REVIEW ARTICLE

The ABC's of Acid-Base Balance

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A step-wise systematic approach can be used to determine the etiology and proper management of acid-base disorders. The objectives of this article are to: (1) discuss the physiologic processes involved in acid-base disturbances, (2) identify primary and secondary acid-base disturbances based upon arterial blood gas and laboratory measurements, (3) utilize the anion gap for diagnostic purposes, and (4) outline a stepwise approach for interpretation and treatment of acid-base disorders. Case studies are used to illustrate the application of the discussed systematic approach.

KEYWORDS: acid-base

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Although acid-base disorders are frequently encountered in hospital and ambulatory care settings, they are often considered the most difficult areas to understand in medicine. Misdiagnosis due to common misconceptions of acid-base homeostasis often delays identification of the primary disorder, causing a disruption in the delivery of appropriate therapy. By understanding the basic principles of acid-base physiology, the interpretation of acid-base data, and the mechanisms responsible for acid-base perturbations, the clinician should be able to recognize all acid-base disorders and develop a systematic approach for the management of such disorders.

BACKGROUND

In order to identify acid-base abnormalities and develop a treatment plan, it is necessary to first comprehend the mechanisms responsible for acid-base equilibrium. An acid is defined as a substance that can donate a hydrogen ion (H^+), whereas a base is a substance that can accept an H^+. The acidity of body fluids can be expressed in terms of H^+, but due to confusing terminology it was proposed to convert H^+ terminology to pH.[1] When taking the negative logarithm of the H^+ concentration, pH represents a measure of H^+ activity. Optimal function for tissues and organs within the human body depends on maintaining blood pH between 7.10 and 7.60. For purposes of diagnosis, the generally accepted range of normality is pH 7.36 to 7.44. Any pH less than 7.36 is called acidemia and any pH greater than 7.44 is called alkalemia. Acidemia refers to the acid condition of the blood (pH < 7.36), whereas acidosis is the process by which a patient develops acidemia. The same is true for alkalemia and alkalosis.[2]

ABBREVIATIONS: AG, Anion gap; HCO_3, Bicarbonate; CNS, Central nervous system; ECF, Extracellular fluid; Hgb, Hemoglobin; ICU, Intensive care unit; THAM, Tromethamine

When an acid-base disorder occurs, the body attenuates this physiologic change by making adjustments through a compensatory mechanism. Compensation refers to a change of the pH toward normal. When there is a shift in H^+, the body may respond by three different mechanisms: chemical buffering, respiratory compensation, or renal compensation.[2] The most immediate response to rapid changes in body H^+ is by chemical buffering with intracellular and extracellular buffers. Buffers are agents that minimize the abil-

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ity of acids and bases to alter pH when added to a system. Major extracellular buffers in the human body include bicarbonate (HCO_3), hemoglobin (Hgb) and certain proteins, and phosphates. Intracellular buffering involves H^+ entering the cell in exchange for potassium and sodium. Respiration is a second line of defense that acts to restore the ratio of acid to base by altering the amount of CO_2 gas in the body. The amount of CO_2 gas in the body is typically referred to as P_{CO_2}, which represents the pressure exerted by dissolved CO_2 gas in the blood. Although CO_2 is produced in cells, it diffuses into the plasma to combine with water to form carbonic acid (H_2CO_3). Thus, it is helpful to consider P_{CO_2} as an acidic substance that is only controlled by the respiratory system. Changes in the rate and depth of breathing can be used to adjust the pH of body fluids. For example, in the presence of acidemia the body may respond by increasing ventilation and thereby removing excess CO_2. Ventilation rate can change P_{CO_2} and pH of blood in a matter of minutes, with maximal compensation being achieved within 12 to 24 hours. The kidneys are the final buffering system and can affect blood pH by reabsorbing HCO_3, by allowing excess H^+ to be excreted in the urine, and by generating new HCO_3 via acid secretion. Bicarbonate is considered a base, and it reflects a metabolic process (versus a respiratory process) that is only affected by the kidneys. The time required for the kidneys to compensate is slow, requiring several hours to change the extracellular fluid volume compartment and 5-7 days to achieve maximal compensation.

