Acidosis and Alkalosis(4)

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Treatment: Metabolic Acidosis

- Treatment of metabolic acidosis with alkali should be reserved for severe acidemia except when the patient has no "potential HCO_3^-" in plasma.
- Potential [HCO_3^-] can be estimated from the increment (Δ) in the AG (Δ AG = patient's AG – 10).
- It must be determined if the acid anion in plasma is
  - metabolizable (i.e., - hydroxybutyrate, acetoacetate, and lactate)
  - or nonmetabolizable (anions that accumulate in chronic renal failure and after toxin ingestion).
- The latter requires return of renal function to replenish the [HCO_3^-] deficit, a slow and often unpredictable process.

Treatment: Metabolic Acidosis

- Consequently, patients with
  - a normal AG acidosis (hyperchloremic acidosis),
  - a slightly elevated AG (mixed hyperchloremic and AG acidosis),
  - or an AG attributable to a nonmetabolizable anion in the face of renal failure
- should receive alkali therapy,
  - either PO ($NaHCO_3$ or Shohl's solution)
  - or IV ($NaHCO_3$),
  - in an amount necessary to slowly increase the plasma [HCO_3^-] into the 20–22 mmol/L range

Treatment: Metabolic Acidosis

- Controversy exists, however, in regard to the use of alkali in patients with a pure AG acidosis owing to accumulation of a metabolizable organic acid anion (ketoacidosis or lactic acidosis).

- In general, severe acidosis (pH < 7.10) warrants the IV administration of 50–100 meq of $NaHCO_3$, over 30–45 min, during the initial 1–2 h of therapy.

- Provision of such modest quantities of alkali in this situation seems to provide an added measure of safety, but it is essential to monitor plasma electrolytes during the course of therapy, **because the [K+] may decline as pH rises**.

- **The goal is to increase the [HCO_3^-] to 10 meq/L and the pH to 7.20, not to increase these values to normal**.

APPROACH TO THE PATIENT: HIGH—ANION GAP ACIDOSES

- There are four principal causes of a high-AG acidosis:
- (1) lactic acidosis,
- (2) ketoacidosis,
- (3) ingested toxins, and
- (4) acute and chronic renal failure .

Initial screening to differentiate the high-AG acidosis should include

- (1) a probe of the history for evidence of drug and toxin ingestion and measurement of arterial blood gas to detect coexistent respiratory alkalosis (salicylates);
- (2) determination of whether diabetes mellitus is present (diabetic ketoacidosis);
- (3) a search for evidence of alcoholism or increased levels of þ-hydroxybutyrate (alcoholic ketoacidosis);
- (4) observation for clinical signs of uremia and determination of the blood urea nitrogen (BUN) and creatinine (uremic acidosis);
- (5) inspection of the urine for oxalate crystals (ethylene glycol); and
- (6) recognition of the numerous clinical settings in which lactate levels may be increased (hypotension, shock, cardiac failure, leukemia, cancer, and drug or toxin ingestion).

LACTIC ACIDOSIS

- An increase in plasma l-lactate may be
  - secondary to poor tissue perfusion (type A)
    - Circulatory insufficiency (shock, cardiac failure),
  - or to aerobic disorders (type B)
    - malignancies,
    - diabetes mellitus,
    - renal or hepatic failure,
    - thiamine deficiency,
  - D-Lactic acid acidosis, is due to formation of d-lactate by gut bacteria which may be associated with
    - Jejuno-ileal bypass,
    - short bowel syndrome,

Approach to the Patient: Lactic Acid Acidosis

- The underlying condition that disrupts lactate metabolism must first be corrected;
- tissue perfusion must be restored when inadequate.
- Vasoconstrictors should be avoided, if possible, because they may worsen tissue perfusion.
- Alkali therapy is generally advocated for acute, severe acidemia (pH < 7.15) to improve cardiac function and lactate use.
- However, $NaHCO_3$ therapy may paradoxically depress cardiac performance and exacerbate acidosis by enhancing lactate production (HCO_3^- stimulates phosphofructokinase).
- While the use of alkali in moderate lactic acidosis is controversial, *it is generally agreed that attempts to return the pH or [HCO_3^-] to normal by administration of exogenous $NaHCO_3$ are deleterious*.
- A reasonable approach is to infuse sufficient $NaHCO_3$ to raise the arterial pH to no more than **7.2** over 30–40 min.

