In metabolic acid base disorders primary changes occurs in plasma bicarbonate which causes metabolic acidosis or metabolic alkalosis. Reduction in bicarbonate concentration leads to low pH and causes metabolic acidosis, while rise in bicarbonate concentration leads to high pH and causes metabolic alkalosis.

**METABOLIC ACIDOSIS**

**Introduction:**

Metabolic acidosis is a disorder characterized by a low bicarbonate concentration and a low pH. The compensatory reduction in PCO2 due to hyperventilation minimizes the fall in pH. Metabolic acidosis can be produced by three major mechanisms:

1. Increased acid generation (ketoacidosis and lactic acidosis)
2. Loss of bicarbonate via the bowel (diarrhoea, small bowel fistulas) or via the kidneys (carbonic anhydrase inhibitors, renal tubular acidosis) and
3. Diminished renal acid excretion (renal failure or type 1 distal renal tubular acidosis).

**Etiology:**

On the basis of anion gap metabolic acidosis and its etiology can be divided into 2 groups:

1. ‘High anion gap metabolic acidosis’
2. ‘Normal anion gap metabolic acidosis’ (‘hyperchloraemic metabolic acidosis’)

**Clinical Features:**

Clinical presentation in metabolic acidosis is chiefly due to

A. Manifestations of underlying disorders
B. Manifestations of metabolic acidosis

Metabolic acidosis has profound effect on pulmonary, cardiovascular, neurological and musculo-skeletal system.

1. **Respiratory Effects:** Hyperventilation - Kussmaul respirations (deep, regular, sighing respiration) suggests presence of metabolic acidosis. This hyperventilation is more due to increase in tidal volume rather than to respiratory rate. Think of metabolic acidosis in patient with unexplained breathlessness.

2. **Cardiovascular Effects:** Severe academia (pH <7.2) can lead to tachycardia and increased susceptibility for cardiac arrhythmias due to sympathetic overactivity; decreased response to inotropes; and secondary hypotension. The reduced blood pressure in such patients is due to depressed myocardial contractility and arterial vasodilatation, both induced by low pH.

   Shift of potassium out of cells due to acidosis leads to hypokalaemia which can affect heart.

3. **Neurological Effects:** CNS function is depressed with headache, confusion, lethargy, and drowsiness to coma.

4. **Other Effects:** Severe acidosis can cause nonspecific symptoms such as anorexia, nausea, vomiting, and muscle weakness.

Chronic acidemia as with chronic renal failure can cause increased bone resorption leading to rickets in children and osteomalacia in adults.

**Compensation:**

The peripheral chemoreceptors sense the acidaemia and stimulate the respiratory centre. The resulting hyperventilation causes a compensatory decrease in arterial pCO2 which partly returns the arterial pH towards normal.

The increase in ventilation usually

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**Table 1: Causes of Metabolic Acidosis (Classified by Anion Gap)**

<table>
<thead>
<tr>
<th>Normal Anion-Gap Acidosis</th>
<th>High Anion-Gap Acidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Renal Causes</td>
<td>1. Ketoacidosis</td>
</tr>
<tr>
<td>• Renal tubular acidosis</td>
<td>• Diabetic ketoacidosis</td>
</tr>
<tr>
<td>• Carbonic anhydrase inhibitors</td>
<td>• Alcoholic ketoacidosis</td>
</tr>
<tr>
<td>2. GIT Causes</td>
<td>2. Lactic Acidosis</td>
</tr>
<tr>
<td>• Severe diarrhoea</td>
<td>3. Renal Failure</td>
</tr>
<tr>
<td>• Uretero-enterostomy</td>
<td>4. Toxins</td>
</tr>
<tr>
<td>• Small bowel fistula</td>
<td>• Ethylene glycol</td>
</tr>
<tr>
<td>3. Other Causes</td>
<td>• Methanol</td>
</tr>
<tr>
<td>• Recovery from ketoacidosis</td>
<td>• Salicylates</td>
</tr>
<tr>
<td>• Addition of HCl, NH4Cl</td>
<td></td>
</tr>
</tbody>
</table>

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Sanjay Pandya, Rajkot
starts within minutes and is usually well advanced at 2 hours of onset but maximal compensation may take 12 to 24 hours. The expected pCO2 at maximal compensation can be calculated from a simple Winter’s equation:

\[
\text{Expected pCO2} = 1.5 \times (\text{Actual [HCO}_3^-) + 8 \text{ mmHg}
\]

**Diagnosis:**

Proper history elicitation provides clues for the presence of metabolic acidosis and its etiology (eg diabetes, renal failure, severe diarrhoea).

