrogen ion concentration (NRH⁺) and it denotes the hydrogen ion concentration at non-respiratory pH (NRpH).^{[6](#page-6-3)[,7](#page-6-4)}

The net changes in blood pH reflect the sum total alterations in the hydrogen ion concentration in the blood. The sum total alterations in the hydrogen ion concentration in the blood include both the variations due to respiratory and non-respiratory (metabolic) components. These components change in both magnitude and direction (positive or negative). The parameter ΔNRpH (NRpH − 7.4) denotes the (non-respiratory) metabolic component in causing variations in pH. The parameter respiratory change in pH (ΔRpH), that is, pH − NRpH, denotes the respiratory

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How to cite this article: Samuel R. Application of Boston Compensation Rules in the Development of a Stepwise Approach for Novel Diagnostic Arterial Blood Gas Interpretation Method. Indian J Crit Care Med 2023;27(10):717–723.

Source of support: Nil **Conflict of interest:** None

component causing variations in pH. Both the component values are more negative for the acidic effect and more positive for the alkaline effect. Using this innovative idea, a novel pH-based method for ABG interpretation was proposed by the current author and published in previous research articles.^{7[−9](#page-6-5)}

After the identification of one primary acid–base disorder, the compensation rules are applied to find the existence of another(second) primary acid–base disorder. There are no separate compensation rules for acute and chronic conditions in metabolic acid–base disorders but for respiratory acid–base disorders, compensation rules exist separately for acute and chronic conditions.¹⁰⁻¹² Using these compensation rules, the expected $pCO₂$ (Exp $pCO₂$) (for metabolic acid–base disorders) or

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expected HCO_3^- (Exp HCO_3^-) (for respiratory acid–base disorders in acute and chronic conditions) values are calculated. Then the calculated expected values (either pCO₂ or HCO₃⁻) are compared with their actual given values to find whether the changes are due to compensations or second primary (mixed) acid–base disorders[.10](#page-6-6)[–12](#page-6-7)

If the difference (given $pCO₂ - Exp pCO₂$) value is greater than positive, then it indicates the additional existence of respiratory acidosis (Resp Ac) and if their difference (given $pCO₂ - Exp pCO₂$) value is greater than negative, then it indicates the additional existence of respiratory alkalosis (Resp Alk). If the difference (given HCO_3^- – Exp HCO₃⁻) value is greater positive then it indicates the additional existence of metabolic alkalosis (Met Alk) and if their difference (given $HCO_3^- -$ Exp HCO_3^-) value is greater negative then it indicates the additional existence of metabolic acidosis (Met Ac)[.10](#page-6-6)[−12](#page-6-7)

The purpose of this current study is to apply the compensation rules in this novel interpretation method and to develop a fourstepwise approach to interpret the various acid–base disorders.

MATERIALS AND METHODS

A total of 232 ABG analysis samples data were utilized. A modified Henderson equation was applied to verify the consistency of the ABG report.^{7,[12](#page-6-7)[,13](#page-6-8)}

Modified Henderson Equation

Hydrogen ion concentration at actual pH (H⁺) = (24 \times pCO₂)/HCO₃ $pH = 9 - log(H⁺)$

Non-respiratory pH (NRpH) Component Calculation

The NRH⁺ was calculated as follows:^{7[−9](#page-6-5)} NRH⁺: Hydrogen ion concentration at NRpH (pCO₂ 40 mm Hg)

 $NRH^+ = (24 \times pCO_2)/$ Std HCO₃ $NRH^+ = (24 \times 40)/$ Std HCO₃ $NRH^+=960/Std HCO_3; NRpH = 9 - log(NRH^+)$

Respiratory Component ΔRpH (pH − NRpH) Calculation

The respiratory change in pH (Δ RpH) was calculated as follows:^{7-[9](#page-6-5)}

pH = 9 – log(H+); NRpH = 9 – log(NRH+); log(40) is 1.6; log(1) is 0. $pH - NRpH = log(NRH^+/H^+)$ $NRH^{+}/H^{+} = [(24 \times 40)/5 \text{td} HCO_{3}]/[(24 \times pCO_{3})/HCO_{3}]$

 $NRH^{+}/H^{+} = 40 \times [(HCO_{3}/Std HCO_{3})/pCO_{2}]$

Substituting their relationship, the following equation was obtained:

 $pH - NRpH = log(40) + log(HCO₃/Std HCO₃) - log(pCO₂)$ $pH - NRpH = 1.6 + log[(HCO₃/Std HCO₃)/pCO₂]$

The above derived relation helps us to understand the changes in pH due to respiratory component. $7-9$ $7-9$

Novel Postulate of Acid–Base Balance Theory

The set point for the concentration of hydrogen ion is 40 to maintain acid–base homeostasis. The total changes in the hydrogen ion concentration in the blood is denoted as ΔH^+ (where ΔH^+ = H⁺ – 40). The variations in NRH⁺ in the blood is denoted as Δ NRH⁺ (where \triangle NRH⁺ = NRH⁺ − 40). The variations in hydrogen ion concentration due to the respiratory component in the blood is denoted as ΔRH+ (where ΔRH^+ = H^+ − NRH⁺).^{[7](#page-6-4),[9](#page-6-5)[,14](#page-6-9)}

$$
\Delta H^+ = \Delta RH^+ + \Delta NRH^+
$$

The net changes in total or actual pH are due to both the variations in respiratory and non-respiratory (metabolic) component affecting the pH. The homeostatic set point of acid–base balance is at pH of 7.4.[7](#page-6-4),[9,](#page-6-5)[14](#page-6-9)

ΔpH = ΔRpH + ΔNRpH

where Δ pH = (pH – 7.4)

 \triangle NRpH = (NRpH – 7.4) (variations due to non-respiratory component)

 Δ RpH = (pH – NRpH) (variations due to respiratory component)

Compensation Bedside Rules

The Boston method (six rules) using bicarbonate also known as six bicarbonate-based bed side rules are more commonly utilized in clinical practice.^{1,[10](#page-6-6),11} The calculated expected values for either $pCO₂$ or HCO $_3^-$ was denoted as Exp pCO $_2$ or Exp HCO $_3$, respectively. The actual values given in the ABG report data were simply denoted as $pCO₂$ or HCO₃ in the compensation rules.

Six Bicarbonate-based Bedside Rules

The following compensation rules were applied: 1

- Rule for acute respiratory acidosis (Resp Ac): Exp $HCO₃ = 24 +$ $[(pCO₂ - 40)/10]$
- Rule for chronic Resp Ac: Exp $HCO_3 = 24 + 3.5$ [(pCO₂ 40)/10]
- Rule for acute respiratory alkalosis (Resp Alk): Exp $HCO₃ = 24 2$ $[(40 - pCO₂)/10]$
- Rule for a chronic Resp Alk: Exp $HCO_3 = 24 5$ [(40 pCO₂)/10]
- Rule for a Met Ac: Exp $pCO₂ = 1.5 \times HCO₃ + 8$ (range: ± 2)
- Rule for a Met Alk: Exp $pCO₂ = 0.7$ (HCO₃)+ 21 (range: ± 2)

Statistical Analysis

A total of 232 ABG sample data were included as convenience samples and divided into various groups using the values of pH, $pCO₂$, HCO₃, and standard base excess (Std BE). Two-way analysis of variance (ANOVA) statistical test was used to determine any statistically significant distinctions between three or more groups of data indicated by a big *F* value and a small *p* value. Linear regression model was used to study the relationship between the metabolic components Std BE and ΔNRpH. Similarly, the relationship between the respiratory components $pCO₂$ and Δ RpH was studied using this model. The value of R^2 measures the strength of their relationship; $p < 0.05$ was taken to be statistically significant for the linear regression and two-way ANOVA statistical tests.

RESULTS

A total of 232 ABG sample data were utilized. They were classified into six acid–base disorder groups and groups II to VI were again divided into three subgroups using the values of pH, $pCO₂$, HCO₃, and Std BE values which were clearly depicted in [Table 1](#page-2-0). The normal cases were included in group I and mixed acid–base disorders were included in miscellaneous group VI. Based on first primary acid– base disorder, the respiratory and metabolic acid–base disorders were included in the groups II to V.