Lactic Acidosis

- NaHCO3 therapy can cause
  - Fluid overload and hypertension because the amount required can be massive when accumulation of lactic acid is relentless.
  - Fluid administration is poorly tolerated because of central venoconstriction, especially in the oliguric patient.(PE)
- When the underlying cause of the lactic acidosis can be remedied, blood lactate will be converted to HCO_3^- and may result in an overshoot alkalosis.

KETOACIDOSIS Diabetic Ketoacidosis (DKA)

- This condition is caused by increased fatty acid metabolism and the accumulation of ketoacids (acetoacetate and – beta hydroxybutyrate).
- The relationship between the AG and HCO_3^- is typically 1:1 in DKA.
- It should be noted that, because insulin prevents production of ketones, bicarbonate therapy is rarely needed except with extreme acidemia (pH < 7.1), and then in only limited amounts.
- Patients with DKA are typically volume depleted and require fluid resuscitation with isotonic saline. VIP

DRUG- AND TOXIN-INDUCED ACIDOSIS
Salicylates

- Salicylate intoxication in adults usually causes
  - respiratory alkalosis or
  - a mixture of high-AG metabolic acidosis and respiratory alkalosis.
- Only a portion of the AG is due to salicylates.
- Lactic acid production is also often increased.

Treatment: Salicylate-Induced Acidosis

- Vigorous **gastric lavage with isotonic saline** (not $NaHCO_3$) should be initiated immediately, followed by administration of activated charcoal per NG tube.
- In the acidotic patient, to facilitate removal of salicylate, **intravenous $NaHCO_3$** is administered in amounts adequate
  - to alkalinize the urine and
  - to maintain urine output (urine pH > 7.5).
- While this form of therapy is straightforward in acidotic patients, a coexisting respiratory alkalosis may make this approach hazardous.
- Alkalemic patients should not receive $NaHCO_3$.
- **Acetazolamide** may be administered
  - in the face of alkalemia, when an alkaline diuresis cannot be achieved,
  - or to ameliorate volume overload associated with $NaHCO_3$ administration,
  - but this drug can cause systemic metabolic acidosis if HCO_3^- is not replaced.

Treatment: Salicylate-Induced Acidosis

- **Hypokalemia** should be anticipated with an alkaline diuresis and should be treated promptly and aggressively.
- **Glucose-containing fluids** should be administered because of the danger of hypoglycemia.
- Excessive insensible fluid losses may cause severe volume depletion and **hypernatremia**.
- If renal failure prevents rapid clearance of salicylate, **hemodialysis** can be performed against a bicarbonate dialysate.

Alcohols

- Under most physiologic conditions, sodium, urea, and glucose generate the osmotic pressure of blood.

- Plasma osmolality is calculated according to the following expression: Posm = 2Na+ + Glu + BUN (all
- in mmol/L), or, using conventional laboratory values in which glucose and BUN are expressed in
- milligrams per deciliter: Posm = 2Na+ + Glu/18 + BUN/2.8.

- The calculated and determined osmolality should agree within 10–15 mmol/kg H2O.

- When the measured osmolality exceeds the calculated osmolality by >15–20 mmol/kg H2O, one of two circumstances prevails.

  - Either the serum sodium is spuriously low, as with hyperlipidemia or hyperproteinemia (pseudohyponatremia),

  - or osmolytes other than sodium salts, glucose, or urea have accumulated in plasma.

Alcohols

- Examples of such osmolytes include
  - mannitol,
  - radiocontrast media,
  - ethanol,
  - isopropyl alcohol,
  - ethylene glycol,
  - propylene glycol,
  - methanol,
  - and acetone.

- In this situation, the difference between the calculated osmolality and the measured osmolality (**osmolar gap**) is proportional to the concentration of the unmeasured solute.

- With an appropriate clinical history and index of suspicion, identification of an osmolar gap is helpful in identifying the presence of **poison-associated AG acidosis**.

