Acid-Base Disturbance: A Comprehensive Flowchart-based Diagnostic Approach

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Abstract
Approaching acid-base disturbances is considered a medical problem among healthcare practitioners. Practicewise, system-based approach should be used to simplify the diagnosis and facilitate management. Flowcharts are considered education tools that can organize thoughts and standardize care. Using a flowchart approach make the practitioners solve any complex acid-base disturbance and facilitate the teaching of such topic.

Keywords: Acid-base; Metabolic; Respiratory; Acidosis; Alkalosis; Anion gap; Osmol gap; Flowchart

Introduction
The acid-base homeostasis is carefully balanced through a delicate series of interactions which involve organs such as the lungs and kidneys, as well as a complex system of buffers. Optimal body function and metabolic systems are kept in check by maintaining a normal pH (7.35-7.45) of arterial blood. Values less then <7.35 are termed acidemia, whereas values more than >7.45 are referred to as alkalemia. Any disorder that lowers the pH to <7.35 is called acidosis, while a disorder that increases the pH >7.45 is called alkalosis [1-3]. The Henderson-Hasselbalch equation describes the Regulation of the systemic pH by means of metabolic and respiratory components [4]:

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

The equation demonstrates that the pH is determined by bicarbonate ([HCO₃⁻] the metabolic component) and carbon dioxide (PCO₂ the respiratory component) ratio [4,5].

The main categories of acid base disturbances include: respiratory disorders (acidosis and alkalosis) and metabolic disorders (acidosis and alkalosis). Notably, respiratory disorders are expressed primarily as changes in PCO₂ while metabolic disorders are expressed primarily as changes in HCO₃⁻ [6,7].

Acid-base analysis can be a complicated and time-consuming process, not to mention a confusing topic among practicing physicians and clinical trainees. Diagnostic evaluation of acid-base disturbances, coupled with clinical data, can provide vital information to guide clinicians in making important management decisions in patient care. However if not properly applied, such an important ancillary test can become confusing and hinder health care providers especially in the critically ill.

Flowcharts are considered arbitrary illustrations, also known as a logical illustration, which is well schematized and text-redundant. These types of visual illustrations serve to facilitate the learning process and promote knowledge acquisition [8]. In this article, a simplified flowchart is demonstrated to provide a diagnostic frame-work for healthcare professionals when interpreting acid-base disturbances in the clinical setting and as a tool for medical education in a work-based environment.

Review
The flowchart developed consists of five basic steps. Depending on standard values employed in the hospital at which the healthcare provider is working, the acid-base result can be simply categorized as low, normal or high (Figure 1).

The 5 steps are as follow:
Step 1: Check the pH
Step 2: Check the PCO₂
Step 3: Check the HCO₃⁻ (if PCO₂ is normal)
Step 4: Calculate the compensation
Step 5: Calculate the anion gap (AG).

Explanation of the Five Steps
Step 1: Check the pH. If the result is low (<7.35), this means there is acidemia and if high (>7.45), then alkalemia is present. On the contrary, if the pH is normal (7.35-7.45), then the provider should proceed to the next step in order to determine the likelihood of a mixed acid-base disturbance.

Step 2: Check the PCO₂. If academia is present, then a low PCO₂ (<35 mmHg) indicates a metabolic acidosis, while a high PCO₂ (>45 mmHg) indicates respiratory acidosis. On the other hand if alkalemia is present, then a low PCO₂ indicates a respiratory alkalosis, as well as a metabolic alkalosis if PCO₂ is high. Alternatively, if a normal pH with low PCO₂ is encountered, then a mixed respiratory alkalosis and metabolic acidosis is likely. Although, a normal pH with a high PCO₂ means a mixed respiratory acidosis and metabolic alkalosis is present. In the event where the PCO₂ is within normal range (35-45 mmHg) [2], proceed to the next step.

Step 3: If the PCO₂ value is normal, then HCO₃⁻ should be checked. It is important to mention that even if an abnormal PCO₂ is encountered, the HCO₃⁻ is still useful in calculating the degree of compensation later on. In other words, checking HCO₃⁻ at this stage in the presence of a normal PCO₂ value is used to support the diagnosis of either acidemia or alkalemia.

