SPECIFICITIES OF ACID-BASE BALANCE DISORDERS IN CHILDREN

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Abstract

The balance between the production and elimination of acids and bases is essential for the homeostasis of the organism. Disturbances of this balance (metabolic and respiratory acidosis and alkalosis and mixed disorders) are secondary, arising from other diseases and injuries, so their treatment is primarily etiological. In the diagnosis of acid-base imbalance, gas analyses of arterial blood play a key role, which is also a guide in therapy, but the anamnesis, physical examination, and other diagnostic methods should not be neglected either. Although the basic elements of the diagnosis and treatment of acid-base disorders, as well as the etiology and pathogenesis are very similar in children and adults, there are still numerous specificities related to children's age, which are listed in this paper.

Keywords: acid-base balance, disorders, children

Introduction

For the body's homeostasis, it is essential to maintain a balance between the production and elimination of acids and bases. Disruptions in this balance are secondary, resulting from and/or manifesting as a disease or injury, rather than being a disease in themselves. These imbalances can be respiratory, metabolic, or mixed, depending on the underlying cause[1]. Therefore, when interpreting arterial blood gas analyses (the most crucial element for diagnosing and guiding the treatment of these disturbances) it is essential to consider the complete clinical picture, perform a physical examination, and be aware of other diagnostic elements, especially in complex cases involving multiple primary disturbances. The body employs various methods and mechanisms to compensate for acid-base disorders, but compensation is limited by various factors. It is crucial to understand the expected degree of compensation, apply symptomatic treatment, and, most importantly, address the underlying cause that led to the primary disturbance or disease. Severe acidosis (pH < 6.8) and severe alkalosis (pH > 8) are nearly impossible to cure, making early diagnosis and timely treatment crucial. Despite many similarities between acid-base disorders in children and adults, there are numerous specific considerations related to pediatric patients, both in terms of the causes of these disturbances and their diagnosis and treatment[2].

Parameters for assessing acid-base status

The assessment of acid-base status is based on the values of several parameters: pH (hydrogen ion concentration), pCO_2 (partial pressure of carbon dioxide), HCO_3 (bicarbonates), BE/BD (base excess/base deficit), and BB (buffering bases). These parameter values do not differ between pediatric, adolescent, and adult age groups.

The concentration of hydrogen ions is always the first step in evaluating and assessing acid-base balance disturbances. It is a general parameter that indicates whether a bodily fluid is in balance, in acidosis, or alkalosis. This parameter does not indicate the nature of the disturbance, only whether a disturbance exists. The concentration of hydrogen ions is numerically expressed as pH, which was defined by Sørensen in 1908 as the negative logarithm of the hydrogen ion concentration (pH = -log H^+)[3]. The calculation (or expression) of pH values can also be performed using the Henderson-Hasselbalch equation, which represents the relation between the metabolic and respiratory components, and takes into account the dissociation constant of carbonic acid (pK) and the solubility coefficient of carbon dioxide (α)[4, 5]. The equation is: pH = pK + log HCO_3/ α pCO_2. High pH values correspond to low concentrations of hydrogen ions (alkalosis), while low pH values correspond to high concentrations of free hydrogen ions, indicating high acidity (acidosis).

The partial pressure of carbon dioxide (pCO_2) is a parameter of the respiratory component of acid-base status[6]. The partial pressure of carbon dioxide (pCO_2) is a direct indicator of the adequacy of alveolar ventilation and an indirect indicator of the concentration of carbonic acid in body fluids. A significant increase in pCO_2 (hypercapnia) indicates respiratory acidosis, while a decrease (hypocapnia) indicates respiratory alkalosis. The normal arterial pCO_2 value is

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Table 1. Expected compensatory response to acid-base disorders

