EDUCATIONAL COMMENTARY – ARTERIAL BLOOD GASES: ACID-BASE BALANCE

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LEARNING OUTCOMES

On completion of this exercise, the participant should be able to

- identify the important buffering systems in the human body.
- explain the Henderson-Hasselbalch equation and its relationship to the bicarbonate/carbonic acid buffer system.
- explain the different acid-base disorders, causes associated with them, and compensatory measures.
- evaluate acid-base status using patient pH and $pCO_2$ and bicarbonate levels.

Introduction

Arterial blood gas values are an important tool for assessing oxygenation and ventilation, evaluating acid-base status, and monitoring the effectiveness of therapy. The human body produces a daily net excess of acid through normal metabolic processes: cellular metabolism produces carbonic, sulfuric, and phosphoric acids. Under normal conditions, the body buffers accumulated hydrogen ions ($H^+$) through a variety of buffering systems, the respiratory center, and kidneys to maintain a plasma pH of between 7.35 and 7.45. This tight maintenance of blood pH is essential: even slight changes in pH can alter the functioning of enzymes, the cellular uptake and use of metabolites, and the uptake and release of oxygen. Although diagnoses are made by physicians, laboratory professionals must be able to interpret arterial blood gas values to judge the validity of the laboratory results they report.

Maintenance of Plasma pH

The body has several mechanisms to maintain plasma pH, including the lungs, the kidneys, and buffering systems. The lungs provide an immediate response, eliminating hydrogen ions as exhaled carbon dioxide ($CO_2$); the kidneys provide a slower response, resorbing bicarbonate ($HCO_3^-$) excreting hydrogen ions in the urine. The body’s buffer systems correct changes in pH by pairing a weak acid with its corresponding salt and include hemoglobin, phosphate, plasma protein, and bicarbonate. Of these buffer systems, hemoglobin accounts for 80% of the buffering, and plasma proteins and phosphates account for about 14% and 1%, respectively. Although it only accounts for approximately 5% of the buffering
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capacity of the plasma, the bicarbonate/carbonic acid buffer system is considered the most important of the four.¹

The following equation describes the bicarbonate/carbonic acid buffer system:

\[
\text{HCO}_3^- + \text{H}^+ \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{CO}_2 + \text{H}_2\text{O}
\]

To maintain homeostasis, the bicarbonate/carbonic acid buffer system neutralizes excess acids by combining \text{HCO}_3^- with the \text{H}^+ to form carbonic acid (\text{H}_2\text{CO}_3), which then dissociates, forming \text{CO}_2 and water (\text{H}_2\text{O}) that can be released from the body through respiration.

Essential to understanding and interpreting arterial blood gases, the Henderson-Hasselbalch equation is a mathematical formula that shows the relationship of a buffer system and the resulting pH. The equation is expressed as:

\[
\text{pH} = \text{pK}_a' + \log \left( \frac{c_{\text{A}^-}}{c_{\text{HA}}} \right)
\]

where \text{A}^- is the conjugate base in a buffer system (\text{HCO}_3^-), \text{HA} is the weak acid in a buffer system (\text{H}_2\text{CO}_3), and the \text{pK}_a' is the pH at which the acid is 50% dissociated.

The equation can be applied to the bicarbonate/carbonic acid buffer system and modified to reflect measureable blood gas values as:

\[
\text{pH} = 6.1 + \log \left( \frac{c_{\text{HCO}_3^-}}{0.03 \times p_{\text{CO}_2}} \right)
\]

where 6.1 is the \text{pK}_a' of \text{H}_2\text{CO}_3 at 37°C and \text{H}_2\text{CO}_3 in mmol/L is expressed as 0.03 \times p_{\text{CO}_2}, the \text{CO}_2 tension in mmHg². From the equation, it is apparent that pH is directly related to changes in \text{HCO}_3^- and inversely related to changes in \text{pCO}_2. The numerator of the equation is typically referred to as the \textit{metabolic component} and the denominator is referred to as the \textit{respiratory component}. By maintaining a ratio of \text{HCO}_3^- to \text{H}_2\text{CO}_3 (or \text{pCO}_2) of 20:1, the body is able to maintain a plasma pH of 7.4.

Acid-Base Disorders

\textit{Metabolic Acidosis (Primary Bicarbonate Deficit)}

Metabolic acidosis, or primary bicarbonate deficit, is the most common of the acid-base disorders and is caused by loss of bicarbonate, either directly or through the buffering of excess acid. The bicarbonate deficit results in a decreased ratio of bicarbonate to \text{pCO}_2, with a resulting drop in pH. There are two types of metabolic acidosis: those causing an increased anion gap and those with a normal anion gap. Anion gap, the difference between unmeasured anions and cations, was originally used as a quality
control tool, because a “gap” exists between routinely measured anions and cations (Na+, K+, Cl −, and HCO3−). An increase in unmeasured anions increases the gap. Metabolic acidosis with an increased anion gap results from conditions where bicarbonate is consumed in buffering of excess acids. These excess acids can result either from anions produced from endogenous metabolic processes (e.g., ketoacids and lactic acids) or exogenous products (e.g., methanol and ethylene glycol) that metabolize to acids. The mnemonic device MUDPILES is commonly used to denote the eight underlying mechanisms that increase the metabolic anion gap: methanol intoxication, uremia of renal failure, diabetes or ketoacidosis, paraldehyde intoxication, isoniazid toxicity, lactic acidosis, ethylene glycol intoxication, and salicylate intoxication. Normal anion gaps are associated with metabolic acidosis due to loss of bicarbonate through the kidneys or gastrointestinal tract. Causes of metabolic acidosis with a normal anion gap include diarrhea and renal tubular acidosis. In metabolic acidosis, the body compensates by stimulating hyperventilation to lower pCO2, thereby raising the pH.

Metabolic Alkalosis (Primary Bicarbonate Excess)

Metabolic alkalosis, or primary bicarbonate excess, results in an increased pH due to an increased bicarbonate to pCO2 ratio. The bicarbonate excess can result from the addition of excess base to the system or excessive loss of acid. The addition of exogenous base is seen in individuals receiving excess intravenous bicarbonate or with those who overuse antacids. Metabolic alkalosis is also seen with citrate toxicity following massive blood transfusions, as the citrate in the blood products is metabolized to bicarbonate. Prolonged vomiting and nasogastric suctioning result in an increased loss of chloride ions (Cl −), leading the kidneys to increase retention of HCO3− to counter the sodium ions (Na+) resorbed by the renal tubules. Prolonged use of diuretics promoting loss of H+ in the urine also leads to retention of HCO3− and therefore metabolic alkalosis. The body responds to the increased pH by depressing the function of the respiratory system, thereby retaining CO2. With an increase in CO2, the bicarbonate to pCO2 ratio is decreased, resulting in a decrease in pH.

Respiratory Acidosis

Any condition that diminishes the elimination of CO2 will cause CO2 to accumulate in the blood, lowering the bicarbonate to pCO2 ratio, resulting in a decrease in blood pH or respiratory acidosis. Depression of the respiratory center by alcohol, barbiturates, narcotics, CNS trauma or tumors, or intracranial hemorrhage can all lead to retention of CO2. Respiratory disorders such as chronic obstructive pulmonary disease (COPD), severe asthma, or weakened respiratory muscles, also lead to increased pCO2 as the body struggles to eliminate CO2. The kidneys compensate by retaining HCO3− and increasing excretion of H+. The resulting increase in the ratio of bicarbonate to pCO2 returns the pH to normal.
Respiratory Alkalosis

In respiratory alkalosis, a primary deficit of CO2 is caused by an increased rate and/or depth of respiration. The resultant decreased pCO2 causes the ratio of bicarbonate to pCO2 to increase and, therefore, the pH to increase. Excessive elimination of CO2 resulting in respiratory alkalosis is seen most frequently in emotionally induced hyperventilation. Other causes of respiratory alkalosis include overstimulation of breathing due to febrile states, and the initial stages of salicylate overdose. Pulmonary disorders such as pneumonia, asthma, and pulmonary emboli can also lead to respiratory alkalosis with increased oxygen needs. As a compensatory measure, the kidneys attempt to normalize blood pH by increasing excretion of HCO3− to the urine and reclaiming H+. The Table summarizes the relationship between pH, HCO3−, and pCO2 in all four of the simple acid-base disorders.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>pH</th>
<th>Primary Defect</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>Decreased</td>
<td>Decreased HCO3−</td>
<td>Decreased pCO2</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>Increased</td>
<td>Increased HCO3−</td>
<td>Increased pCO2</td>
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</tr>
</tbody>
</table>

Abbreviation: ABG, arterial blood gas.

