Acid Base Disorders

ACOI 2017
Board Review
Case Studies
Disclosures

Nothing to declare
High Anion Gap Acidosis Case 1

40 yo gentleman presenting to ER with coma
labs: pH 7.14/ pCO2 15; Na 138/ K 6.4/ Cl 100/ HCO3 5; BS 100/ BUN 18/ S-Osm 340/ ETOH 0/ALB 4.0
funduscopic showed optic neuritis
How do you approach the differential of this acid base disorder?
Case 1

1. Acidosis or alkalosis - ACIDOSIS
2. Metabolic or respiratory - METABOLIC
3. Compensation appropriate - YES
5. Δ gap = Δ HCO3 - YES

Corrected anion gap = 2.5 X (4-albumin)
High Osmolar Gap Acidosis

when there is a high osmolar gap (>20) as well as a high anion gap the differential includes methanol, ethylene glycol, and propylene glycol intoxication.

no other gapped acidosis will increase the osmolar gap to this extent.

osmolar gap = s-osm (meas) - s-osm (calc)

ABNORMAl > 10 mosm, PATHOLOGIC > 20
High Osmolar Gap Acidosis

methanol leads to formic acidosis with CNS and optic toxicity (lethal dose > 15 ml)

ethylene glycol leads to glycolic and oxalic acidosis with renal and CNS toxicity with needle shaped crystals on UA (lethal dose 1-1.5 ml/kg)

treatment of both is ETOH or fomepizole to block alcohol dehydrogenase and/or dialysis

Propylene glycol usually occurs with lorazepam infusion (drug diluent)
Cost $3000 dollars/treatment
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Substance(s) Causing Toxicity</th>
<th>Clinical and Laboratory Abnormalities</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholic (ethanol) ketoacidosis</td>
<td>β-hydroxybutyric acidAcetoacetic acid</td>
<td>Metabolic acidosis</td>
<td>May be most frequent alcohol-related disorder; mortality low relative to other alcohols; rapidly reversible with fluid administration; increase in S0sm inconsistent</td>
</tr>
<tr>
<td>Methanol intoxication</td>
<td>Formic acidLactic acidKetones</td>
<td>Metabolic acidosis, hyperosmolality, retinal damage with blindness, putaminal damage with neurologic dysfunction</td>
<td>Less frequent than ethylene glycol; hyperosmolality and high anion gap acidosis can be present alone or together; mortality can be high if not treated quickly</td>
</tr>
<tr>
<td>Ethylene glycol intoxication</td>
<td>Glycolic acidCalcium oxalate</td>
<td>Myocardial and cerebral damage and renal failure; metabolic acidosis, hyperosmolality, hypocalemia</td>
<td>More frequent than methanol intoxication; important cause of intoxications in children; hyperosmolality and high anion gap acidosis can be present alone or together</td>
</tr>
<tr>
<td>Diethylene glycol intoxication</td>
<td>2-Hydroxyethoxyacetic acid</td>
<td>Neurological damage, renal failure, metabolic acidosis, hyperosmolality</td>
<td>Very high mortality possibly related to late recognition and treatment; most commonly results from ingestion in contaminated medications or commercial products; hyperosmolality may be less frequent than with other alcohols</td>
</tr>
<tr>
<td>Propylene glycol intoxication</td>
<td>Lactic acid</td>
<td>Metabolic acidosis, hyperosmolality</td>
<td>May be most frequent alcohol intoxication in ICU; minimal clinical abnormalities; stopping its administration is sufficient treatment in many cases</td>
</tr>
<tr>
<td>Isopropanol intoxication</td>
<td>Isopropanol</td>
<td>Coma, hypotension, hyperosmolality</td>
<td>Hyperosmolality without acidosis; positive nitroprusside reaction</td>
</tr>
</tbody>
</table>
Calcium oxalate monohydrate crystals  Urine sediment viewed under polarized light showing coarse, needle-shaped calcium oxalate monohydrate crystals. These crystals have a similar appearance to hippurate crystals. Courtesy of W Merrill Hicks, MD.
High Anion gap without High Osmolar Gap