Two-way ANOVA statistical analysis was done between various acid–base disorder groups for the traditional (pCO₂, HCO₃, and Std BE) and novel ABG interpretation method (ΔNRpH and ΔRpH) separately. A statistically significant differences between various groups was found using the *F* and *p* values for the novel ABG interpretation method and shown in the [Table 2.](#page-2-1)

Table 1: Classification into various acid–base disorder groups

Groups	Classification into various acid-base disorder groups based on first primary acid-base disorder					
Group I	Normal: 25 cases					
	Resp Ac: 32 cases					
Group II	Resp Ac 1: $(HCO3$ from 22 to 26 mmol/L)					
	Resp Ac 2: (HCO ₃ $>$ 26 \leq 35 mmol/L)					
	Resp Ac 3: (HCO ₃ $> 35 \le 42$ mmol/L)	9				
	Resp Alk: 53 cases					
Group III	Resp Alk 1: (HCO ₃ $> 8 \le 18$ mmol/L)	14				
	Resp Alk 2: (HCO ₃ > 18 < 22 mmol/L)	16				
	Resp Alk 3: (HCO ₃ from 22 to 26 mmol/L)	23				
	Met Ac: 47 cases					
Group IV	Met Ac 1: $pCO2$ from 13 to 25 mm Hg	14				
	Met Ac 2: pCO ₂ from 26 to 34 mm Hg					
	Met Ac 3: $pCO2$ from 35 to 45 mm Hg	16				
	Met Alk: 34 cases					
Group V	Met Alk 1: $pCO2$ from 35 to 45 mm Hg	12				
	Met Alk 2: $pCO2$ from 46 to 55 mm Hg	15				
	Met Alk 3: $pCO2 \ge 56$ mm Hg					
	Miscellaneous groups: 41 cases					
Group VI	Miscellaneous 1 (\downarrow pH, \uparrow pCO ₂ with \downarrow HCO ₃)	11				
	Miscellaneous 2 (normal pH, \uparrow pCO ₂ with \uparrow HCO ₃)	16				
	Miscellaneous 3 (normal pH, \downarrow pCO ₂ with \downarrow HCO ₃)	14				

Table 2: Two-way ANOVA statistical analysis between various acid–base disorder groups for the traditional ($pCO₂$, HCO₃, and Std BE) and novel ABG interpretation method (ΔNRpH and ΔRpH)

The compensation rules will help in recognizing the alterations due to compensation or second primary acid–base disorder in the groups II to V. The Exp $pCO₂$ for metabolic acid–base disorders or $Exp HCO_3^-$ for respiratory acid–base disorders (in acute and chronic conditions) are calculated using the compensation rules and then compared with their respective given values (either $pCO₂$

Fig. 1: Relationship between Std HCO₃ and NRH⁺

Fig. 2: Relationship between Std HCO₃ and NRpH

or HCO₃⁻). If both values are closer and their difference is within acceptable limits, then it denotes changes due to compensations. If their difference is larger, then it indicates the existence of second primary acid–base disorder. The larger their difference greater the severity of the condition.^{10[−12](#page-6-7)}

The value of pH from 7.35 to 7.45 denotes the normal level, so the normal ΔpH (pH – 7.4) value is from –0.05 to +0.05. Acidic pH is indicated by ΔpH value of below −0.05 and alkaline pH is indicated by Δ pH value of above +0.05.^{9,15} Also, Δ RpH is calculated using the derived equation and ΔNRpH is calculated using their relationship (ΔpH = ΔRpH + ΔNRpH) Then Δ pH value is correlated with the individual values. If the changes are within the normal reference value, then it is normal. ΔRpH values are more negative for Resp Ac and more positive for Resp Alk. ΔNRpH values are more negative for Met Ac and more positive for Met Alk.^{9[,12](#page-6-7)[,15](#page-6-11)}

The NRH⁺ was computed using the value of Std HCO₃. The relations between Std HCO₃, NRH⁺, and NRpH are depicted in [Figures 1](#page-2-2) and [2.](#page-2-3) As the NRH⁺ value rises, the Std HCO₃ value falls and *vice versa*. However, as the NRpH rises, the Std HCO₃ also rises and *vice versa*. The value of Std BE from −2 to +2 mmol/L denote the normal level and abnormal negative values are seen in Met Ac

Fig. 3: Relationship between Std BE and NRH+

Fig. 4: Relationship between Std BE and ΔNRpH (NRpH − 7.4)

and abnormal positive values are noticed in Met Alk.^{14[,15](#page-6-11)} The Std BE, NRH⁺, and ΔNRpH are graphically depicted in [Figures 3](#page-3-0) and [4](#page-3-1). It is obviously seen that NRH⁺ is increased in Met Ac and decreased in Met Alk. In Met Ac ΔNRpH value is more negative and in Met Alk its value is more positive. This ΔNRpH is identical and comparable to the Std BE and their relationship was clearly depicted in [Figure 4](#page-3-1).

