Step-wise Approach to Acid-base Evaluation

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**Introduction:**

Acid-base abnormalities are commonly seen as renal emergencies in any intensive care units attached to nephrology department. A step-wise approach to acid-base evaluation is essential for their proper understanding and management.

**CASE HISTORY**

A 57 years old hindu female house-wife, a known case of diabetes for last 8 years was initially treated with Glipizide (5mg) daily. Currently she was on DBI-TD (Phenformin) 1 tab twice a day with meals. She was seen in Urology OPD for left loin pain with microscopic haematuria due to calculus in the middle third of ureter. Her renal functions were normal and she was advised IVU. Next day morning she developed loose motions 8-10 times, with nausea and vomiting. She got admitted to hospital at 2.45pm. with increasing breathlessness.

On examination her general condition was poor. She had tachycardia, acidotic breathing with BP systolic 80mm of Hg. She was dehydrated and pale. Systemic examination: Respiratory system bilateral equal air entry. No wheeze or crackles, CVS: heart sounds were normal, no murmur. PA: Mild distension with peristalsis present. CNS : patient conscious but drowsy, no focal neurological deficit.

Laboratory evaluation showed Hb: 12 gms/dl Total WBC 29500/cmm with 92% polymorphs and 8% lymphocytes. Urine : pH: Acidic, Sp. gravity 1025, protein +1, glucose and ketone absent, Leucocytes 10-15/HPF, erythrocytes occasional.

Arterial Blood gases showed -

\[
\begin{align*}
\text{PO}_2 & : 92.8 \text{ mm of Hg} \\
\text{PCO}_2 & : 22.5 \text{ mm of Hg} \\
\text{HCO}_3 & : 3.4 \text{ mEq/Lit} \\
\text{TCO}_2 & : 4.4 \\
\text{O}_2 \text{ Sat} & : 88.10\% \\
\end{align*}
\]

Renal profile showed -

\[
\begin{align*}
\text{Na}^+ & : 135 \text{ mEq/Lit} \\
\text{K}^+ & : 8.3 \text{ mEq/Lit} \\
\text{Cl}^- & : 90 \text{ mEq/Lit} \\
\text{HCO}_3^- & : 3.4 \text{ mEq/Lit} \\
\text{Blood urea} & : 115 \text{ mg/Lit} \\
\text{S. Cr.} & : 3.00 \text{ mg/Lit} \\
\text{Blood glucose} & : 412 \text{ mg/dl} \\
\end{align*}
\]

**CASE DISCUSSION**

Here is a patient with NIDDM - on phenformin, with renal calculus disease, who developed loose motions, vomiting, following IVU preparation. She was admitted with dehydration, hypotension and acidotic breathing.

*Que.* What acid base disturbances will you expect considering underlying condition?

*Ans.* 1 Metabolic acidosis due to (a)Lactic acidosis, (b) Diabetic keto-acidosis, (c) Diarrhoea with bicarbonate loss, (d)Renal tubular acidosis, (5) Renal Failure.

*Ques.* How will you evaluate this acid base disturbance (How will you interpret this ABG)?
TABLE I
Estimating the Hydrogen Ion Concentration From pH

\[ \Delta 0.3 \]

<table>
<thead>
<tr>
<th>pH</th>
<th>7.1</th>
<th>7.2</th>
<th>7.3</th>
<th>7.40</th>
<th>7.5</th>
<th>7.6</th>
<th>7.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>([H^+])</td>
<td>78</td>
<td>60</td>
<td>50</td>
<td>40</td>
<td>32</td>
<td>26</td>
<td>20</td>
</tr>
</tbody>
</table>

A change in pH of 0.3 will either double or halve the \([H^+]\).

**Within narrow limits 0.01 change in pH is equivalent to a change of 1 mEq/L of \([H^+]\)**

*Ans.* Step 1: Check validity

1) Using the Henderson equation it can be checked if the report of various parameters of the ABG report are compatible.

\[
H = 24 \times PCO_2 \\
HCO_3
\]

From table I & II pH 6.828 = H of approx. 160

From using parameters from ABG

\[
H = 24 \times 22.5 = 158.9 \\
3.4
\]

means this ABG is compatible or valid.

**Step 2: Obtain minimum diagnosis.**

a) Look at pH
   - Acidaemia
   - Alkalemia

b) Match with PCO\(_2\) or HCO\(_3\) :
   - Metabolic
   - Respiratory

Look at Table III

Patient's pH is decreased HCO\(_3\) is decreased and PCO\(_2\) is decreased means this report is compatible with metabolic acidosis.

**Step 3: Is it simple or Mixed acid base disturbance?**

Applying compensations = Table IV

Predicated PCO\(_2\) = \(3.4 \times 1.5 + (8 \pm 2)\)

11 - 15 mm of Hg

This patient's observed PCO\(_2\) is 22 mm of Hg which is much higher than predicted, suggesting mixed disorder i.e. metabolic acidosis with respiratory acidosis.