Disorder	Parameter (primary)*	Adequate compensatory response (outline)	Mathematical model for calculating expected compensation
Respiratory acidosis	↑pCO_2	for every 10 mmHg ↑pCO_2 there is an ↑HCO_3 of 1 mmol/L	Ac.: ↑HCO_3 by 0.1 x (I pCO_2 - 40) →pH ↓ by 0.008 x (I pCO_2 - 40) Chr.: ↑HCO_3 by 0.4 x (I pCO_2 - 40)
Respiratory alkalosis	↓pCO_2	for every 1.3 kPa ↓pCO_2 there is an ↓HCO_3 of 2 mmol/L	Ac. HCO_3 se ↓ by 0.2 x (40 - I pCO_2) →pH se ↑ by 0.008 x (40 - I pCO_2) Chr. HCO_3 ↓ by 0.4 x (40 - I pCO_2)
Metabolic acidosis	↓HCO_3	for every 1 mmol/L ↓HCO_3 there is an ↓pCO_2 of 1.2-1.3 kPa	pCO_2 ↓ by 1-1.5 x (24 - I HCO_3)
Metabolic alkalosis	↑HCO_3	for every 1 mmol/L ↑HCO_3 there is an ↑pCO_2 6-8 mmHg (1 kPa)	pCO_2 ↑ by 0.25-1 x (I HCO_3 - 24)

Legend: ↑-increase; ↓-decrease; **Ac.** - acute; **Chr.** - chronic; **I** - measured (or actual) value.
Note: *parameter that is primarily altered (elevated or decreased value).

5.33 kPa (40 mmHg), with variations from 4.7 to 6 kPa (35-45 mmHg), while in venous blood, this value is 6-8 mmHg higher[6].

Bicarbonates (HCO_3) are the most important parameter of the metabolic component, as they are routinely and easily measured and represent the largest portion of the blood's buffering bases. A significant increase in bicarbonate levels indicates metabolic alkalosis, while a decrease indicates metabolic acidosis. Under standard conditions, the normal concentration of bicarbonates in arterial blood is 24 ± 2 mmol/L, and it is 1-3 mmol/L lower in venous blood.

Base excess and base deficit represent deviations from the normal values of bicarbonates. Normal BE/BD values range from ± 2.3 to ± 3.2 mmol/L. The practical significance of determining BD is that it is used to calculate the amount of bicarbonate needed to correct metabolic acidosis[1, 7].

Buffering bases represent the sum of the concentrations of all conjugate bases (bicarbonates, plasma proteins, and hemoglobin) in one liter of blood, depending on hemoglobin concentration. The normal value in adults is 375 mEq/L[1, 7].

Physiological regulation of acid-base balance

In the case of an acid-base imbalance, the body attempts to compensate using various mechanisms. Regulation of acid-base status involves the respiratory center, chemoreceptors, and buffers, which can be either physical-chemical (such as blood and tissue fluid buffers) or physiological (such as the lungs and kidneys). Compensatory mechanisms are useful, especially in the initial phase (when the imbalance occurs), but they are insufficient to correct the disorder entirely. Therefore, it is essential to address the underlying cause of the imbalance, i.e., to treat the root cause of the disorder[8].

The primary indicator of whether compensation exists (and is adequate) is if the values of HCO_3 and pCO_2 are shifted in the same direction (i.e., both are either decreased or increased from normal values). Whether the change in these parameters is primary or compensatory depends on the extent of the deviation. It is crucial to know the expected numerical values of compensatory changes for the corresponding parameters (Table 1). If the deviations are within the expected compensatory response range, it indicates a simple (primary) disorder that has been adequately compensated. However, if the compensatory response is greater, smaller, or absent compared to expectations, it suggests mixed (complex) disorders, meaning multiple primary disturbances are present simultaneously[1, 8].

In pediatric patients, Winter's formula is particularly useful for assessing the degree of compensation, specifically the expected decrease in pCO_2 in cases of metabolic acidosis. The formula is as follows: $pCO_2 = (1{,}5 \times HCO_3) + 8 \pm 2$ mmHg. This formula is appropriate for estimating the maximum respiratory compensation for metabolic acidosis. Respiratory compensation for metabolic disturbances has its limits, with the maximum possible hyperventilation resulting in a pCO_2 as low as 10-15 mmHg.