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To calculate $\Delta$, use the rule of "4".

\[ \text{pH: } 7.35 - 7.45 \]
\[ \text{PCO}_2: 35-45 \text{ mmHg} \]
\[ \text{HCO}_3: 22-26 \text{ mEq/L} \]
\[ \text{AG: } 10-14 \text{ mEq/L} \]
\[ \text{Cl: } 98-106 \text{ mEq/L} \]

*Another formula can be used here (Winter’s formula): $(\text{PCO}_2 = 1.5 \times \text{HCO}_3 + 8 \pm 2)$

**Another formula can be used here: $(\text{PCO}_2 + 0.9 \times \text{HCO}_3 + 9 \pm 2)$

Serum triglycerides $>800$ mg/dL.

AG: anion gap; AGMA: anion gap metabolic acidosis; NAGMA: non-anion gap metabolic acidosis

Note: Bold boxes indicate mixed disturbances.

**Figure 1:** Acid-base disturbance flowchart.
If acidaemia with a normal PCO₂ and low HCO₃ (<22 mEq/L) is present, this would suggest metabolic acidosis. However, if the HCO₃ is within normal range (22 – 26 mEq/L) [9] or high (>26 mEq/L), then respiratory acidaemia and metabolic acidaemia are present. Although, if alkalemia with a normal PCO₂ and high HCO₃ is evident, this situation indicates metabolic acidaemia. Whereas a normal or low HCO₃ indicates both respiratory and metabolic acidaemia. However, if the pH and PCO₂ are normal, while the HCO₃ is low, then a mixed respiratory acidaemia and metabolic acidaemia is likely. Alternatively, a normal pH and PCO₂ with a high HCO₃ would indicate the presence of a mixed respiratory acidaemia and metabolic acidaemia. In case of normal values of pH, PCO₂ and HCO₃ then proceed to step 4 in the flowchart.

Step 4: Calculate the compensation (Table 1).

Metabolic acidaemia: The decrease in PCO₂ is approximately equal to 1.25 times the decrease in HCO₃ [10]. Therefore, the degree of compensation can be calculated using this formula:

\[
(\Delta \text{PCO}_2) = 1.25 \times \Delta \text{HCO}_3
\]

Winter's formula \((\text{PCO}_2 = 1.5(\text{HCO}_3) + 8 ± 2)\) can be used to determine the expected degree of compensation as well [11]. If the PCO₂ is more than expected, then respiratory acidaemia is likely. While if it is less than expected, then there is respiratory acidaemia as well.

Metabolic alkalosis: The increase in PCO₂ is approximately equal to 0.6 times the increase in HCO₃ [10]. Therefore, the degree of compensation can be estimated using the following formula:

\[
(\Delta \text{PCO}_2) = 0.6 \times \Delta \text{HCO}_3
\]

Alternatively, a different formula can be used \((\text{PCO}_2 = 0.9(\text{HCO}_3) + 9 ± 2)\) to calculate the degree of compensation in the presence of metabolic alkalosis [12].

If the calculated PCO₂ is more than expected, then a respiratory acidaemia is present. While a calculated PCO₂ that is less than expected suggests the presence of a respiratory acidaemia as well.

Respiratory acidaemia: This can either be defined as acute or chronic respiratory acidaemia. In acute respiratory acidaemia (2-3 days), there is 1 mEq/L increase in HCO₃ for every 10 mmHg increase in PCO₂ that is, a one to ten ratio (1:10). On the other hand, in chronic respiratory acidaemia (>3 days), there should be 4 mEq/L increase in HCO₃ for every 10 mmHg increase in PCO₂, meaning a four to ten ratio (4:10) [13].

Therefore, if the estimated change in HCO₃ and PCO₂ \((\Delta \text{HCO}_3/\Delta \text{PCO}_2)\) are determined, then three possible conclusions are likely: a value of 0.1 indicates acute respiratory acidaemia and a value of 0.4 suggests chronic respiratory acidaemia. However, a value between 0.1 – 0.4 would indicate acute on chronic respiratory acidaemia.

Alternatively, if the value is <0.1, then metabolic acidaemia is present, while if the estimated change is >0.4, then metabolic alkalosis is likely.

Respiratory alkalosis: In a similar manner, this can either be defined as acute or chronic respiratory alkalosis. In acute respiratory alkalosis (2-3 days), there is 2 mEq/L decrease in HCO₃ for every 10 mmHg decrease in PCO₂, that is, a two to ten ratio (2:10). On the contrary, in chronic respiratory alkalosis (>3 days), there will be a 5 mEq/L decrease in HCO₃ for every 10 mmHg decrease in PCO₂, meaning a five to ten ratio (5:10) [12].

Therefore, if the estimated change in HCO₃ and PCO₂ are determined \((\Delta \text{HCO}_3/\Delta \text{PCO}_2)\), then three possible conclusions are likely: a value of 0.2 which indicates acute respiratory alkalosis and a value of 0.5 would suggest chronic respiratory alkalosis. However, a value between 0.2-0.5 suggests an acute on chronic respiratory alkalosis. Alternatively, if the estimated change is <0.2, then there is also a metabolic acidaemia, while if the result is >0.5, a metabolic alkalosis exists as well.

Step 5: Calculate the anion gap. This step must be done regardless of the previous results and even if all parameters are normal. The anion gap can be calculated using this formula:

\[
\text{Na} - (\text{Cl} + \text{HCO}_3)
\]

High anion gap (>15 mEq/L): This would suggest the presence of a metabolic acidaemia regardless of prior estimations and means an anion gap metabolic acidaemia exists if acidaemia was already determined in the previous steps.

In this case, the delta gap \((\Delta \text{gap})\), or estimated degree of change anticipated in the anion gap should be calculated using this formula:

\[
(\text{AG} – 12) – (\Delta \text{HCO}_3)
\]

The normal range of the \(\Delta \text{gap}\) is \([-6) – (+6)] \ [14]. If the \(\Delta \text{gap}\) is ≤ -6, then this would indicate either one of the following: a mixed AGMA and NAGMA, or AGMA with chronic respiratory alkalosis and compensating hyperchloremic acidaemia. However if \(\Delta \text{gap}\) is ≥ +6, this would mean AGMA with metabolic alkalosis is likely [15].

In any patient with an AGMA, it is necessary to calculate an osmol gap which can help predict potentially life-threatening toxic alcohol ingestion.

The osmol gap can be determined as follows:

Osmol gap = measured osmolality – calculated osmolality

The calculated osmolality is easily estimated using this formula:

\[
\text{Calculated Osmolality} = 2(\text{Na}) + \text{Glucose/18} + \text{BUN/2.4} + \text{ETOH/4.6}
\]
When the measured osmolality differs by 10-15 mOsm/kg H2O from the calculated osmolality, the presence of an unmeasured substance should be considered [1,16]. However, it is important to mention that toxic alcohol ingestion cannot be excluded by a normal osmol gap level and needs to be carefully considered within the context of the patient presentation [17]. Causes of increased osmol gap (MMEGGLI) are listed below:

- Methanol
- Mannitol
- Ethanol
- Ethylene glycol
- Glycine
- Glycerol
- Lactate
- Isopropyl alcohol

Normal anion gap: If acidosis was determined in the previous steps, then a normal anion gap (10 – 14 mEq/L) [13] suggests normal anion gap metabolic acidosis (NAGMA). Consequently, there should be a 1 mEq/L increase in chloride (above the normal of 100), and 1 mEq/L decrease in HCO3 (±5). If the decrease in HCO3 is less than expected, then this would indicate both NAGMA and metabolic alkalosis [10].

Very low or negative anion gap: In this situation, careful consideration of an underlying additional metabolic cause should be examined, namely hypoalbuminemia, as the anion gap is affected by a low albumin level. In other words, with every 1 g/dl decrease in serum albumin, the anion gap will decrease by 2.5 mEq/L [18].

In the end, after going through the steps mentioned above and reviewing the possible causes of each condition (Table 2), the interpretation and subsequent correction of an acid-base problem should always be evaluated in context of the clinical data obtained from the patient’s history and physical exam findings [19,20].

Discussion

Although the evaluation of acid-base disturbances can be a daunting task, a simplified and yet organized approach with the clinical presentation in mind can help aid healthcare practitioners in making crucial management decisions that are vital to patient care. The flowchart, as mentioned previously, serves to help those responsible for patient care approach acid-base abnormalities in a more standardized fashion, creating a framework for further management strategies. It is important to mention that many explanations are available which address the issue of acid-base interpretation, but in the proposed flowchart, a more practical approach is emphasized, eliminating unnecessary steps which could hinder the overall evaluation.

As with any flowchart, there are certain restrictions to its use. Conditions in which a patient cannot compensate metabolic acidosis, such as being intubated, can hinder the application of the flowchart. In addition, the values in the flowchart are not fixed and may differ depending on laboratory standard reference values used. Another circumstance in which such a flowchart may not be accurate is in pregnant patients. Differences in values found during pregnancy are considered acceptable physiological changes as pregnant women tend to have a higher pH and lower PCO2 secondary to normal compensatory measures.

Table 2: Causes of acid-base disturbances.

<table>
<thead>
<tr>
<th>Metabolic acidosis</th>
<th>AGMA (MUDPILERS ACT)</th>
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<tbody>
<tr>
<td>Methanol intoxication</td>
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<td>Uremia</td>
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<tr>
<td>Diabetic ketoacidosis</td>
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<td>Paraldehyde</td>
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<td>Isoniazide</td>
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<td>Lactic acidosis</td>
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<td>Ethanol</td>
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<td>Rhabdomyolysis</td>
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<td>Salicylates</td>
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<tr>
<td>Alcoholic ketoacidosis</td>
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<tr>
<td>Cyanide, Carbon monoxide</td>
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<tr>
<td>Toluene</td>
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<td>NAGMA</td>
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<td>GI bicarbonate loss (diarrhea).</td>
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<tr>
<td>Renal tubular acidosis</td>
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<td>Carbonic anhydrase inhibitors.</td>
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<td>Ureteral diversions</td>
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<td>Rapid normal saline rehydration.</td>
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<tr>
<td>Respiratory acidosis</td>
<td>Central nervous system depression</td>
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<td>Pleural disease (pneumothorax, pleural effusion)</td>
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<td>Lung disease (ARDS, COPD, pulmonary edema, pneumonia)</td>
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<td>Airway obstruction</td>
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<td>Neuromuscular disorders (Guillain-Barré syndrome, myasthenia gravis)</td>
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<tr>
<td>Thoracic injury (flail chest)</td>
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<tr>
<td>Metabolic alkalosis</td>
<td>Volume contraction (vomiting, gastric suction, diuretics)</td>
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<td>Excess glucocorticoids or mineralocorticoids (eg, Cushing’s syndrome)</td>
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<td>Hypokalemia</td>
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<tr>
<td>Bartter’s syndrome</td>
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<tr>
<td>Alkalai ingestion/infusion</td>
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<tr>
<td>Post-respiratory acidosis</td>
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<tr>
<td>Respiratory alkalosis</td>
<td>CNS disease (Cerebrovascular accident)</td>
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<td>Toxins (Salicylates)</td>
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<td>High altitude</td>
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<td>Severe anemia</td>
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<td>Pregnancy</td>
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<tr>
<td>Lung disease/hypoxia (asthma, pneumonia, pulmonary embolism, pulmonary edema, pulmonary fibrosis)</td>
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<tr>
<td>Anxiety</td>
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<tr>
<td>Cirrhosis of the liver</td>
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<td>Septicemia</td>
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</table>

Future study in this regard should aim to further validate this conclusion, as well as to address the issue of the use of such a flowchart as an educational tool for educational purposes.

Conclusion

Acid-base disturbances are common problems and can be the result of numerous disease entities. Integrating the patient's clinical data which includes; history and physical examination findings, with a step-wise systematic flowchart approach, can aid healthcare providers in overcoming diagnostic dilemmas and subsequently take appropriate action. In addition, a flowchart-based approach facilitates the learning process and can be a useful teaching tool when addressing complex acid-base disturbances.

Authors’ Contributions

Alshehri AA reviewed the literature, designed the flowchart and wrote the
Acknowledgements

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Note: The application is available for free in the following link: https://itunes.apple.com/sa/app/abg-test/id887189397?mt=8

References