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NEW EQUATION CORRELATING DELTA GAP AND OTHER METABOLIC AND RESPIRATORY COMPONENTS IN ARTERIAL BLOOD GAS FOR MIXED ACID BASE DISORDERS

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ABSTRACT **Background:** Mixed acid base disorders are very common in intensive care unit patients but its interpretation remains a challenging task. The delta gap or delta ratio is applied to identify it. But this concept of delta gap and its correlation with other metabolic components and respiratory acid base disorders are very confusing and difficult to understand. A newer equation is derived for the delta gap by the current author that helps in the better correlation, understanding and interpretation of mixed acid base disorders. The aim of the current research study is to derive a newer equation that correlates delta gap with other metabolic and respiratory components and to apply it to interpret the Arterial Blood Gas (ABG) report for complex acid base disorders. **Methods:** Using the already known equation that correlates the Stewarts acid base parameters (strong ion difference and non-volatile weak acids), anion gap, bicarbonate, pCO2 and Non-Respiratory hydrogen ion concentration, a newer relation is derived for delta gap. This newer relation correlates the delta gap with other metabolic and respiratory components in ABG interpretation. 5 ABG data are cited as examples to explain this newer and derived equation for delta gap to understand and identify the mixed acid base disorders. **Results:** This newer relation of Delta Gap correlates various parameters of the acid base disorders. So it is much easier to identify the hidden acid base disorders. **Conclusion:** This newer equation helps in better understanding of the concept of hidden acid base disorders that helps to identify the mixed acid base disorders which are not uncommon in intensive care unit patients. The application of this new equation may provide an easier and quicker approach to interpret complex acid base disturbances frequently encountered in the emergency medical conditions that needs prompt management.

KEYWORDS : Delta Gap, mixed acid base disorders, hidden acid base disorders

INTRODUCTION:

In arterial blood gas (**ABG**) interpretation, **pCO_2** is used as the respiratory component but many metabolic components are there. **Bicarbonate** is calculated using Modified Henderson equation. It is highly influenced by pCO_2 and is a **marker** of metabolic acid-base disturbances. Both **bicarbonate** and **Standard base excess** does not denote the causative mechanism of metabolic acid base disturbances.[1-4] The hydrogen ion concentration calculated using **standard bicarbonate** denote the **Non-respiratory hydrogen ion concentration**. The non-respiratory hydrogen ion concentration is higher in metabolic acidosis and lower in metabolic alkalosis.[5,6,7] The **Physicochemical** approach using **Stewart's theory** of acid base balance is employed to describe the **causative mechanism** of metabolic acid base disorders. The parameters like **strong ion difference** (SID) and plasma concentration of **weak non-volatile acids** namely albumin and phosphate (**A^-** or **A^-tot**) are utilized in it.[3,8,9,10]

The difference between sum of strong cations and strong anions is called the **apparent strong ion difference** (SIDa) which is balanced by the **buffer base** (**effective strong ion difference** [SID_e= ([HCO_3^-] + [A^-]]) to preserve electrical neutrality.[8,9,10] **Sodium** and **chloride** are the main strong ions and the principal contributors to the **main strong ion difference** (SIDm = {Na^+} - {Cl^-}).[11-14]

Strong Ion gap (SIG) denotes the difference between SIDa and SID_e. The concept of **strong ion gap** (SIG) is similar to **anion gap** (AG) that denotes the unmeasured ions. The anion gap is highly affected by changes in concentration of non-volatile weak acids (A^- tot) mainly albumin and it has to be corrected for it [where **AG = (SIG + A^- tot)**].[8,9,10,15] The **non-respiratory hydrogen ion** concentration is **inversely** proportional to the **Strong ion difference** and **directly** proportional to the total concentration of **non-volatile dissociated weak acids** (A^- or A^- tot) and directly proportional to the **anion gap** (AG).[13,15,16]