**Step 4: Determine the Anion Gap**

\[
\text{AG} = \text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-) \\
\text{Normal} = 12 \pm 4 = 8 \text{ to } 16
\]

\[
\text{AG} = 135 - (3.4 + 90) \\
= 135 - (93.4) \\
= 41.6
\]

This is high anion gap acidosis.

**Step 5: Is it triple disorder?**

*Ans.* Look for metabolic acidosis with delta (\(\Delta\)) Anion Gap.

a) \(\Delta\ AG = AG\) calculated - AG normal.

\[
\Delta\ AG = 41.6 - 12.0 \\
= 29.6
\]

b) \(\text{HCO}_3^- + \Delta\ AG = "Starting HCO}_3^-" \)

\[
3.4 + 29.6 = 33.0 \text{ mEq/L}
\]

Starting \(\text{HCO}_3^- = 33.00 \text{ mEq/L}\)

Abnormally high "starting HCO\(_3\)" indicates metabolic alkalosis. This suggests that patient had triple disorder - metabolic acidosis + respiratory acidosis + metabolic alkalosis.
Q. What are the causes of high-anion gap acidosis?
A. 1) Uremia
2) Lactic acidosis
3) Ketoacidosis
4) Intoxications: Salicylates, Ethylene glycol, ethanol and paraldehyde.

Q. What are possible causes of hyperkalemia in this patient?
A. 1) Renal Failure
2) Shift of K+ from intracellular to extracellular compartment due to acidosis.
3) Type IV RTA in diabetes hyporeninimic-hypoaldosteronism.

This patient’s serum lactate level done on admission was 35mg/dl (normal 5.7 to 22.00mg/dl). This suggest lactic acidosis. Patient had hypotension, hypokalaemia, dehydration and hyperglycemia. Patient received 100cc of 7.5% of HOC3 IV over 15 min. and 100cc in 500cc of saline, 100cc saline per hour as infusion. Inj. calcium gluconate 10cc 10% IV. slowly for emergency treatment of hyperkalaemia. Human actrapid insulin 10 units IV. stat and 6 units/hour. as infusion for hyperglycemia and antibiotics ceftazidime and ciprofloxacin. After stabilization of blood pressure, patient received haemodialysis with bicarbonate bath for 4 hours twice in two days. Patient recovered uneventfully and was discharged with normal renal function and acid-base status after 7 days. This patient had phenformin induced lactic acidosis which was complicated by diarrhoea vomiting and dehydration.

Q. What is mechanism by which phenformin can induce lactic acidosis?
A. The mechanism by which phenformin can induce lactic acidosis is probably related to disruption of mitochondrial membrane, impairing the transport of reducing equivalent at this site and thus inhibiting gluconeogenesis in liver and kidney. This leads to lactate under utilization and accumulation. The mortality rate of patients with this condition has been reported to be about 50 to 60 percent.

Q. What are causes of lactic Acidosis?
A. The causes of lactic Acidosis are:

1) Type A (Associated with hypoxia) poor tissue perfusion.
   1. Shock - Cardiogenic
   2. Acute hypoxaemia
   3. Carbon monoxide poisoning
   4. Severe anaemia
   5. Severe congestive cardiac failure.

II. Type B1 (Associated with systemic disorders)
   1. Diabetes Mellitus
   2. Liver failure
   3. Neoplastic diseases
   4. Sepsis
   5. Convulsions

Type B2 (Associated with drug and toxins)
   1. Biguanides (Phenformin and metformin), fructose, sorbitol, xylitol
   2. Ethanol, methanol
   3. Cyanide, nitroprusside
   4. Salicylates

Type B3 (Associated with inborn errors of metabolism)
   1. Glucose - 6 - phosphate deficiency
   2. Fructose - 6 diphosphate deficiency
   3. Pyruvate dehydrogenase and carboxylase deficiency
   4. Defective oxidative phosphorylation.

III. Miscellaneous:
   1. Ingestion of lactic acid milk
### TABLE III

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Primary event</th>
<th>Secondary compensation</th>
<th>$H$</th>
<th>$pH$</th>
<th>$PCO2$</th>
<th>$HCO3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic Acidosis</td>
<td>Acids or loss of bases</td>
<td>Hyperventilation</td>
<td>↑</td>
<td></td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td></td>
<td>of bases</td>
<td>by lung $\rightarrow$ $PCO2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic Alkalosis</td>
<td>Retention of bases, loss of acids</td>
<td>Hypoventilation</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td></td>
<td>by lung $\rightarrow$ $PCO2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Acidity</td>
<td>Inability of lung to excrete $CO2$</td>
<td>Kidney regeneration</td>
<td></td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td></td>
<td>of $HCO3$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Alkalosis</td>
<td>Increase excretion of $CO2$ by lung</td>
<td>Excretion of $HCO3$ by</td>
<td></td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kidney</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\downarrow$ decreased $\uparrow$ increased $\rightarrow$ Leads to

2. D-lactic acidosis in short bowel syndrome.

**Q.** What are options of treatment in lactic acidosis?

**A.**
1) Treatment of underlying cause.
2) Restoration of tissue perfusion and oxygenation
3) Alkalization
4) Insulin in phenformin induced lactic acidosis.
5) Dichloroacetate
6) Dialysis using high bicarbonate buffered dialysate.

**Q.** What is the goal of alkali therapy?

**A.** The goal of alkali therapy is to prevent / reverse the detrimental consequences of severe acidemia especially those affecting the cardiovascular system. To accomplish this goal, give sodium bicarbonate (7.5%) in amount that will return blood PH to a safer level of about 7.20.

**Q.** How to achieve a target of 7.20?

**A.** There is no simple prescription for reaching this target since several ongoing and at a time competing process can affect the acid base status (e.g. increased net lactic acid production, vomiting or renal failure). One can use Henderson equation or simple formula like: $HCO3$ in mEq = Body wt. in Kg x deficit x 0.5 (bicarbonate space taken as 50% of body wt.) Thus to raise plasma bicarbonate from 8 to 12 mEq per lit in 50 kg patient, one should administer $4 \times 50 \times 0.5$ i.e. 100mEq of sodium bicarbonate. Except in cases of extreme acidemia, sodium bicarbonate should be dispensed as an infusion over a period of several minutes to few hours. Follow-up monitoring of the patient's acid-base status will determine additional alkali requirement.

**Q.** What are risks of alkali therapy?

**A.**
1) Hypernatremia and hyperosmolality
2) Fluid overload
3) Hypokalemia
4) Hypocalcemia and precipitation of tetany
5) Overshoot alkalosis
6) Paradoxical worsening of intracellular acidosis.
7) Increase in haemoglobin oxygen affinity with decrease in oxygen delivery to all tissues.

**Q.** What is role of Dichloroacetate in lactic acidosis?

**A.** Dichloroacetate stimulates pyruvate kinase, thereby accelerating the oxidation of pyruvate to acetylcoenzyme A. Although the effect of dichloroacetate in experimental lactic acidosis were impressive and the initial clinical observations were promising; a control clinical study failed to demonstrate a substantial advantage of dichloroacetate over conventional management of lactic acidosis.
TABLE IV
APPROACH TO A PATIENT WITH ACID-BASE IMBALANCE

↓ HCO₃, ↓ PCO₂,
↓ Metabolic Acidosis
↓ (Predicted PCO₂ = 1.5(HCO₃) + 8 ± 2)
↓ Observed PCO₂
  Equal to Predicted
  Simple Metabolic Acidosis
  Metabolic Acidosis + Respiratory Alkalosis

↓ Observed PCO₂
  Lower than Predicted
  Metabolic Acidosis + Respiratory Alkalosis

↓ Observed PCO₂
  higher than Predicted
  Metabolic Acidosis + Respiratory Acidosis

↓ pH
↓ < 7.38
↓ Acidosis
↓ (Predicted HCO₃ = Acute PCO₂, 10 → ↑ HCO₃, 3-4 mEq/L
  Chronic PCO₂, 10 → ↑ HCO₃, 3-5 mEq/L)
↓ Alkalosis
↓ > 7.45
↓ Respiratory Acidosis
↓ Observed HCO₃
  Equal to Predicted
  Simple Respiratory Acidosis
  Respiratory Acidosis + Metabolic Alkalosis
↓ Observed HCO₃
  Lower than Predicted
  Respiratory + Metabolic Acidosis
↓ Observed HCO₃
  Higher than Predicted
  Respiratory Acidosis + Metabolic Alkalosis
TABLE V
PH > 7.45 ALKALOSIS

↑ HCO₃, ↑ PCO₂

Metabolic Acidosis

(Predicted PCO₂ = (0.9 x HCO₃) + 9 ± 2) or
(ΔPCO₂ = 0.6 x ΔHCO₃)

Observe PCO₂
Equal to Predicted
Simple Metabolic Acidosis

Observe PCO₂
Lower than Predicted
Metabolic Acidosis + Respiratory Alkalosis

Observe PCO₂
Higher than Predicted
Metabolic Acidosis + Respiratory Acidosis

↑ PCO₂, ↑ HCO₃

Respiratory Acidosis

(Predicted HCO₃ = Acute PCO₂ × 10 → ↑ HCO₃, mEq/L
Chronic↑PCO₂ mm Hg/10 → ↑ HCO₃ 5 mEq/L)

Observe HCO₃
Equal to Predicted
Simple

Observe HCO₃
Lower than Predicted
Respiratory + Metabolic Acidosis

Observe HCO₃
Higher than Predicted
Respiratory + Metabolic Alkalosis

REFERENCES