**Uremia** - gap 20, GFR < 15ml/min

**Salicylates** - severe respiratory alkalosis, drug levels should always be checked – lactic acidosis

**Lactic acidosis** - diagnosis of exclusion A, B and D

**Pyroglutamic acidosis** – critical illness, females and acetaminophen use. Urine 5-oxyproline
High Anion gap without High Osmolar Gap

Ketoacidosis – abnormal glucagon/insulin ratio

- **diabetic** - acetone positive, BS > 200
- **alcoholic** - during abstinence and BS < 200, acetone may be negative
- **starvation** - diagnosis made by history, acetone may be negative

Beta hydroxybutyric acid is the major ketone body in all ketoacidosis
High Anion Gap Acidosis - Treatment

Treatment of organic acidosis is controversial with physiological data on both sides.

Clinically there is no evidence of improved patient survival.

Therefore, treatment with bicarbonate is reserved for a pH < 7.1 with refractory hypotension or arrhythmia.
High Anion Gap Acidosis - Summary

The presence of a high anion gap as well as a high osmolar gap leads to the diagnosis of intoxication with ethylene glycol or methanol.

The treatment of both are the same (ETOH, fomepizole and dialysis).

Optic neuritis is seen in methanol intoxication.

Propylene glycol occurs only in inpatients.
High Anion Gap Acidosis

Recent reports
Pyroglutamic Acidosis – Acquired Form

Pyroglutamic acid accumulates during times of glycine deficiency (critical illness, pregnancy and malnutrition) which will deplete glutathione.

Usually occurs in women (urine 5-oxyproline).

Glutathione is also depleted by acetaminophen use.

Syndrome – unexplained high anion gap acidosis, use of acetaminophen and change in mental status in the setting of critical illness.
Propylene Glycol Intoxication

Propylene glycol (PG) is a solvent used in IV medications (lorazepam)

Use of lorazepam infusions at > 0.1 mg/kg/hr may cause accumulation of PG leading to a high osmolar high anion gap acidosis (lactic acidosis)

Treat with fomiperazole
Propofol Infusion Syndrome

Occurs in critically ill patients
Myocardial failure, rhabdomyolysis, metabolic acidosis hypertriglycerideridemia and renal failure
Anion gap may be elevated (?? lactic acidosis)
Risk related to duration (> 48 h) and intensity of infusion
Infusion > 4mg/kg/hr
Diethylene Glycol

Substitute for glycerol by disreputable companies selling to developing nations
Causes CNS and PNS symptoms
Causes AKI
Generation of 2-hydroxyethylacetate (HEAA)
Drug induced Lactic Acidosis

Linezolid – usually occurs with prolonged therapy (5-6 weeks)

Metformin – occurs in patients with contraindications given the drug (liver disease, > Stage 3 CKD, CHF, critical illness, peri-operative state, and IV contrast)

HAART HIV – chronic use of many drugs have been implicated (didanosine, stavudin

Misc – mangosteen, clenbuteral
D-LACTIC ACIDOSIS

Recent reports of gapped metabolic acidosis in patients with short bowel syndrome
Occurs after ingesting a large CHO load
Confusion, gapped metabolic acidosis and negative lactate levels
Treatment – antibiotics and NPO
Case 2 - Hyperchloremic Metabolic Acidosis

an elderly man present with tachypnea, diarrhea and weakness

labs - pH 7.24/ pCO2 24; Na 140/ K 6.7/ Cl 120/ HCO3 10; urine pH 5.0/ U Na 40/ U K 20/ U Cl 50

How do you approach the differential of this acid base disorder?
Case 2

1. Acidosis or alkalosis - ACIDOSIS
2. Metabolic or respiratory - METABOLIC
3. Compensation appropriate - YES
4. Anion gap – NORMAL (10)
5. $\Delta$ gap = $\Delta$ HCO3 - YES
6. Osmolar gap - NONE
Urine Anion Gap