Interpretation of Arterial Blood Gases

In order to most precisely evaluate acid-base status, an arterial (instead of venous) blood gas is usually preferred. Arterial blood represents a mixture of blood from various parts of the body compared to venous blood obtained from an extremity which reveals information primarily about that extremity. Arterial blood also identifies the ability of the lungs to oxygenate the blood. Mixed venous blood samples can yield information about tissue oxygenation, but cannot determine the contribution of the heart versus lungs. Thus, normal arterial oxygenation confirms normal lung function, but low oxygen concentration in mixed venous blood could indicate that the heart, lungs, or both are failing.

Table 1. Normal Blood Gas Values

	Arterial Blood	Venous Blood
pH*	7.40 (7.35–7.45)	7.36 (7.33–7.43)
P_{O_2}†	80–100 mm Hg	35–40 mm Hg
P_{CO_2}‡	35–45 mm Hg	41–51 mm Hg
HCO_3§	22–26 mEq/L	24–28 mEq/L
O_2 saturation‖	≥ 95%	70% - 75%
Base excess¶	–2 to +2	0 to +4

**pH = identifies the presence of acidemia or alkalemia.*
†P_{O_2} = pressure exerted by oxygen dissolved in the plasma.
‡P_{CO_2} = pressure of dissolved CO_2 gas in the blood.
§HCO_3 = bicrobanate.
‖O_2 saturation = percentage of oxygen that hemoglobin is carrying related to the total amount the hemoglobin could carry.
¶Base excess = primarily reflects the concentration of bicarbonate and is affected only by metabolic processes; positive values reflect metabolic alkalosis and negative values reflect metabolic acidosis.

Table 1 lists the parameters and normal values commonly reported in an arterial blood gas (ABG). Acid-base disturbances are typically classified according to the cause, resulting in an acidosis (pH < 7.35) or an alkalosis (pH > 7.45). The causes are either respiratory in nature due to changes in breathing rate and pattern or metabolic as a result of an accumulation of fixed acids (e.g., ketones) or excessive loss of bicarbonate (e.g., pancreatic fluid). The best method to accurately and consistently identify the etiology for acid-base disturbances is to employ a systematic, stepwise approach. Five simple steps can be used to identify the primary acid-base disorder and the body's attempt to compensate.[3] This approach is summarized in Table 2.

1. Evaluate the pH

First evaluate the ABG to determine the presence of acidemia or alkalemia. A normal pH is any value between 7.35 and 7.45. Any value < 7.35 indicates acidemia, while a value > 7.45 represents alkalemia. A normal pH may reflect a normal blood gas, or, alternatively, the presence of full compensation in which the P_{CO_2} and HCO_3 will be outside the normal ranges.

2. Identify the primary process: respiratory or metabolic

Normal P_{CO_2} is any value between 35 and 45 mm Hg. It is important not to confuse P_{CO_2} (mm Hg) in the ABG report with CO_2 (mEq/L) in the serum electrolyte report. "CO_2" is reported on the serum electrolyte report in mEq/L and represents total CO_2, which is a combination of HCO_3 and dissolved CO_2/H_2CO_3 in the blood. Since CO_2/H_2CO_3 are

Table 2. Systematic Approach to Arterial Blood Gas Interpretation[3]

1. Evaluate the pH to determine the presence of acidemia or alkalemia.
2. Determine whether the primary process is respiratory or metabolic.
3. Calculate the "gaps."
4. Check for the degree of compensation.
5. Determine whether there is a 1:1 relationship between anions in the blood.

only a small fraction of the total CO_2 in a serum sample, total CO_2 is considered equal to HCO_3.