The value of $pCO₂$ from 35 to 45 mm Hg denotes the normal level. So, the normal value of the parameter ($pCO₂ - 40$ mm Hg) is from −5 to +5 mm Hg.^{14,15} The relationship between ΔRpH (pH – $NRpH$) and $pCO₂$ were clearly depicted and graphically analyzed in [Figure 5.](#page-3-2) The link between $pCO₂$ and the ratio (HCO₃/Std HCO₃) depicted in [Figure 6](#page-3-3) clearly shows that the ratio was directly affected by $pCO₂$ values. The value of the ratio (HCO₃/Std HCO₃) is one at $pCO₂$ 40 mmHg because of identical bicarbonate and Std HCO₃ values. The ratio (HCO₃/Std HCO₃) values are higher (>1) for increased pCO₂ and lesser (<1) for decreased pCO₂. The value of Δ RpH is zero at pCO₂ 40 mm Hg because of identical bicarbonate and Std HCO₃ values and the magnitude of log 1 is zero. The value of Δ RpH (pH – NRpH) is negative for higher pCO₂ levels (>40 mm Hg) which indicates the acidic effect of increased $pCO₂$ and positive for lower pCO₂ levels (<40 mm Hg), which indicates the alkaline effect of decreased pCO₂.

Fig. 5: Relationship between pCO₂ and ΔRpH (pH – NRpH)

Fig. 7: Linear regression plot between Std BE and ΔNRpH (NRpH − 7.4)

The relation between Std BE and ΔNRpH was analyzed using linear regression plot and shown in [Figure 7](#page-3-4). It was found to be statistically significant with R^2 -value of 0.93 and $p < 0.0001$.

Fig. 8: Linear regression plot between pCO₂ and ΔRpH (pH −NRpH)

Similarly, the relation between $pCO₂$ and Δ RpH was analyzed using linear regression plot and shown in [Figure 8.](#page-4-0) It was found to be statistically significant with R^2 -value of 0.96 and $p < 0.0001$. The relationship of metabolic (non-respiratory) and respiratory components in Novel ABG interpretation method were compared and shown in [Table 3.](#page-4-1) The physiological approach, Std BE approach and novel ABG interpretation method citing with few example cases including normal and mixed, metabolic acid–base disorders and respiratory acid–base disorders were shown in [Tables 4](#page-4-2) to [6](#page-5-0), respectively.

Discussion

The novel acid–base balance theory states that net or total changes in hydrogen ion concentration or actual pH is due to both the variations in respiratory and non-respiratory (metabolic) components affecting the hydrogen ion concentration or pH in the acid–base homeostasis.^{7[,9,](#page-6-5)[16](#page-6-12)}

Furthermore, ΔpH, ΔRpH, and ΔNRpH values are more negative for acidosis and their values are more positive for alkalosis. Also, ΔNRpH is more negative for Met Ac and ΔRpH is more negative for Resp Ac. Similarly, ΔNRpH is more positive for Met Alk and ΔRpH is more positive for Resp Alk. If the variations in pH due to metabolic (ΔNRpH) and respiratory component (ΔRpH) are equal in magnitude but opposite in direction (one positive and the other negative), then the net change in pH denoted by ΔpH is zero. If changes in both the metabolic(ΔNRpH) and respiratory (ΔRpH) components are involved, it denotes either compensations or mixed acid–base disorders[.7,](#page-6-4)[9](#page-6-5)[,12](#page-6-7)[,15](#page-6-11)

A stepwise approach is developed for this novel ABG interpretation method. In step 0, the modified Henderson equation was applied to verify the consistency of the ABG report. The pH and total change in pH (ΔpH) is checked in step 1 to find whether it is normal, acidic or alkaline. Then in step 2, the Δ pH is compared and correlated with the individual components of respiratory