HCO₃ is either resorbed (prox) or regenerated (distal).
To regenerate HCO₃ - NH₄ is formed distally.
In an acidic urine \( \text{Na+K+NH₄} = \text{Cl} \).
NH₄ can not be measured therefore 
\( \text{Cl} > \text{Na+K} \) if NH₄ is present
NL DISTAL FX

If \( \text{Cl} \leq \text{Na+K} \) then distal urinary acidification is impaired (UAG abnormal).
Urine Anion Gap

the urine anion gap is useful in distinguishing disorders with normal ammonium excretion from those with abnormal excretion

Normal UAG – Proximal RTA or non renal acidosis (diarrhea etc.) \((Cl > Na + K)\)

Abnormal UAG - CKD (lack of NH4 production), distal RTA Type I and IV or aldosterone deficiency \((Cl \leq Na + K)\)
Hyperchloremic Metabolic Acidosis

Normal Urine NH4 (Cl > Na + K)

this is due to HCO3 loss with normal distal tubular function

**GI** - loss of HCO3 due to diarrhea, urinary diversion or pancreatic fistulae

**Renal** - proximal RTA (type 2) leads to renal HCO3 loss with normal distal regeneration. May be associated with other proximal defects (Fanconi’s), hypergammaglobulinemia, drugs (toluene, toperimate, zonisamide, tenofovir, azetazolamide) or multiple myeloma
Hyperchloremic Metabolic Acidosis

Abnormal NH4

**Classic Distal** - a defect in the proton pump leads to a U pH > 5.5 and acidosis (*Type 1*) (ampho B, HyperPTH, Sjogren’s, medullary sponge kidney)

**Hyperkalemic Distal** - a defect in the aldo sensitive collecting duct leads to acidosis and hyperkalemia with preserved renal acidification (*Type 4*) (obstruction, aldo resistance)

**NH3 Defect** - CKD leads to abnormal NH3 production with preserved urinary acidification (GFR < 30)
Impaired ammonium excretion in chronic renal failure. Urinary excretion of ammonium (NH4) in normals (solid line) and patients with chronic renal failure (dashed line) at baseline and after an acid load. The plasma bicarbonate concentration fell from 27 to 22 meq/L in normals and from 22 to 14 meq/L in CRF following the acid load. Ammonium excretion rose markedly in normal subjects, but was low at baseline and did not increase in the patients with CRF despite a greater degree of metabolic acidosis. (Data from Welbourne, T, Weber, M, Bank, N, J Clin Invest 1972; 51:1852.)
<table>
<thead>
<tr>
<th>Defect</th>
<th>U pH</th>
<th>UAG</th>
<th>K (serum)</th>
<th>GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal RTA (II)</td>
<td>&lt; 5</td>
<td>NI</td>
<td>Low</td>
<td>nl</td>
</tr>
<tr>
<td>Distal RTA (I)</td>
<td>&gt; 5</td>
<td>Low</td>
<td>Low</td>
<td>NI</td>
</tr>
<tr>
<td>Distal RTA (IV)</td>
<td>&lt; 5</td>
<td>Low</td>
<td>High</td>
<td>NI to low</td>
</tr>
<tr>
<td>CKD</td>
<td>&lt; 5</td>
<td>Low</td>
<td>NI to high</td>
<td>&lt; 30</td>
</tr>
</tbody>
</table>
Hyperchloremic Metabolic Acidosis
Summary
the patient had a hyperchloremic metabolic acidosis with an abnormal urine anion gap - no NH4 excretion despite acidosis.
urinary acidification was preserved eliminating Type 1 RTA (U pH < 6.5).
hyperkalemia was consistent with a Type 4 RTA.
Figure 4. Correlation between central venous and arterial blood gas values for pH
Figure 5. Correlation between central venous and arterial blood gas values for PCO2
Figure 6. Correlation between central venous and arterial blood gas values for HCO\textsubscript{3}
Arterial and central venous blood gas values ($n = 190$)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Arterial</th>
<th>Venous</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.37</td>
<td>7.34</td>
<td>.027</td>
</tr>
<tr>
<td>pCO2</td>
<td>38.4</td>
<td>42.3</td>
<td>-3.8</td>
</tr>
<tr>
<td>HCO3</td>
<td>22.4</td>
<td>23.2</td>
<td>-0.80</td>
</tr>
</tbody>
</table>
Venous Blood Gas