If alkalemia is present and the P_{CO_2} is less than 35 mm Hg, then the primary disorder is respiratory dysfunction. It is helpful to think of P_{CO_2} as an acidic substance when interpreting ABGs, thus a deficiency or low amount of an acidic substance would be consistent with an alkalemic state. A normal HCO_3 is any value between 22 and 26 mEq/L. If the HCO_3 is > 26 mEq/L, then the primary disorder has a metabolic cause since HCO_3 is considered a basic substance. There may be a situation in which two primary disorders coexist. If the P_{CO_2} is < 35 mm Hg and the HCO_3 is > 26 mEq/L, primary respiratory alkalemia and metabolic alkalemia are occurring simultaneously. A respiratory etiology is the primary process for acidemia when the P_{CO_2} exceeds 45 mm Hg. If the HCO_3 is < 22 mEq/L, then the primary disorder has an underlying metabolic cause. A primary metabolic acidemia may coexist with a primary respiratory acidemia when the HCO_3 is < 22 mEq/L and the P_{CO_2} is > 45 mm Hg, respectively.

3. Always calculate the anion gap

The anion gap (AG) is an additional tool that can be used to assist in evaluating acid-base disturbances. This calculated value represents the difference between the serum concentrations of positively charged ions (cations) and negatively charged ions (anions). This calculation is based upon the concept of electrical neutrality, which states that the number of cations and anions in serum must be equal. Thus, the anion gap is usually calculated by subtracting the sum of measured serum anions, HCO_3 and chloride, from measured cations, namely serum sodium. Typically, unmeasured anions, such as phosphates, sulfates, organic acids, and proteins exceed unmeasured cations (i.e., calcium, potassium, magnesium), thus the AG is 10 ± 4 mEq/L. Each 1 mEq/L increase in the AG should occur with an equal 1 mEq/L decrease in HCO_3. When the AG is > 14 mEq/L, this indicates that the presence of a metabolic acidosis should be investigated. The AG does have limitations, though, and a normal AG does not exclude the possibility of the accumulation of unmeasured anions. Yet, when the AG exceeds 25 mEq/L, a metabolic acidosis is always present.

4. Always check for the degree of compensation

The human body has compensatory mechanisms for returning the abnormal pH toward normal. During compensation, the component NOT involved in the primary disorder is adjusted in an effort to correct the pH. For example, in a primary metabolic alkalemia the compensatory respiratory response—hypoventilation—results in a high P_{CO_2}. As a general rule, the increase in P_{CO_2} should equal 0.6 times the increase in the HCO_3 concentration. For example, if the HCO_3 increased to 37 mEq/L from a normal value of 25 mEq/L, the appropriate compensation for the P_{CO_2} is 47 [(12 × 0.6) = 7.2 + normal P_{CO_2} of 40 = 47 mm Hg]. In this case, if the actual P_{CO_2} is > 50 mm Hg an additional primary respiratory acidemia is occurring. If the P_{CO_2} is < 44 mm Hg, a primary respiratory alkalemia is occurring. The body compensates for metabolic acidemia by increasing the loss of P_{CO_2} via the lungs. For compensation of metabolic acidemia, the decrease in P_{CO_2} should equal a factor of 1.3 times the decrease in HCO_3. For instance, if the HCO_3 decreases to 17 mEq/L from 25 mEq/L (a decrease of 8), the P_{CO_2} should decrease to 30 mm Hg from 40 mm Hg [40 – (1.3 × 8) = 30]. Conversely, if the P_{CO_2} were > 33 mm Hg an additional primary respiratory acidemia would be present; if the P_{CO_2} were below 27 mm Hg, a primary respiratory alkalemia would be in coexistence with the primary metabolic acidemia.

5. Check for a 1:1 relationship of acid-base substances

The rationale for this concept is based upon the earlier stated premise that cations and anions in the serum should be equal. If there is a discrepancy, the application of this concept will assist in identification of an underlying metabolic alkalemia not detected by using the previously mentioned rules. For example, in the presence of an increased anion gap metabolic acidemia, the bicarbonate concentration should decrease by 1 mEq/L for every 1-point increase in the AG.

When the bicarbonate concentration decrease is less than the increase in the AG, an underlying metabolic alkalemia may be present. This "inequality" can be explained by the fact that the serum bicarbonate is higher than expected for the AG because the bicarbonate started at a higher level as a result of the underlying alkalosis.

Case Studies

A collection of case studies is used to illustrate the application of this five-step approach to interpret ABGs, discuss the etiology of acid-base disorders, and develop an appropriate treatment plan. A summary of equations used in the case studies is provided in Table 3.

Table 3. Equations for Analysis of Acid-Base Disorders[3]

1. Anion Gap (AG) = Sodium – (Bicarbonate + Chloride)
2. Compensation for Metabolic Acidosis
   ↓ in P_{CO_2} = 1.3 x ↓ HCO_3
3. Compensation for Metabolic Alkalosis
   ↑ in P_{CO_2} = 0.6 x ↑ HCO_3
4. Compensation for Respiratory Acidosis
   Acute: for every 10 mm Hg increase in P_{CO_2}, HCO_3 increases by 1 mEq/L
   Chronic: for every 10 mm Hg increase in P_{CO_2}, HCO_3 increases by 4 mEq/L
5. Compensation for Respiratory Alkalosis
   Acute: for every 10 mm Hg decrease in P_{CO_2}, HCO_3 decreases by 2 mEq/L
   Chronic: for every 10 mm Hg decrease in P_{CO_2}, HCO_3 decreases by 4 mEq/L
6. Increased AG Metabolic Acidosis
   each 1-point ↑ in AG should be equaled by a 1 mEq/L ↓ in HCO_3
7. Normal AG Metabolic Acidosis
   each 1 mEq/L ↑ in chloride should be equaled by a 1 mEq/L ↓

Case 1

A 2-year-old, 13 kg male with a history of Hirschsprung's disease is postoperative day 2 following a small bowel resection. His nasogastric tube is connected to low intermittent suction and draining copious amounts of green fluid. Urine output has decreased to 0.3 mL/kg/hr despite receiving maintenance intravenous fluids of dextrose 5%/0.2% normal saline. Laboratory values and ABG on room air are as follows:

Sodium 144 mEq/L, Potassium 3.2 mEq/L, Chloride 94 mEq/L,

ABG: pH 7.52, P_{O_2} 90 mm Hg, P_{CO_2} 48 mm Hg, HCO_3 39 mEq/L.

Step 1: Elevated pH indicates the presence of alkalemia.

Step 2: The primary process is metabolic since the HCO_3 is elevated and P_{CO_2} is not decreased.

Step 3: Calculate the gaps.
AG = 144 – (39 + 94) = 11 mEq/L. A normal AG is 10 ± 4 mEq/L, thus the AG is normal.

Step 4: Check for the degree of compensation. The increase in P_{CO_2} is 8.4 (0.6 × 14), thus 40 + 8.4 = 48.4. The calculated increase in P_{CO_2} of 48.4 mm Hg is equal to the measured P_{CO_2} of 48 mm Hg, thus the metabolic alkalemia is fully compensated.

Step 5: Determine the 1:1 relationship. This calculation is not necessary.

The mechanism for metabolic alkalosis in this case is a result of a loss of H^+ from gastrointestinal fluids via the nasogastric tube. Other etiologies for metabolic alkalosis are summarized in Table 4. Of special note is the ability of medications to cause this disorder. Both loop and thiazide diuretics promote a disproportionate excretion of chloride in relation to bicarbonate. Administration of high-dose penicillin antibiotics (e.g., carbenicillin, ticarcillin) enhances the secretion of potassium and hydrogen ions because they act as nonreabsorbable anions. Alkali administration via sodium bicarbonate or organic acids converted to bicarbonate, such as lactate, acetate, and citrate, may also contribute to metabolic alkalemia.

Certain situations require acute management of the alkalemic state. Severe alkalemia may have adverse consequences, such as tetany, muscle weakness, ileus, and predisposition to arrhythmias as a result of decreased ionized calcium and intracellular shifts of potassium, magnesium and phosphorus.[4] Treatment modalities for management of metabolic alkalosis can be remembered with the mnemonic **CARP**: **C**hloride, **A**ldosterone**, R**enal perfusion, **P**otassium. In the patient with adequate renal function, the first step is to maximize the patient's ability to excrete excess bicarbonate by correcting extracellular fluid (ECF) volume depletion with 0.9% saline (Na**C**l). Then minimize **A**ldosterone production, administer IV fluids to improve **R**enal perfusion, and supplement **P**otassium chloride. If alkalemia is due to gastric losses, the patient is usually ECF volume-depleted, chloride-depleted, and potassium-depleted. Initiation of histamine$_2$-receptor (H_2) antagonists or proton pump inhibitors may be useful in decreasing gastric acid losses. If alkalemia is diuretic-induced, potassium and ECF vol-

Table 4. Causes of Metabolic Alkalosis

Extracellular Fluid or Chloride Depletion
loss of gastrointestinal fluid (i.e., vomiting, nasogastric suction)
Post hypercapnea
Medications
diuretic therapy (loop and thiazides)
extended penicillins (carbenicillin, ticarcillin)
Mineralocorticoid excess
hyperaldosteronism

ume is often depleted. Converting to potassium-sparing diuretics may help prevent recurrences. If the ECF volume is severely contracted, temporarily stopping or reducing the dose of diuretics until the disorder has resolved may be required. Alkalemia due to high-dose corticosteroid administration may necessitate changing to a corticosteroid with lower mineralocorticoid activity such as dexamethasone or methylprednisolone. Acetazolamide may be used to promote bicarbonate diuresis if adequate renal perfusion is present. Rarely, intravenous HCl has been used to treat severe metabolic alkalemia, but it must be extemporaneously prepared by a pharmacist since it is not commercially available. Concentrated HCl is mixed with intravenous fluids to make 0.1 N HCl in 5% dextrose and must be administered via a central vein. If a patient is receiving parenteral nutrition, chloride salts (e.g., NaCl, KCl) of electrolyte solutions may be used and H_2-antagonists can be added to the formulation.

Case 2

A 9-year-old female with a history of Crohn's disease is admitted to the hospital with a perforated bowel and peritonitis. After undergoing surgery for a colectomy and peritoneal irrigation, she is transferred to the intensive care unit (ICU). Postoperatively, she becomes septic with a temperature of 103°F. ABG and laboratory values upon arrival to the ICU are as follows: pH 7.12, P_{CO_2} 19 mm Hg, HCO_3 5 mEq/L,

Sodium 140 mEq/L, Potassium 4.8 mEq/L, Chloride 105 mEq/L.

Step 1: Acidemia is present since the pH is < 7.35.

Step 2: The primary process is metabolic since the bicarbonate is decreased and the P_{CO_2} is not increased.

Step 3: Anion gap is dramatically elevated: 140 – (105 + 5) = 30 [normal AG = 10 ± 4].

Step 4: Compensation for metabolic acidosis is calculated using the following formula: $\Delta P_{CO_2} = 1.3 \times$ decrease in HCO_3. The decrease in bicarbonate is 20 (25 – 5 = 20), so the P_{CO_2} should decrease to 14 mm Hg ($\Delta P_{CO_2} = 1.3 \times 20 = 26$; 40 – 26 = 14). The compensation for the metabolic acidemia is not complete because the P_{CO_2} of 19 mm Hg is slightly high for normal compensation. Thus, the P_{CO_2} is consistent with a mild superimposed respiratory acidosis. A second disorder, respiratory acidosis, is present.

Step 5: 1:1 Relationship – The bicarbonate decrease of 20 (25 – 5 = 20), is close enough to the AG of 18 (30 – 12 = 18) to exclude an underlying metabolic alkalosis.

The mechanism for metabolic acidosis in this case is lactic acidosis in association with the patient's septic shock. Calculation of the AG is useful because it reveals information about the probable cause and the most appropriate therapy for the acidosis. Clinical causes of a metabolic acidosis with an increased anion gap are summarized in Table 5. Metabolic acidosis with a normal anion gap (hyperchloremic acidosis) is usually caused by either gastrointestinal bicarbonate loss, altered renal function, or the use of certain medications.

Management of patients with metabolic acidosis depends on the origin of the disorder. If the acidosis is due to gastrointestinal losses, correction involves treating the underlying cause. In Case 2, the appropriate therapy would be management of the septic shock. Severe acidemia can precipitate adverse consequences such as reduced cardiac output, decreased strength of respiratory muscles, hyperkalemia, progressive obtundation and coma.[4] Alkalinizing agents are available for the treatment of metabolic acidosis. Sodium bicarbonate is the cornerstone of alkali therapy. Because of risks associated with bicarbonate therapy, specific dosing guidelines must be followed. As a general rule, sodium bicarbonate is not used as a treatment modality unless a patient is experiencing life-threatening adverse consequences (i.e., cardiovascular depression) or displays a pH < 7.20 with circulatory instability. Sodium bicarbonate is not recommended during cardiac arrest. The predominant source of acid in the tissues is accumulated CO_2 due to inadequate circulation, thus administration of sodium bicarbonate will exacerbate tissue acidosis. The role of alkali therapy in lactic acidosis is contro-

Table 5. Causes of Metabolic Acidosis

Increased Anion Gap – Think of the mnemonic: **A MUDPIE**
Aspirin
Methanol
Uremic renal failure
Diabetic ketoacidosis and other forms of ketoacidosis
Paraldehyde
Ischemic or idiopathic lactic acidosis
Ethylene glycol
Normal Anion Gap
Gastrointestinal losses of HCO_3
Diarrhea
Enteric fistula
Pancreatic fistula
Ureteral diversions
Uretero-sigmoidostomy
Ileal bladder
Ileal ureter
Renal tubular acidosis
Proximal
Distal
Buffer deficiency (phosphate, ammonia)
Medications
Carbonic anhydrase inhibitors (i.e., acetazolamide)
Amphotericin B

versial. Since most cases of lactic acidosis are due to inadequate tissue perfusion, the potential for poor clearance of bicarbonate-generated CO_2 exists in some tissues when bicarbonate therapy is used. Effective treatment goals with bicarbonate therapy include reversing the detrimental consequences of severe acidemia by returning the pH to approximately 7.20 and the plasma bicarbonate to 10 mEq/L. To estimate the amount of sodium bicarbonate to achieve this goal, multiply the apparent volume of distribution of bicarbonate (0.5 L/kg) × body weight (kg) × (desired [HCO_3] – current [HCO_3]).[4] For a 30 kg patient with a plasma HCO_3 of 5, the calculated dose of sodium bicarbonate is 75 mEq infused as an intravenous infusion over 1-2 hours [(0.5)(30)(5) = 75]. To avoid risks associated with bicarbonate therapy, it has been recommended to add two 50-mL injections of 8.4% sodium bicarbonate to one liter of 0.2% normal saline.[4] An 8.4% solution contains 1 mEq of sodium and 1 mEq of bicarbonate, so this manipulation would render this solution nearly isotonic (~140 mEq sodium per liter).

Excessive administration of sodium bicarbonate has been associated with several problems. Increased P_{CO_2} generation and a worsening of acidosis in the central nervous system may occur as a result of CO_2 that freely diffuses across the blood brain barrier and cell membranes more readily than bicarbonate. "Overshoot alkalosis" may result from aggressive exogenous bicarbonate loading. Bicarbonate is consumed as a buffer for ketone bodies or lactic acid and regenerated when these organic acids are later metabolized, thus the patient may develop excess ECF bicarbonate once the underlying cause of the acidosis is corrected. Overcompensation may occur because bicarbonate equilibrates slowly across the blood brain barrier. A systemic alkalemia may result because the brainstem areas that control ventilation continue to sense severe acidosis even after the systemic pH has been increased with exogenous bicarbonate. Because of the tremendous load of sodium associated with undiluted sodium bicarbonate (1000 mEq sodium per liter), severe pulmonary edema and hypernatremia may develop. Caution must be exercised when using this therapy in patients with congestive heart failure and renal failure. Coadministration of loop diuretics may prevent this complication. If the patient is receiving parenteral nutrition, acetate salts of electrolyte solutions (i.e., sodium acetate, potassium acetate) may be used in the formulation. However, these are often regarded as unreliable sources because their alkalinizing properties are dependent on their conversion to bicarbonate which may be influenced by liver disease or circulatory failure. Dichloroacetate and Carbicarb are two investigational agents used to treat metabolic acidosis, but these are not routinely available in most practice settings. Tromethamine (THAM) is commercially available in the United States, but no therapeutic advantage to sodium bicarbonate has been demonstrated. THAM corrects metabolic acidosis by combining with hydrogen ions from carbonic acid to form bicarbonate and a cationic buffer. Its use is limited by the potential for severe inflammation, vascular spasms, and tissue necrosis if infiltration occurs.

The oral route may be used for alkali replacement. Sodium bicarbonate tablets are often used for maintenance therapy in patients with chronic bicarbonate losses (i.e., renal tubular acidosis). Many patients dislike the taste of the tablets, so baking soda (60 mEq bicarbonate/tsp) may be used as an alternative. Shohl's solution (sodium citrate/citric acid) is a liquid dosage form preferred by some patients. Citrate preparations, however, may increase gastrointestinal absorption of aluminum and this may be a problem in renal failure patients.

Case 3

A 5-year-old, 25 kg boy sustained severe head injuries, a grade IV splenic laceration, a tibia-fibula fracture, and a pulmonary contusion after being hit by a car while riding his bicycle. He is stabilized and transferred to the intensive care unit with the following laboratory values and ABG on admission: Sodium 135 mEq/L, Potassium 3.1 mEq/L, Chloride 103 mEq/L, pH 7.51, P_{CO_2} 25 mm Hg, HCO_3 22 mEq/L.

Step 1: Alkalemia is present since the pH > 7.45.

Step 2: The primary process is respiratory because the P_{CO_2} is < 40 mm Hg and the HCO_3 is not increased.

Step 3: AG is normal [135 – (103 + 22) = 10].

Step 4: Compensation for respiratory alkalemia is calculated by the following formula: the HCO_3 decreases by 2 mEq/L for every 10 mm Hg decrease in P_{CO_2} (for acute respiratory alkalosis). Since the decrease in P_{CO_2} is 15 (40 – 25 = 15 mm Hg), the calculated decrease is 3. In this case, the calculated decrease is identical to the actual decrease (25 – 22 = 3), so only acute respiratory alkalemia is present with normal compensation. If the situation is chronic (> 3 days), the degree of compensation varies: for every P_{CO_2} decrease of 10 mm Hg, the HCO_3 decreases by 4 mEq/L. If the calculation of the degree of metabolic compensation is not close to the actual value for the HCO_3 (± 2 mEq/L), an additional primary metabolic disorder is present.

Step 5: 1:1 Relationship – Since the AG is normal, the bicarbonate decrease of 3 (25 – 22 = 3) is the same as the chloride increase of 3 (103 – 100 = 5). Thus, no underlying metabolic alkalosis exists.

The mechanism for respiratory alkalosis in this case is decreased P_{CO_2} from ventilation in excess of CO_2 production due to head trauma. Other clinical causes for respiratory alkalosis are summarized in Table 6. Management of respiratory alkalosis primarily involves treating the underlying cause. In mechanically ventilated patients, it may be necessary to suppress patient-triggered breaths with opiates or sedative agents.

Case 4

A 6-year-old female with steroid-dependent asthma presents to the Emergency Department with labored breathing after several days of persistent diarrhea. She is treated with intravenous steroids, aerosolized bronchodilators, and oxygen, but her breathing continues to worsen. Laboratory values and ABG are as follows: Sodium 137 mEq/L, Potassium 2.1 mEq/L, Chloride 111 mEq/L, pH 6.94, P_{CO_2} 60 mm Hg, HCO_3 15 mEq/L.

Table 6. Causes of Respiratory Alkalosis

Psychogenic hyperventilation
Anxiety
Hypoxia
Severe asthma
Pneumonia
Pulmonary embolus
Congestive heart failure/pulmonary edema
Infection
Gram-negative sepsis
Fever
Increased intracranial pressure
Head trauma
Stroke/hemorrhage
Tumor
Salicylate toxicity
Liver disease
Excessive mechanical ventilation

Step 1: Acidemia is present (pH < 7.35).

Step 2: The primary process is both respiratory (P_{CO_2} > 40 mm Hg) and metabolic (HCO_3 is decreased).

Step 3: AG is normal [137 – (111 + 15) = 11].

Step 4: Compensation – There is no need to perform this calculation since the coexistence of two academic abnormalities confirms the absence of compensation.

Step 5: 1:1 Relationship – In a normal AG metabolic acidosis, any decrease in HCO_3 should be equal to the increase in chloride. The change in HCO_3 was 10 mEq/L (25 – 15 = 10) and the chloride level increased by 11 mEq/L (111 – 100 = 11), so the relationship of HCO_3 to chloride was approximately 1:1. Thus, no underlying metabolic alkalosis is present.

In situations of mixed acid-base disorders (i.e., metabolic and respiratory acidosis), it is often helpful to determine the primary process in order to determine the most appropriate management. Measurement of urinary electrolytes can be employed to differentiate the cause of the normal AG metabolic acidosis.[3] The kidney responds to gastrointestinal HCO_3 loss with a compensatory loss of ammonium in the urine, thereby acidifying the urine. Ammonium is the predominant

Table 7. Causes of Respiratory Acidosis

Impaired Central Nervous System (CNS)
CNS disease (e.g., injury, neoplasm, infection)
Drug/poison (e.g., opiates, alcohols, anesthetics)
Metabolic (e.g., anoxia)
Mechanical
Airway obstruction (e.g., severe asthma, foreign body, tumor)
Pneumothoraces
Neuromuscular
Spinal cord injury
Paralyzing agents
Muscular dystrophy
Guillain-Barré, ALS, MS
Loss of gas exchange area
Severe pneumonia
Severe pulmonary edema
Emphysema
Massive pulmonary embolus

unmeasured cation and its excretion is usually accompanied by chloride. A urine delta gap can be calculated by subtracting urinary chloride from urinary sodium and potassium (i.e., urine delta gap = [urinary sodium + urinary potassium] – urinary chloride). Under normal circumstances, 20 – 40 mEq/L of ammonium is excreted each day in the urine, and the urine delta gap has a negative value of –20 to 0 mEq/L. The normal response to an acid load is an increase in renal production of ammonia, with an increase in urine ammonium excretion. In metabolic acidosis, ammonium excretion should increase dramatically if acidification is intact, resulting in a large negative urine delta gap (–20 to –50 mEq/L). If a defect in renal acidification is present (i.e., renal tubular acidosis), ammonium excretion is impaired and the urine delta gap is a positive value.

Knowledge of this patient's urinary electrolytes confirmed that the likely cause of the normal anion gap metabolic acidosis was the diarrhea. However, should this patient's treatment begin with administration of sodium bicarbonate to correct the metabolic process, the potassium concentration would further decline due to an intracellular shift causing additional muscle weakness and potentially a fatal respiratory collapse. The mechanism for the respiratory acidosis in this case is the patient's hypoventilation from severe airway obstruction and fatigue. Other causes for respiratory acidosis are listed in Table 7. The patient is treated with mechanical ventilation for the respiratory acidosis and aggressive intravenous potassium chloride replacement for her hypokalemia.[5] When potassium exceeds 3.3 mEq/L, the patient can slowly be treated with sodium bicarbonate if the pH remains less than 7.20. Dosing guidelines for sodium bicarbonate are the same as previously outlined.

In summary, acid-base disorders are common in both hospitalized and ambulatory patients. These disorders may exist as single or mixed entities as illustrated in the case studies. A systematic approach to acid-base disturbances can assist the clinician in identifying all the abnormalities present so that appropriate treatment can be initiated and its response can be accurately monitored.

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