Basic characteristics of acid-base balance disorders

Acid-base imbalance manifests through four primary disorders: respiratory acidosis, respiratory alkalosis, metabolic acidosis, and metabolic alkalosis. Additionally, there are mixed (complex) disorders, which involve the simultaneous presence of multiple primary disorders, most commonly two. Almost all combinations of primary disorders are possible, except for respiratory acidosis and respiratory alkalosis, and metabolic acidosis and metabolic alkalosis[8].

Acidosis is defined as a disorder that adds acid or removes base from body fluids. Conversely, alkalosis is a disorder that removes acid or adds base to body fluids. Acidemia and alkalemia are conditions where the plasma pH is measurably shifted. Metabolic acid-base disorders indicate primary deviations in bicarbonate concentration, while respiratory disorders indicate primary deviations in carbon dioxide (CO_2) concentration, or carbonic acid (H_2CO_3)[1].

Respiratory acidosis

Respiratory acidosis is a pathological process in which alveolar ventilation is primarily decreased relative to the metabolic production of carbon dioxide, resulting in hypercapnia, or a positive carbon dioxide balance. It is characterized by an increase in the partial pressure of carbon dioxide (pCO_2 > 6 kPa), an increase in the concentration of free hydrogen ions, i.e., a decrease in pH (pH < 7.35), and a compensatory increase in bicarbonate[10].

The causes of respiratory acidosis are numerous and include diseases, injuries, and conditions that lead to hypoventilation, which can occur at the level of the respiratory center or the thoracic cavity. Depression of the respiratory center can be caused by brain injuries and tumors, encephalitides, and other intracranial diseases, as well as drugs and toxins with depressant effects. Injuries and diseases affecting any segment of the thoracic cavity (such as bone structures, respiratory muscles, airways, pulmonary parenchyma, or pleural space) can result in hypercapnia.

In the pediatric age group, the most common causes of respiratory acidosis are: hypoventilation (due to CNS depression from medications or stroke, neuromuscular diseases), intrinsic lung diseases (severe pneumonia, pulmonary edema, pulmonary hemorrhage), and airway obstruction (upper airway - croup, foreign body aspiration, or lower airway - bronchial asthma, bronchiolitis)[10].

The clinical picture is nonspecific and depends on the type and progression of the disorder leading to respiratory acidosis. Acute hypercapnia manifests as feelings of agitation, anxiety, fear, reduced mental activity, and headaches. The dominant symptom is a sense of air deprivation, resembling suffocation. In severe cases, there may be disturbances of consciousness ranging from agitation to somnolence, stupor, and coma. Chronic hypercapnia, often associated with chronic pulmonary or neuromuscular diseases, causes apathy, drowsiness, decreased concentration and memory, headaches, tachycardia, and vasomotor disturbances[8].

Treatment of respiratory acidosis primarily involves addressing the underlying cause and aims to normalize pulmonary ventilation. In addition, oxygen therapy and other forms of supportive or symptomatic treatment are applied. Oxygen therapy can be administered via spontaneous inhalation of oxygen through a mask or nasal cannula, or various modes of non-invasive or invasive mechanical ventilation, depending on the degree and severity of respiratory insufficiency[7].

Respiratory alkalosis

Respiratory alkalosis primarily represents an increase in alveolar ventilation relative to metabolic carbon dioxide production. Chemically, this results in: hypocapnia (pCO_2 < 4.7 kPa), decreased hydrogen ion concentration (increased pH > 7.45), and compensatory decrease in bicarbonate[11].

The causes of respiratory alkalosis include direct or reflex stimulation of the respiratory center, leading to hyperventilation and increased elimination of CO_2. Direct stimulation of the respiratory center occurs in the following conditions: excitement, fear, severe pain, initial phase of salicylate intoxication, Gram-negative sepsis, CNS damage, neurotic and hysterical states, etc. Reflex stimulation of the respiratory center happens via peripheral chemoreceptors and intrathoracic receptors (heart failure, pneumonia, bronchial asthma attacks, pulmonary fibrosis, pulmonary embolism, foreign bodies in the airways, etc.).