Results in same clinical outcomes as ABGs
Low CO widens the difference
Kaplan-Meier analysis to assess the probability of reaching ESRD for the two groups. Bicarbonate Supplementation Vs. Control

de Brito-Ashurst I et al. JASN 2009;20:2075-2084
A. Dietary protein intake on 4-month patient dietary records.

B. mPNA (g/kg) over 4 months.

C. Mid-arm muscle circumference (cm) over 4 months.

D. Plasma albumin (g/L) over 4 months.

E. Serum potassium (mmol/L) over 4 months.

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Metabolic Alkalosis

A normotensive ice skater presents with weakness
Labs : pH 7.54/ pCO2 45; Na 140/ K 2.8/ Cl 95/ HCO3 38; U Cl 50 U Na 70
Repeat U Cl < 20
How do you approach the differential of this acid base disorder?
Case 3

1. Acidosis or alkalosis - ALKALOSIS
2. Metabolic or respiratory - METABOLIC
3. Compensation appropriate – YES
4. Anion gap – NORMAL (7)
5. $\Delta$ gap = $\Delta$ HCO3 – YES
6. Osmolar gap - NONE
Metabolic Alkalosis

**Generation** - loss of HCl from kidneys or GI tract

**Maintenance** - because of prerenal state, hyperaldosteronism, and hypokalemia the body is unable to excrete HCO3

**Cl responsive** - when Cl is given it will shut off the maintenance phase and allow the kidney to excrete HCO3 by restoring volume and normalizing aldosterone production

**Cl unresponsive** - even when Cl is given it will not shut off aldosterone production
Cl Responsive Alkalosis

When NaCl and KCl are given they restore volume and replete K and Cl shutting off aldosterone production.

This plus the correction of the prerenal state allow the kidneys to excrete excess HCO3.

Treatment - administration of NaCl and KCl
Metabolic Alkalosis Cl Responsive

**Diuretic alkalosis** - U Cl < 20 after diuretics are stopped

**Chloridarrhea** - congenital or villous adenoma

**Posthypercapnic** - usually with chronic respiratory acidosis

**Gastric alkalosis** - hypokalemia due to renal K wasting

**Milk Alkali** – hypercalcemia, AKI, and alkalosis

**Cystic Fibrosis** – skin Cl loss
Milk Alkali Syndrome

Historically due antacids and large quantities of milk to treat PUD
Modern –large amount of Ca carbonate and Vit D leading to alkalosis, hypercalcemia and AKI
Calcium acts like a loop diuretic
Cl Unresponsive Alkalosis

This group of disorders is all have elevated aldosterone or defects in kidney. However, this is not volume (NaCl) responsive but rather volume independent. Administration of NaCl will not inhibit aldo nor will it correct the prerenal state. Treatment - diamox, HCl, spironolactone.
Metabolic Alkalosis Cl Unresponsive

**Primary aldo excess** - pharmacologic or primary aldosteronism

**Secondary aldo excess** - CHF, cirrhosis, RAS, ?Barter’s, hypomagnesemia

**Primary renal Cl loss** - Barter’s syndrome (furosemide pump), Gitelman’s syndrome (thiazide pump), Liddle’s syndrome and diuretics
Metabolic Alkalosis - Summary

Patient had a metabolic alkalosis with high urine Cl initially due to diuretic abuse.
Stopping the diuretic stopped the loss of urinary Cl.
She had an eating disorder – Diuretic abuse.
Metabolic Alkalosis Update

Permissive hypercapneic ventilation – current recommendations for ventilation in the setting of acute lung injury. Use of HCO3 for pH < 7.2. This may lead to posthypercapneic alkalosis

Performance enhancement – use of NaHCO3 pre exercise will enhance performance
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