Mixed Acid-Base Disorders

Mixed acid-base disorders frequently result from the simultaneous presentation of respiratory and metabolic disorders. Combinations of respiratory and metabolic disorders can be difficult to diagnose and assess, as the pH can be elevated, decreased, or normal. Mixed disturbances are commonly detected by failure of the compensatory measures or an abnormal anion gap. When evaluating acid-base status in a mixed disorder, pH serves as a useful therapeutic guide; when used alone, though, pH is a poor indicator of acid-base status. An example of a common mixed acid-base disturbance is a patient with severe vomiting and hyperventilation secondary to pain. In this example, the patient exhibits both respiratory alkalosis and metabolic alkalosis.

Evaluation of Acid-Base Status

To evaluate acid-base status, the relationship between bicarbonate and pCO2, as described in the Henderson-Hasselbalch equation, must be kept in mind. Changes in pH are directly related to changes in
bicarbonate and inversely related with $pCO_2$, and the ratio of bicarbonate to $pCO_2$ must be 20:1 to maintain a normal blood pH of 7.4. It is also important to recognize arterial blood gas values outside of the established reference ranges:

\[
\begin{align*}
\text{pH} &= 7.35 - 7.45 \\
\text{pCO}_2 &= 35 - 45 \text{ mmHg} \\
\text{HCO}_3^- &= 22 - 26 \text{ mmol/L}^3
\end{align*}
\]

When interpreting an acid-base disorder, certain steps should be followed:

1. Evaluate the pH for acidosis (<7.35) or alkalosis (>7.45).

2. Assess $pCO_2$ to determine whether the respiratory component is the causative agent. The Henderson-Hasselbalch equation tells us that pH inversely responds to changes in $pCO_2$; therefore, if the pH is inversely related to the $pCO_2$, the disorder is due to a respiratory disturbance. If the pH and $pCO_2$ are not headed in opposite directions, the disorder is due to a metabolic disturbance and should be reflected in the $HCO_3^-$ concentration in a direct relationship with the pH.

3. Evaluate for compensation. Compensation for acid-base disorders is accomplished by altering the factor not primarily affected. If the disorder is due to a respiratory disturbance, the kidneys (or metabolic component) will respond to correct the ratio of $HCO_3^-$ to $pCO_2$ to return pH to normal by increasing or decreasing $HCO_3^-$ concentration. If the disorder is due to a metabolic disturbance, the lungs (or respiratory component) will respond by increasing or decreasing respiration to increase or decrease $pCO_2$. When evaluating for compensation, if the $HCO_3^-$ and $pCO_2$ results are headed in the same direction, compensation is occurring.

Summary

Although arterial blood gas interpretation for diagnosis or therapeutic monitoring is not within the purview of most laboratory personnel, understanding the body’s mechanisms for maintaining homeostasis is essential to assessing the validity of arterial blood gas results. The human body is under constant demand to buffer acids produced through cellular metabolism, and, under normal circumstances, it does so quite efficiently through various buffering systems. As illustrated by the Henderson-Hasselbalch equation, healthy lungs and kidneys function to maintain a 20:1 ratio of bicarbonate to carbonic acid, maintaining a blood pH of 7.4. Acid-base imbalances may arise with many pathologic conditions, along with a resultant change in blood pH as well as electrolyte imbalances. Although acid-base disturbances are routinely classified into four simple categories, acid-base status evaluation is rarely simple, owing to the compensatory measures the body uses to correct the imbalance and maintain homeostasis.
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References


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