In children, the most common causes of respiratory alkalosis are encapsulated in the mnemonic acronym AMISH: Ammonia (elevated ammonia - in hepatic encephalopathy); Anxiety; Medications (medications, especially progesterone, salicylates); Increased Intracranial Pressure (elevated intracranial pressure); Sepsis; Hypoxemia; Hyperthermia[12].

In the pathogenesis of respiratory alkalosis, hypoxia of any etiology plays a crucial role, leading to a drop in pO_2 < 8 kPa (60 mmHg), which triggers hyperventilation and respiratory alkalosis. Acute hypoxia is observed in conditions such as pulmonary edema, severe acute bronchial asthma attacks, severe pneumonia, hypotension, etc. Chronic hypoxia is associated with diseases like pulmonary fibrosis, anemia, cyanotic heart defects, and can also occur at high altitudes.

The clinical picture of respiratory alkalosis depends on the disorder that led to it, as well as whether it developed acutely or gradually. Acute hypocapnia (resulting from hyperventilation lasting from a few minutes to several hours) manifests clinically as dizziness, irritability, visual disturbances, tachycardia, and arrhythmias. Chronic hypocapnia, resulting from prolonged exposure to etiological factors, presents with similar but more subtle symptoms. Treatment of respiratory alkalosis must focus on reducing hyperventilation and addressing the underlying etiological factor.

Metabolic acidosis

Metabolic acidosis is a pathological state characterized by an excess of strong acids in body fluid, marked by a decrease in bicarbonate (HCO_3 < 20 mmol/L), a decrease in pH value (pH < 7.35), and an increase in the concentration of free hydrogen ions. This results in a compensatory decrease in pCO_2. There are three types (clinical forms) of metabolic acidosis: ketoacidosis, lactic (lactic acid) acidosis, and uremic (uric acid) acidosis.

The most common cause of metabolic acidosis in both adults and children is increased endogenous acid production, which occurs in the context of circulatory disturbances

such as shock, hypoxia, intoxication, or certain systemic diseases. Decreased acid excretion is the second most common cause in adults and the third in children, typically occurring in kidney diseases such as renal insufficiency or renal tubular acidosis, but it can also be of non-renal origin (e.g. hypoaldosteronism). Increased loss of base is the second most common cause in children and the third in adults, resulting from conditions such as diarrhea, vomiting, or intestinal fistulas. Rarely, the cause can be excessive exogenous acid intake (e.g. sodium chloride, ammonium chloride, amino acids), which occurs in accidental (children) or intentional (adults - suicide) ingestion of strong acids, or very rarely, iatrogenic causes (inadequate parenteral nutrition, excessive NaCl administration).

In children, congenital metabolic disorders are significant causes of metabolic acidosis and are often overlooked, particularly in newborns. For exogenous acid intake and toxic substances, iron ingestion is a common cause of metabolic acidosis in newborns in the US, due to excessive iron supplementation by mothers during pregnancy. Toxic alcohol poisoning is very rare in children (unlike in adults) and is always accidental, but even minimal doses (< 5 mL) can be fatal for children. It's important to remember that alcohols are present not only in alcoholic beverages but also in various everyday products (e.g. propylene glycol in cosmetics, and methanol in antifreeze). Additionally, in children, "benzodiazepine acidosis" can occur, which is extremely rare in adults, particularly if they receive large doses intravenously or via continuous infusion (e.g. in intensive care units)[13].

Ketoacidosis is the most common form of metabolic acidosis in both adults and children. There are three types of ketoacidosis: diabetic ketoacidosis (the most common type across all age groups), alcoholic/alcoholism ketoacidosis (not seen in children, but is the second most common type in adults), and starvation ketoacidosis (results from fasting or starvation). While starvation ketoacidosis is rarely observed in adults and tends to be mild, it is much more common in children, can develop very quickly, and may be severe. It often occurs in conditions where children refuse food and fast, such as during lower respiratory infections and gastroenteritis, and less commonly in epilepsy, diets, etc.

Common features for all three types of ketoacidosis are: decreased bicarbonate levels and increased ketone bodies in the blood and urine. Symptoms and signs, especially in diabetic ketoacidosis (DKA), are not specific and can resemble those of acute appendicitis, potentially leading to diagnostic errors, particularly in children. Additionally, dehydration and hypokalemia are present in all three types of metabolic acidosis, which is critical for treatment decisions. In DKA, despite the high blood glucose levels, the first step in treatment is rehydration, followed by insulin administration and potassium replacement[15].

Lactic acidosis is defined as a state of acidosis where lactate concentration in the blood is significantly elevated. Normal lactate levels are < 2 mmol/L (typically around 1 mmol/L). Mild lactic acidosis occurs at levels of 2-4 mmol/L, while levels > 4-5 mmol/L indicate very severe acidosis and poor prognosis, especially if this condition persists for more than 24 hours. While lactic acidosis is commonly associated with poor perfusion and shock (which is the most frequent case), this is not always the situation. According to the classification by Cohen and Woods (1976), there are two types of lactic acidosis: with circulatory disorders (Type A) and without circulatory disorders (Type B), which can be seen in some malignancies (e.g. lymphoma), decompensated diabetes mellitus, severe liver disease, etc[14, 15].

Uremic acidosis occurs due to decreased reabsorption and decreased excretion of NH_4, leading to urine acidification[16]. Retention of organic and inorganic anions (primarily sulfates and phosphates) leads to a significant increase in anion gap[18-22]. The most pronounced electrolyte disturbances in uremic acidosis are a significant decrease in bicarbonate (HCO_3 = 10-12 mmol/L) and hyperkalemia (K^+ is highest in terminal chronic kidney failure). There is also a chronic decrease in Ca^{++}, leading to secondary hyperparathyroidism. Phosphorus, magnesium, and sulfate levels are elevated.

The use of bicarbonate in the treatment of metabolic acidosis initially seems to be an obligatory and most logical approach[17]. However, bicarbonate replacement must be done with great caution and based on strict indications, as its use carries risks of complications. This is particularly important because bicarbonate is administered in the form of sodium bicarbonate ($NaHCO_3$), which introduces a significant amount of sodium into the body, thereby doubling the risks[18]. The most common and significant risks of bicarbonate administration include:

- *tetania* (due to rapid plasma alkalization and the resulting hypocalcemia);

- cardiac arrhythmias (particularly if administered in boluses through a central venous catheter), which can be fatal if concentrated solutions are used;

- hypertension and edema (including pulmonary edema) are caused by excess sodium, which binds water, rather than by the bicarbonates themselves;

- electrolyte imbalance (hypokalemia and hypocalcemia).

Due to the aforementioned risks of complications, it is recommended that bicarbonates be used only in cases of severe metabolic acidosis[19]. Indications for the use of bicarbonates are: pH < 7.20 (some authors suggest < 7.10), hyperkalemia (K > 5.5 mmol/L), acidic urine, lactate level > 2 mmol/L, and bicarbonate level < 15 mmol/L. It is also a rule that bicarbonates should never be replaced until normal values are reached but only up to values of 18-20 mmol/L. The dosage of bicarbonates for parenteral use can be calculated

using formulas (e.g. Astrup, Levitski) or empirically. The most accurate method is based on blood gas analyses, specifically the measured base deficit, and considering the patient's body weight (BW), using Astrup's formula: 0.3 x BD x BW[20]. This formula is also applied in pediatric age groups, with the coefficient used to multiply body weight and base deficit being 0.4 for neonates and 0.52 for preterm infants[21].

Metabolic alkalosis

Metabolic alkalosis is a pathological condition characterized primarily by an excess of bases or a deficiency of acids, resulting in a positive bicarbonate balance. Laboratory characteristics of this disorder include: decreased concentration of hydrogen ions (increased pH), elevated bicarbonate levels, and compensatory increase in the partial pressure of carbon dioxide[22].

Causes of this disorder include: excessive loss of chloride, hydrogen, and potassium (due to prolonged vomiting or gastric suction, diarrhea, diuretic therapy, liver cirrhosis), endocrine disorders (such as hypoparathyroidism, hyperfunction of the adrenal cortex -hyperaldosteronism, hypercortisolism), or excessive intake of bases (such as $NaHCO_3$, antacids), which can occur due to inadvertent ingestion (e.g. in children) or iatrogenic causes (e.g. treatment of metabolic acidosis with excessive doses of bicarbonate).

The clinical picture depends on the extent of the pathological process leading to the alkalosis. Compensated and partially compensated metabolic alkalosis may be asymptomatic or present with minimal symptoms such as general weakness, fatigue, reduced muscle tone, and nausea. In cases of pronounced alkalosis, symptoms may include disorientation, nausea, vomiting, muscle tremors, slowed breathing, the occurrence of extrasystoles, and potentially hypotension.

Treatment of this disorder must focus on addressing the underlying cause: preventing vomiting, discontinuing diuretic use, reducing aldosterone and glucocorticoid secretion (or surgically removing hormonally active adrenal cortex tumors), etc. Symptomatic treatment aims to normalize circulation and microcirculation and correct blood volume. In severe cases, acidic solutions may be used, but with great caution - diluted, administered exclusively through a central venous catheter, and only via slow intravenous infusion due to potential complications (such as venous thrombosis)[23].

Mixed disorders

Mixed disorders involve the simultaneous presence of multiple primary disturbances. Typically, two primary disturbances are present, but occasionally a third may also be involved. Mixed disorders are very complex and challenging in terms of diagnosis and treatment[22, 23].

Respiratory acidosis and metabolic acidosis are the most common mixed disorders of acid-base balance. They occur in chronic obstructive pulmonary diseases, pulmonary edema, hypokalemic myopathy, and after cardiac arrest.

Respiratory alkalosis and metabolic alkalosis are the rarest but most severe acid-base balance disorders, as they have the highest mortality rate. They can occur during pregnancy (due to hyperventilation and vomiting) and are most commonly seen in patients undergoing controlled artificial ventilation who receive massive blood transfusions.

Respiratory acidosis and metabolic alkalosis can be observed in patients with chronic obstructive pulmonary disease which also have hypertension treated with diuretics. This disorder can be identified by high pCO_2 levels along with (very) high bicarbonate levels. The simultaneous presence of these two primary disorders is challenging to diagnose because each tends to shift the pH in the opposite direction. As a result, the pH value can be completely normal despite the presence of two severe disorders[1].

Respiratory alkalosis and metabolic acidosis occur in conditions where lactic acid hyperproduction is combined with excessive hyperventilation (e.g. severe liver damage, and salicylate poisoning). As with the previous example, the simultaneous presence of both acidosis (metabolic) and alkalosis (respiratory) can result in a normal or only slightly altered pH value[22, 23].

Electrolytes in acid-base disorders

Electrolytes play a crucial role in metabolic processes and in maintaining acid-base balance[24]. Their significance lies in maintaining osmotic pressure, distributing water in different body compartments, sustaining optimal pH levels, and contributing to the excitability of cardiac and skeletal muscles (particularly calcium). They also play a role in catalyzing enzymatic processes (as cofactors for many enzymatic systems). The ionic exchange of electrolytes between intracellular and extracellular spaces is also crucial for enhancing the blood's buffering capacity (especially potassium and chloride).

Disruption of electrolyte balance is also associated with acid-base disorders, primarily metabolic ones[23, 24]. In metabolic acidosis, there is a predominance of cations, while in metabolic alkalosis, there is a predominance of anions. However, there are no strict rules about which electrolytes are shifted and in which direction. The bicarbonate ion levels are always decreased in metabolic acidosis and increased in metabolic alkalosis. For other ions, there is no strict rule: Sodium is typically shifted in the same direction as bicarbonates (but deviations from normal values are less pronounced than for bicarbonates), while potassium is always decreased in metabolic alkalosis and often increased in metabolic acidosis, though it can also be normal or decreased. Chloride is always elevated in metabolic alkalosis

and usually decreased in metabolic acidosis, though it can also be elevated in hyperchloremic metabolic acidosis. The importance of electrolyte imbalance in acid-base disorders is particularly emphasized by Stewart's concept of acid-base balance[25, 26].

Treatment of electrolyte disorders is based on replenishing the deficient electrolytes, but this should be done cautiously, usually through slow intravenous infusions. However, if electrolytes are in excess, correcting these imbalances is generally more challenging and requires careful management to remove excess from the body. The fundamental rule in treating electrolyte imbalances is that both replacement and elimination must be performed very slowly (typically with infusion solutions), generally at a rate of about 0.5 mmol/h, regardless of the electrolyte or the specific disorder involved.

The anion gap (AG) is the difference between the sum of the major cations and the sum of the major anions in the plasma: $AG = (Na^+ + K^+) - (Cl^- + HCO^-_3) = 12 \pm 2$. The presence of an elevated anion gap indicates the presence of metabolic disorders affecting acid-base balance[13, 22]. The AG is typically elevated in metabolic acidosis due to the presence of excess acids and acidic metabolic products. To help remember the causes of metabolic acidosis with an increased AG, the mnemonic "MUDPILES" is used, which includes: Methanol; Uraemia (renal failure); Diabetic, alcoholic, or starvation ketoacidosis; Paracetamol, Propylene glycol, Paregoric; Inborn errors of metabolism, Iron, Ibuprofen, Isoniazid; Lactic acid; Ethylene glycol; Salicylates (aspirin)[13].

There are also, although less common, metabolic acidoses with a moderately elevated or normal anion gap. A helpful acronym to identify the causes of these types of metabolic acidosis is "DR. C": Diarrhoea; Renal tubular acidosis (types I, II, IV), or medication-induced (hypoaldosteronism); Chloride excess (hyperchloremic metabolic acidosis), which can occur due to excessive doses of normal saline during fluid resuscitation, hyperalimentation, or increased gastrointestinal reabsorption of chloride due to fistulae.

The Urinary Anion Gap (UAG) is also useful to calculate in certain situations, especially in children. The UAG is calculated by subtracting the chloride concentration in urine from the sum of sodium and potassium concentrations: $UAG = U_{N}^{+} + U_{K}^{+} - U_{Cl}^{-}$. The UAG can be either positive or negative due to the presence of unmeasured ions in the serum and excessive excretion of protons (cations), particularly ammonium. A positive UAG is seen in renal tubular acidosis, where there is an inability to acidify the urine despite systemic acidosis, meaning an inability to secrete ammonium[27].

Regarding electrolyte balance/imbalance, similar principles apply to both adult and pediatric populations. However, special caution should be taken when interpreting the Urinary Anion Gap (UAG) and Anion Gap (AG) in newborns during the first few weeks of life due to dynamic changes at that age. AG and UAG may be unreliable because of the immaturity of the renal tubular system. In newborns, low bicarbonate levels may be considered normal, with HCO_3 levels around 16 mmol/L being typical.

The Importance of blood gas analysis in the diagnosis and treatment of acid-base disorders

Arterial blood gas (ABG) analysis is the most critical diagnostic criterion for acid-base disorders. ABG tests alone are sufficient for diagnosing simple (uncomplicated) acid-base imbalances. However, in the case of mixed disorders, ABG remains essential but insufficient on its own for diagnosis. In such cases, additional evaluation is required, including medical history (or heteroanamnesis), clinical presentation, physical examination, biochemical analyses, urine analysis, and other diagnostic methods. When obtaining blood samples for gas analysis, it is crucial to always use the same type of blood (arterial, venous, or capillary), as the composition of these blood types differs in terms of all acid-base parameters[1, 22].