Boston Compensation Rules for Novel Diagnostic ABG Method

Table 5: Comparison of physiological, Std BE, and novel ABG interpretation method for metabolic acid-base disorders													
S.No.	pН							pCO , $Exp pCO$, pCO ₂ - $Exp pCO$, HCO ₃ Std HCO ₃ Std BE \triangle NRpH (NRpH - 7.4) \triangle RpH (pH - NRpH) \triangle pH (pH - 7.4)					
Compensation rule for metabolic acidosis													
	7.24	$\overline{22}$	-22.1	-0.1	9.4		$12.1 -17.99$	-0.308	0.148	-0.160			
	7.36	- 25	29.15	-4.15	14.1		$17.4 -11.35$	-0.151	0.111	-0.040			

 7.15 42 29.9 12.1 14.6 14.4 −14.25 −0.233 −0.017 −0.250 *Compensation rule for metabolic alkalosis* 7.54 35 41.93 −6.93 29.9 30.5 7.37 0.093 0.047 0.140 7.45 39 39.97 −0.97 27.1 27.2 3.11 0.043 0.007 0.050 7.48 63 53.83 9.17 46.9 40.9 23.40 0.220 −0.140 0.080

and non-respiratory change in pH using their relationship (Δ pH = ΔRpH + ΔNRpH).

Steps 1 and 2 denote the initial evaluation in the identification of acid–base disorder. The component that directly correlates with ΔpH in magnitude and direction (positive or negative) is identified. It denotes the first primary acid–base disorder. The changes in the other component are either secondary to compensations or due to second primary acid–base disorder. In the step 3, appropriate compensation rules are applied based on the first primary acid– base disorder. This is to find whether the given (pCO₂ or HCO₃⁻) and expected values (pCO₂ or HCO₃⁻) are similar or deviating. The patient history and clinical correlation will help us to differentiate the acute or chronic conditions for respiratory disorders.

If the levels of pCO_2 or HCO₃⁻ in compensation rules are expected (i.e., the given and the expected values are similar), then the changes in the other component is secondary to compensations. If the levels of pCO_2 or HCO_3^- in compensation rules are unexpected (i.e., the given and the expected values are deviating) then it denotes the additional existence of second primary acid–base disorder indicating a mixed disorder. In step 4, the type of acid–base disorder is identified and interpretation is done using the other ABG parameters, patient history and clinical correlation.

The physiological approach is more popular among the methods used for ABG interpretation. Bicarbonate is a highly variable quantity not only influenced by $pCO₂$ but also by individual metabolic components.^{[1,](#page-6-0)12} In the traditional approach, the pH (no unit) is compared with the pCO₂ (unit is mm Hg), HCO₃[–] (unit is mmol/L) and standard base excess (unit is mmol/L) and all of their units are different. Many patients in critically ill situation presents with different pH, pCO₂, and HCO₃ $^-$ values, so it makes an ABG interpretation an arduous task that poses a stress especially on the junior medical staffs. The individual contribution to the pH change by the respiratory component $pCO₂$ and the metabolic components $\mathsf{HCO_3}^-$ and Std BE cannot be easily inferred in these methods.

The limitation of the present study is that the demographic data of the patients were not available. The patient history and clinical conditions were not applied to differentiate the acute or chronic conditions for respiratory disorders. The strength of this pH based novel ABG interpretation method is that these derived formulas does not require any additional ABG parameter to be measured. So, it can be easily calculated in the blood gas analyzer by upgrading its software. The superiority of this method is that it directly correlates and compares the ΔpH with respiratory and nonrespiratory component affecting the pH and all of their units are similar (all the three pH parameters have no unit). It appears to be a simple task for the initial assessment of acid–base disorder which were clearly depicted in Tables 4 to 6 citing with examples. These example cases were taken from the total 232 cases and represent the various acid–base disorder groups. It is much easier to see the variations in magnitude as well as the normal, acidic, or alkaline side deviation using the changes in the direction either moving toward more positive alkaline side or moving toward more negative acidic side. The individual contribution to the pH change by the respiratory and the non-respiratory (metabolic) component can be easily inferred which has a significant role in the identification and understanding of mixed acid–base disorders.

CONCLUSION

The understanding and application of the postulate of the novel acid–base balance theory may help to view and overcome the problems in acid–base homeostasis in a different perspective but in a holistic and integrated approach. The stepwise approach in this novel diagnostic ABG interpretation method appears to be much more user-friendly providing an interpretation of various acid–base disorders easily and quickly.

Clinical Significance

This innovative method may help to overcome the confusing and challenging task of ABG interpretation for the junior medical staff.

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