Main aspects of assessment of metabolic acidosis are

- First: Diagnose metabolic acidosis
- Second: Diagnose the cause
- Third: Approach to metabolic acidosis

1. **Diagnosis of Metabolic Acidosis**

The only definitive way to diagnose metabolic acidosis is by simultaneous measurement of serum electrolytes and arterial blood gases.

Basic criteria for the diagnosis of a simple metabolic acidosis

- Low ‘bicarbonate’ and Low pH confirm diagnosis of a simple metabolic acidosis.

Other clues for the diagnosis of metabolic acidosis in simple and mixed disorders

- **Anion gap:** High (> 20) anion gap alert the clinician to the presence of a high anion gap metabolic acidosis. This can be extremely useful in sorting out complicated mixed disorders. (AG = Na – (Cl + HCO3) = 12 +/- 2).

- **Calculation for compensation:** It is important to diagnose metabolic acidosis in case of respiratory disorders. If actual value of HCO3 is lesser than calculated expected value in patient with respiratory disorder, it is suggestive of associated metabolic acidosis.

- **Delta Gap:** Compare the increase in anion gap with the fall in HCO3. In high anion gap metabolic acidosis it is difficult to diagnose coexisting: hidden normal anion gap metabolic acidosis and metabolic alkalosis. Delta ratio is a useful diagnostic tool particularly in such difficult situations.

In metabolic acidosis of increased anion gap type, the fall in HCO3 is generally equal to the rise in plasma anion gap. If the fall in HCO3 markedly exceeds the rise in anion gap, it is suggestive of coexisting hidden normal anion gap metabolic acidosis. If the rise in plasma anion gap substantially exceeds the fall in HCO3, there is coexisting hidden metabolic alkalosis.

2. **Diagnose the cause of metabolic acidosis**

Important investigations to establish etiological diagnosis of metabolic acidosis are:

- Urine tests for glucose and ketones
- Plasma glucose
- Urea and creatinine
- Ketone level
- Lactate level

3. **Approach to metabolic acidosis**

In assessing a patient with metabolic acidosis, important investigations to narrow down underlying etiological diagnosis are:

- **Anion gap:** Anion gap divides metabolic acidosis into two major subgroups (a) Normal anion gap and (b) High anion gap metabolic acidosis.

- **Urinary anion gap:** The urinary anion gap is defined as (UNa + UK) - UCl and is an indirect estimation of urinary ammonium excretion. The normal range is –10 to +10. Urinary anion gap divides causes of normal anion gap metabolic acidosis into two major subgroups: renal and gastrointestinal causes. If urinary anion gap is positive (10 mEq/L or more) it favours renal causes (e.g. renal tubular acidosis), while urinary anion gap is negative (-10 to -50 mEq/L) it suggests gastrointestinal causes (e.g. diarrhea) of normal anion gap metabolic acidosis.

- **Osmolar gap:** Normal osmolar gap is 10-15 (Osmolar gap = Measured osmolality – Calculated osmolality). Osmolar gap can narrow the differential diagnosis of high-AG metabolic acidosis. Osmolar gap is high in acidosis due to ethylene glycol, methanol, ethanol, isopropyl alcohol and uremia.

**TREATMENT OF METABOLIC ACIDOSIS**

Treatment of metabolic acidosis includes

1. **Specific management of underlying disorder**

As a rule treat underlying disorder meticulously. It is the most important measure and may be the only required treatment for mild to moderate acidosis. Different causes of acidosis have some different specific management principles.

2. **Alkali therapy**

Bicarbonate administration should be reserved only for selective patients with severe acidemia. Treatment of all acidaemia with NaHCO3 is not only unnecessary but can also be detrimental.

3. **Correct volume and electrolyte deficits**
ALKALI THERAPY IN METABOLIC ACIDOSIS

NaHCO₃ should be administered judiciously in selected patients of metabolic acidosis.

A. Why to treat metabolic acidosis?

Exogenous alkali is often required for the prompt reduction of severe acidemia and associated detrimental effects. Kussmaul's breathing, cardiac arrhythmias, hypotension, impaired response to pressure agents, hyperkalemia etc. are the life threatening complications.