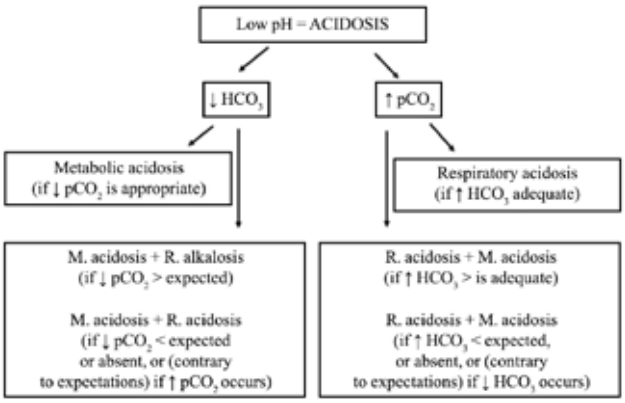
Arterial blood is the most suitable for gas analysis because, in addition to standard acid-base parameters, it allows the monitoring of oxygenation parameters, which are important for assessing lung oxygenation and calculating the alveolar-arterial oxygen difference. However, arterial puncture is an invasive, painful, and costly procedure that carries risks of complications such as bleeding, hematoma, infection, thrombosis, embolization distal to the puncture site, and, although very rarely, hand ischemia that may require amputation. Therefore, the procedure must be performed by a well-trained professional using proper technique.

Venous blood is rarely used in the evaluation of acid-base status. The values of acid-base parameters obtained from venous blood differ significantly from arterial values only in terms of oxygenation parameters (pO_2 and SAT), and there is no specific correlation between arterial and venous blood for these parameters. However, for acid-base balance parameters (pH, pCO_2, and HCO_3), there is a good correlation, with venous blood being slightly more acidic than arterial blood. Venous pH is typically 0.3-0.5 lower, bicarbonate levels are 1-3 mmol/L lower, and pCO_2 is about 6 mmHg higher compared to arterial values. Lactate levels are the same in both venous and arterial blood.

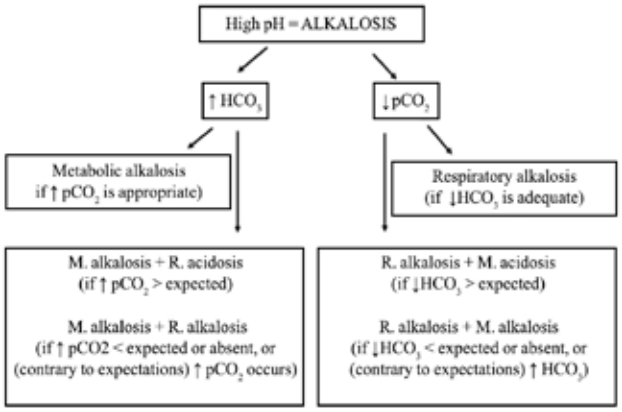
Capillary blood gas analysis is performed using special heparinized glass capillary tubes. This technique is most commonly used in infants, with the sample taken from the earlobe or the fingertip. In hypotensive patients, capillary blood should be avoided not only for gas analysis but also for other laboratory tests (such as glucose levels).

Interpreting gas analyses requires expertise and a thorough understanding of the topic, especially when dealing with complex acid-base disorders (Scheme 1 and 2)[1, 28].

Scheme 1. Interpretation of acidosis



Scheme 2. Interpretation of alcalosis



When analyzing acid-base status parameters, it's important to follow the recommended sequence of steps:

1. Check pH (determine if the condition is acidosis or alkalosis),

2. Determine the primary disorder (identify whether it is metabolic or respiratory),

3. Assess compensation (this helps determine the presence of mixed disorders),

4. Define the disorder and make a differential diagnosis.

When interpreting gas analyses, it's important to monitor the trend of parameters.

Conclusion

Acid-base imbalances are secondary manifestations of respiratory and metabolic disorders. Diagnosis is based on arterial blood gas analyses and monitoring the trend of acid-base parameters - pH, partial pressure of carbon dioxide, and bicarbonate levels. However, additional diagnostic methods are necessary, especially when dealing with mixed disorders. Acid-base disturbances, particularly metabolic ones, are often accompanied by electrolyte imbalances. Treatment of these disorders is complex. Along with causal therapy, which depends on the underlying cause of the disturbance, symptomatic treatment is crucial, primarily focused on improving perfusion and oxygenation.

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