Simple acid base disorders are easy to interpret but in emergency and intensive care unit patients, complex acid base disorders are frequently encountered, so arterial blood gas (ABG) remains a challenging one. The concept of **hidden acid base disorders** and triple acid base disorders are difficult to understand and interpret. **Delta ratio** or **Delta Gap** is used to assess elevated anion gap metabolic acidosis and to evaluate for the presence of mixed acid–base disorders.[17,18,19]

Delta Gap is calculated only if the anion gap is elevated. If anion gap is normal then delta gap calculation is not required. The **interpretation** is done based on the **memorization** of the reference values given for the different acid base disorder conditions. So it remains an **arduous task** to understand and interpret the mixed and hidden acid base disorders. The **aim** of this current research study is to **derive a newer equation** that correlates delta gap with other metabolic and respiratory components and to apply it to interpret the ABG report for complex acid base disorders.

METHODS:

The compensation rules for respiratory and metabolic acidosis to be applied for the cited examples are mentioned below.[20]

Rule for Acute Respiratory Acidosis:

Expected [HCO_3] = 24 + {(Actual pCO_2 - 40) / 10}

Rule for Chronic Respiratory Acidosis:

Expected [HCO_3] = 24 + 3.5 {(Actual pCO_2 - 40) / 10}

Rule for a Metabolic Acidosis:

Expected pCO_2 = 1.5 **X** [HCO_3] + 8 (range: +/- 2)

The normal **reference** range for **delta gap** from **-6 to + 6** mmol/L denote **High Anion Gap Metabolic Acidosis only.** If the value is **>+6,** then it denotes either **Metabolic Alkalosis or Respiratory Acidosis.** If the value is **< - 6,** then it denotes either **Non-Anion Gap Metabolic Acidosis or Respiratory Alkalosis.**[17] The relation between bicarbonate and strong ion difference is given below.[12,13,14]

SIDa - (A^-tot + SIG) = HCO3 ;

Main strong ion difference **SIDm = {Na^+} - {Cl^-}**

The calculated **anion gap** has to be **corrected** for the given **serum albumin** level. The **albumin corrected anion gap**, **delta ratio** and **delta gap** are calculated using the following formulae which are mentioned below.[16,17,18]

Albumin Corrected Anion Gap = Anion Gap + 2.5 x (4.4 - Observed Albumin g/dl)

Delta Ratio:

delta ratio = $\Delta AG / \Delta HCO_3^-$

ΔAG = Calculated Anion Gap - Normal Anion Gap

$\Delta AG = Na^+ - (Cl^- + HCO_3^-) - 12$

$\Delta HCO_3^- = 24 - HCO_3^-$

Delta Gap or Bicarbonate Gap:

Delta Gap = $\Delta AG - \Delta HCO_3^-$

Delta Gap = $Na^+ - Cl^- - HCO_3^- - 12 - 24 + HCO_3^-$

Delta Gap = Na^+ - Cl^- - 36

The **above simple equation** of **delta gap** for **quick assessment** of mixed metabolic acid base disorder **already exist in literature**.[21] In the above relation, Main strong ion difference [SIDm = $\{Na^+\}$ - $\{Cl^-\}$] parameter is substituted and the following relation between **delta gap** and **strong ion difference** is obtained which clearly shows that delta gap is **directly proportional** to the main strong ion difference.

Delta Gap = SIDm – 36
Delta Gap ∞SIDm

The **following** relation is the **applied equation** already derived and published **by** the **current author** in previous research articles.[13,15,16]

SIDa - (A^-tot + SIG) = {960/ NRH^+}X (HCO3/Std HCO3)
Where **NRH^+ = 960/Std HCO3** and **AG = (SIG + A^-tot)**
Combining the **last two relations** involving the **delta gap** and **strong ion difference**, the following relations are obtained.

SIDa - (A^-tot + SIG) ∞ 1 / NRH^+
Substituting delta gap and anion gap relation in the above relationship, the following is obtained.

{Delta Gap + 36 - (AG)} ∞ 1 / NRH^+
The **constant value** can be **omitted** for using proportionality. So, the **following newer relations are obtained**.
{Delta Gap - AG} ∞ 1 / NRH^+
Delta Gap ∞SIDm ∞1 / NRH^+
Delta Gap ∞ SIDm ∞ (HCO3/ Std HCO3) ∞ pCO2

The above **three newly derived relationship** relates the **delta gap** with the other **metabolic** and **respiratory components** of Arterial Blood Gas.

RESULTS:

Total value of the parameter {SIDa - (A^- tot + SIG)} denotes bicarbonate numerically only if all the ions and parameters are measured [SIDa - (A^- tot + SIG) = HCO3]. But all the ions are not measured routinely due to certain practical difficulties in laboratory measurements and higher costs. So, for practical convenience, in clinical practice the **main strong ion difference** and the **weak acid albumin** concentration can be compared and correlated with the **bicarbonate** using the **corrected anion gap** and **calculated delta gap (Delta Gap = SIDm – 36)** to understand the **causative mechanism** of the metabolic acid base disturbances and to **detect** the presence of **hidden** acid base disorders to identify **mixed acid base disorders**. **5 examples** of ABG data are shown in the **table 1** to compare and correlate Stewart's Acid Base Parameters with Bicarbonate, anion gap and delta gap. The **relationship** between **delta gap** and other **metabolic** and **respiratory components** of arterial blood gas in different acid base disorder conditions are clearly shown in **table 2**.

Table 1: Calculation, Correlation and Application of Delta Gap

S.No	pH	pCO2 mmHg	HCO3 mmol/L	Na mmol/L	Cl mmol/L	Alb g/dl	AG	Corrected AG	SIDm (Na-Cl)	Delta Gap
1	7.4	40	24	145	100	4	21	22	45	9
2	7.4	40	24	140	105	4	11	12	35	NA
3	7.09	34	10	135	112	2	13	19	23	-13
4	7.37	65	36	125	75	1.5	14	21.25	50	14
5	7.33	30	15	117	92	0.6	10	19.5	25	-11

Table 2: Relationship between Delta Gap and other Metabolic and Respiratory Components of ABG

Delta Gap Value	Clinical Condition
Delta Gap: > +6	Metabolic Alkalosis: Increased SID result in lower Non-Respiratory Hydrogen Ion Concentration leading to Metabolic Alkalosis
	Respiratory Acidosis: Increased SID is also seen in increased ratio 1 (HCO3/Std HCO3) which is related to Increased pCO2 leading to Respiratory Acidosis.
Delta Gap: < - 6	Non Anion Gap Metabolic Acidosis: Decreased SID result in higher Non-Respiratory Hydrogen Ion Concentration leading to Metabolic Acidosis.
	Respiratory Alkalosis: Decreased SID is also seen in decreased ratio 1 (HCO3/Std HCO3) which is related to decreased pCO2 leading to Respiratory Alkalosis.
Delta Gap: 0 ± 6 (- 6 to + 6)	High Anion Gap Metabolic Acidosis Only
Novel Relations Applied	Delta Gap ∞ SIDm ∞ 1 / NRH+ Delta Gap ∞ SIDm ∞ (HCO3/Std HCO3) ∞ pCO2 Where SIDm = {Na+} - {Cl-}

DISCUSSION:

In ABG interpretation, the **primary** acid base disorder is **initially identified** using the pH, pCO_2 & HCO_3 values and then assessed for the presence of **second** acid base disorder.

In **case 1**, the pH, pCO_2 & HCO_3 values are normal but the **anion gap** is **elevated**. The calculated **delta gap** value is **9 (>+6)** indicating the presence of **hidden metabolic alkalosis**. The **bicarbonate** value is **normal** (**SIDa - (A^- tot + SIG) = HCO3**) because the elevated anion gap (where **AG = SIG + A^-tot**) is seen along with elevated strong ion difference and so the sum total becomes normal. So, bicarbonate is a marker and does not explain its causative mechanism.[3,4,15] If only the bicarbonate value is seen, the identification of hidden acid base disorder may be missed. In **case 2**, the pH, pCO_2 & HCO_3 values are normal and same as in case 1, but here the sodium and chloride values are different. The anion gap value is normal. Delta gap calculation is not needed as the anion gap is not elevated.