- Three alcohols may cause fatal intoxications:
  - ethylene glycol,
  - methanol,
  - and isopropyl alcohol.

- All cause an elevated osmolal gap, but only the first two cause a high-AG acidosis.

Ethylene Glycol

- Ingestion of ethylene glycol (commonly used in **antifreeze**) leads to a metabolic acidosis and severe damage to the CNS, heart, lungs, and kidneys.

- The increased AG and osmolar gap are attributable to ethylene glycol and its metabolites, oxalic acid, glycolic acid, and other organic acids.

- Diagnosis is facilitated by recognizing
  - **oxalate crystals** in the urine,
  - the presence of an **osmolar gap** in serum,
  - and a **high-AG acidosis**.

- Treatment should not be delayed while awaiting measurement of ethylene glycol levels in this setting.

Treatment: Ethylene Glycol—Induced Acidosis

- This includes the
  A. prompt institution of a saline or osmotic diuresis,
  B. thiamine and pyridoxine supplements,
  C. fomepizole or ethanol,
  D. and hemodialysis.

- **Fomepizole**, although expensive, is the agent of choice and offers the advantages of a predictable decline in ethylene glycol levels without excessive obtundation during ethyl alcohol infusion.

- **Hemodialysis** is indicated
  - when the arterial pH is <7.3,
  - or the osmolar gap exceeds 20 mOsm/kg.

Methanol

- The ingestion of methanol (wood alcohol) causes metabolic acidosis, and its metabolites formaldehyde and formic acid cause **severe optic nerve and CNS damage**.
- Lactic acid, ketoacids, and other unidentified organic acids may contribute to the acidosis.
- Due to its low molecular mass (32 Da), an osmolar gap is usually present.
- Treatment: Methanol-Induced Acidosis
  - This is similar to that for ethylene glycol intoxication,
    - including general supportive measures,
    - fomepizole,
    - and hemodialysis (as above).

Isopropyl Alcohol

- Ingested isopropanol is absorbed rapidly and may be fatal when as little as 150 mL of rubbing alcohol, solvent, or de-icer is consumed.

- A plasma level >400 mg/dL is life-threatening.

- Isopropyl alcohol differs from ethylene glycol and methanol in that
  - the parent compound, not the metabolites, causes toxicity,
  - and an **AG acidosis is not present because acetone is rapidly excreted**.

- Isopropanol alcohol toxicity is treated by
  - watchful waiting and supportive therapy;
  - IV fluids,
  - pressors,
  - ventilatory support if needed,
  - and occasionally hemodialysis for prolonged coma or levels >400 mg/dL.

RENAL FAILURE

- The hyperchloremic acidosis of moderate renal insufficiency is eventually converted to the high-AG acidosis of advanced renal failure.
- Poor filtration and reabsorption of organic anions contribute to the pathogenesis.
- As renal disease progresses, the number of functioning nephrons eventually becomes insufficient to keep pace with net acid production.
- Uremic acidosis is characterized, therefore, by a reduced rate of NH_4^+ production and excretion.
- **The acid retained in chronic renal disease is buffered by alkaline salts from bone.**
- Despite significant retention of acid (up to 20 mmol/d), the serum [HCO_3^-] does not decrease further, indicating participation of buffers outside the extracellular compartment.
- Chronic metabolic acidosis results in significant loss of bone mass due to reduction in bone calcium carbonate.
- Chronic acidosis also increases urinary calcium excretion, proportional to cumulative acid retention.

Treatment: Renal Failure

- Because of the association of renal failure acidosis with muscle catabolism and bone disease, both uremic acidosis and the hyperchloremic acidosis of renal failure require oral alkali replacement **to maintain the [HCO3-] between 20 and 24 mmol/L.**
- This can be accomplished with relatively modest amounts of alkali (1.0–1.5 mmol/kg body weight per day).
- Sodium citrate (Shohl's solution) or NaHCO3 tablets (650-mg tablets contain 7.8 meq) are equally effective alkalinizing salts.
- Citrate enhances the absorption of aluminum from the gastrointestinal tract and should never be given together with aluminum-containing antacids because of the risk of **aluminum intoxication**.
- When hyperkalemia is present, furosemide (60–80 mg/d) should be added.