B. Why alkali therapy is given in selected patients, and aimed for only partial correction?

Deleterious effect of NaHCO₃ therapy:
1. Hypernatraemia and volume overload especially in CHF or renal failure
2. CNS acidosis and hypercapnia
3. Hypokalemia and hypocalcaemia
4. Overshoot or rebound alkalosis in organic acidosis (i.e. ketoacidosis, lactic acidosis) due to conversion of accumulated organic anions (lactate, acetoacetate) into bicarbonate.

So to reduce possible complications only partial correction of severe acidemia is desirable.

C. Indications of alkali therapy:

Sodium bicarbonate solutions should NOT be given on a routine basis. Important Indications of alkali therapy are:
1. When blood pH drops below 7.1 to 7.2. Such a severe acidemia can be life threatening.
2. When HCO₃ falls below 10 meq/L. Low HCO₃ needs prompt treatment because
   a. Small, additional fall in HCO₃ can cause a large fatal drop in pH.
   b. Respiratory compensation requires heavy muscular work. Such compensatory hyperventilation for prolonged period can cause fatigue of respiratory muscles especially in elderly and debilitated patients. If fatigue occurs ventilation fails, PCO₂ rises and the patient develops superimposed respiratory acidosis.
3. Treatment of hyperkalemia with metabolic acidosis.

Treatment of acidemia with NaHCO₃ is clearly indicated only in certain circumstances and is probably deleterious in others. Anion gap is a major determinant for the same. Bicarbonate therapy is safe, useful and appropriate in hyperchloremic (normal AG) acidosis. However, in increased AG-organic metabolic acidosis it is controversial; it does not clearly improve mortality, and there are several possible risks.

D. What should be the goal of treatment?

In high AG metabolic acidosis bicarbonate should be started late (pH < 7.1) and discontinued early. NaHCO₃ should be administered judiciously with an aim to return blood pH to a safer level of about 7.15 and bicarbonate must be increased 10 meq/L. The goal is not to increase these values to normal. At this level dysrhythmias become less likely and cardiac contractility and responsiveness to catecholamines will be restored. Patient with acute normal AG acidosis (i.e. diarrhea) needs early bicarbonate therapy and goal of therapy is to maintain HC0₃ at 15mEq/L.

E. How much bicarbonate is needed to achieve the goal?

There is no simple prescription as several factors affect the acid base status (i.e. rate of acid production and bicarbonate loss, respiratory compensation, ECF volume status, and treatment of etiology).

Amount of HCO₃ required =

(Desired HCO₃ - Actual HCO₃) X 0.5 X body weight in kg

Except in cases of extreme acidemia, NaHCO₃ should be administered as an infusion over a period of several minutes to a few hours, rather than a bolus.

F. Precautions taken during NaHCO₃ administration

1. As NaHCO₃ is highly irritant, establish proper large I.V. line for infusion.
2. Avoid I.V. bolus of NaHCO₃, except in an emergency.
3. Correct hypokalemia, before correcting acidosis as intracellular K+ shifting can cause life-threatening hypokalemia.
4. NaHCO₃ should be given with caution in circulatory overload.
5. Never treat just acidosis, treat its etiology simultaneously.
6. Avoid mixing of calcium with NaHCO₃ to avoid precipitation.
7. Avoid mixing of NaHCO₃ with inotropes.

Alternative alkalinizing agents

Carbicarb: Experimentally promising, Carbicarb generates bicarbonate rather than CO₂ while buffering hydrogen ion (CO₃²⁻ + H⁺ = HCO₃⁻). However clinical experience with Carbicarb is limited, and is not commercially available for clinical use.

THAM: Another carbon dioxide consuming, sodium free solution buffer THAM, also limits CO₂ production and increases pH. However THAM is not documented to be clinically more...
**Metabolic Acid Base Disorders**

**Table 2 : Cause of Metabolic Alkalosis**

<table>
<thead>
<tr>
<th>Saline responsive (Urine Chloride &lt; 15 mEq/L)</th>
<th>SALINE RESISTANT (Urine Chloride &gt; 20mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECF Volume Depletion</td>
<td>Normal or Increased ECF Volume</td>
</tr>
<tr>
<td>Vomiting / Gastric suction</td>
<td>Hypertensive</td>
</tr>
<tr>
<td>Diuretic</td>
<td>Hyperaldosteronism</td>
</tr>
<tr>
<td>Hypercapnia correction</td>
<td>Cushing syndrome</td>
</tr>
<tr>
<td>No ECF Vol. Depletion</td>
<td>Normotensive</td>
</tr>
<tr>
<td>NaHCO3 infusion</td>
<td>Bartter’s syndrome</td>
</tr>
<tr>
<td>Multiple transfusion</td>
<td>Severe K+ depletion</td>
</tr>
</tbody>
</table>

Metabolic alkalosis is characterized by primary rise in the plasma bicarbonate HCO₃, causing high pH and compensatory increase in PCO₂ due to alveolar hypoventilation. High HCO₃ and high PCO₂ is also a feature of chronic respiratory acidosis, but the differentiating feature is low pH.