In **case 3**, the primary disorder is **metabolic acidosis**. Using the winters formulae for compensation, additional respiratory acidosis is also seen. The anion gap is normal but the **corrected anion gap** (correction done for lower serum albumin level) is **elevated**. The calculated delta gap value is **– 13(< - 6)** denoting additional presence of **Non-Anion Gap Metabolic Acidosis.** The presence of **triple acid base disorder** involving **high anion gap metabolic acidosis**, **Non-Anion gap metabolic acidosis** and **respiratory acidosis** are seen.

In **case 4**, the primary disorder is **respiratory acidosis**. If the compensation rule for chronic respiratory acidosis is applied then the bicarbonate value is closer to the expected bicarbonate. The anion gap is normal but the **corrected anion gap** is **elevated**. The calculated **delta gap** value is **+14(>+6)** denoting either the additional presence of chronic respiratory acidosis or metabolic alkalosis. In **case 5**, the primary disorder is **metabolic acidosis**. If the compensation rule using the winters formulae is applied, then the pCO_2 value is closer to the expected pCO_2 denoting **only compensation** and no respiratory acid base disorder. The anion gap is normal but the **corrected anion gap** is **elevated**. The calculated delta gap value is **-11(< - 6)** denoting **additional** presence of **Non-Anion Gap Metabolic Acidosis.**

The **strong ion difference** is **inversely** related to **non-respiratory hydrogen ion concentration**, so its value is **decreased** in **metabolic acidosis** (Non-Anion gap metabolic acidosis) and **increased** in **metabolic alkalosis**.[4,6,7,15] The strong ion difference value is affected by **pCO_2** values through the ratio **HCO3/ Std HCO3** (Increased in Respiratory acidosis and decreased in respiratory alkalosis).[15]

Delta gap is calculated only if the anion gap is elevated and to find the presence of additional mixed acid base disorder (**{Delta Gap - AG} ∞ 1 / NRH^+**). The delta gap in the reference range from **-6 to + 6** mmol/L denote High Anion Gap Metabolic Acidosis only.[17] **The delta gap is proportional to the main strong ion differences, so any changes in main strong ion difference will change this delta gap value.** If the **delta gap** value becomes **more negative** (decreasing), then it denotes main strong ion difference value is decreasing denoting metabolic acidosis or respiratory alkalosis. If the **delta gap** value becomes **more positive** (increasing), then it denotes main strong ion difference value is increasing denoting metabolic alkalosis or respiratory acidosis.

Using the relation between delta gap and main strong ion difference (**Delta Gap = SIDm – 36**) the following relations can be obtained. The **delta gap** value is **decreased** in **Non Anion gap metabolic acidosis** and **increased** in **metabolic alkalosis** (**Delta Gap ∞ SIDm ∞ 1 / NRH^+**). Delta gap value is directly **influenced** by **pCO_2** through the ratio HCO_3/Std HCO_3. (**Delta Gap ∞SIDm ∞ (HCO_3/ Std HCO_3) ∞ pCO_2**) So the calculated delta gap value is **increased** in **Respiratory**

acidosis and **decreased** in **respiratory alkalosis**.

CONCLUSION:

These **newer findings** and **relations** may help in increasing the understanding of the **concept** of **delta gap** and its changes with other **metabolic** and **respiratory components** in complex acid base disorders. This method seems to be much easier to understand, correlate, interpret and apply it to **detect hidden** acid base disorders for the **assessment** of **mixed acid base disorders** which are not uncommon in emergency clinical conditions. The earlier **identification** of the **causative mechanism** of the acid base disorders may help in prompt treatment that results in saving the life of the critically ill patients.

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