Pathogenesis:

There are two steps involved in the development of metabolic alkalosis: 1. Generation of metabolic alkalosis and 2. Maintenance of metabolic alkalosis

1. **Generation of metabolic alkalosis:** Mechanism of primary rise in the plasma HCO₃ can be one or more of the following:
   a. The loss of hydrogen ion from upper GI tract (vomiting) or urine (diuretics)
   b. Addition of alkali: Administration of HCO₃ or its precursors as citrate (multiple transfusion of citrated blood)
   c. Disproportionate loss of chloride: The loss of fluid with a high Cl/low HCO₃ concentration (condition referred to as contraction alkalosis)

2. **Maintenance of metabolic alkalosis:** Under normal circumstances the excess in bicarbonate generated by any of these processes is rapidly excreted in the urine. To maintain metabolic alkalosis, impairment in renal bicarbonate excretion is required. Three important factors maintaining metabolic alkalosis are
   a. Volume /chloride depletion
   b. Hypokalemia
   c. Aldosterone excess

**Etiological and differential diagnosis:**

Most important causes of metabolic alkalosis are loss of gastric fluid (i.e. vomiting), diuretics and hyperadrenal states. The most useful factors to determine etiology of metabolic alkalosis are ECF volume, blood pressure, urinary chloride concentration, and serum potassium. Urinary chloride concentration differentiates metabolic alkalosis in two major groups, saline responsive and saline resistant metabolic alkalosis (Table No. 2).

**Clinical features:**

Metabolic alkalosis rarely causes specific manifestations. Common features are:

1. CNS symptoms: Alkalaemia can increase neuromuscular excitability leading to paresthesia, light headache, and carpopedal spasm.
2. CVS symptoms: Hypotension and cardiac arrhythmias are common presentations.
3. Other symptoms: Weakness, muscle cramps and postural dizziness due to hypovolemia; muscle weakness and polyuria due to hypokalemia.
4. Respiratory abnormalities: In moderate to severe metabolic alkalosis, compensatory hypoventilation may cause hypoxia in the patient with preexisting lung disease.

**Diagnosis:**

- Increased HCO₃, pH and compensatory increase in PCO₂
- Expected increase in PCO₂ = 0.75 X Rise in HCO₃
- Serum potassium and chloride are usually low
- Urinary chloride estimation is very useful for etiological diagnosis

**TREATMENT OF METABOLIC ALKALOSIS**

A. Treatment of underlying cause

B. Saline (chloride/volume) responsive alkalosis

1. Aim of therapy is adequate correction of volume depletion, potassium depletion and chloride depletion.
2. I.V. isotonic saline with KCl or Isolyte-G are preferred
infusions to treat metabolic alkalosis due to vomiting, nasogastric suction, or diuretic therapy.

3. Treatment with H2 inhibitors or proton pump inhibitors will reduce gastric acid secretion and will minimize further H+ loss and, therefore, will prevent or reduce metabolic alkalosis due to vomiting or nasogastric suction.

4. Diuretics induced metabolic alkalosis in oedematous patients is difficult to treat where saline should be avoided. It needs dose reduction of diuretics, KCl supplementation, spironolactone or carbonic anhydrase inhibitors.

5. Avoid or discontinue exogenous source of alkali such as NaHCO3 infusions, Ringer’s lactate, acetate or citrate.

6. In rare cases with severe metabolic alkalosis diluted HCl can be given i.v. to lower the plasma HCO3 concentration. Although relatively diluted, 0.1 N hydrochloric acid (HCl) infusions are corrosive and can produce thrombophlebitis. So it must be infused slowly into large veins like subclavian or femoral veins.

7. Dialysis therapy may be helpful in occasional patients with severe metabolic alkalosis, volume overload, and renal failure.

C. Saline (chloride/volume) resistant metabolic acidosis

It needs specific treatment of underlying causes (surgical treatment of pituitary tumor or adrenal adenoma in Cush- ing’s syndrome) or supportive treatment such as spironolactone, correction of hypokalemia, and sodium restriction.

REFERENCES:


