Common Acid/Base Disorders: Causes and Consequences

P. Ryan Killian, PharmD, BCPS
Assistant Professor Clinical Pharmacy
UAMS College of Pharmacy
Critical Care Clinical Pharmacist
Baxter Regional Medical Center
Mountain Home, Arkansas
Disclosure

- I have no financial relationships to disclose

- I will discuss off label use and/or investigational use in my presentation
Goals

- Identify signs and symptoms of common acid/base disorders
- Identify etiology of common acid/base disorders
- Recommend safe and effective pharmacotherapy for common acid/base disorders
- Recommend accurate monitoring for parameters of recommended therapy
Objectives

- Review available pharmacotherapy for common acid/base disorders
- Discuss appropriate monitoring for parameters of recommended therapy
Acid-Base
Acid-Base

I didn't have anything useful to say so I made this pie chart.

Oooh!

It must be true because it's pie.

Oooh!

That worked too well.

I pledge my life and my fortune to the pie!
Acid-Base

100%
Acid-Base

I COULD HAVE E-MAILED YOU MY POWERPOINT DECK, AND YOU COULD HAVE READ IT IN FIVE MINUTES.

BUT I PREFER MAKING YOU SIT HERE FOR AN HOUR WHILE I READ EACH BULLET POINT IN SLOW MOTION.

POINT NUMBER ONE...

YANK THIS AS HARD AS YOU CAN.
Functions of pH

- Respiratory drive
- Electrolyte levels and availability
  - Potassium
  - Calcium
- Enzyme mediated reactions
- Receptor function
THE BASICS

ABG Normal Values:

- pH 7.35-7.45
- PCO₂ 35-45 mmHg
- PO₂ 80-100 mmHg
- HCO₃ 20-28 mEq/L
Acidemia

- high H+, low pH
- result of decreased HCO₃ or increased PCO2

Alkalemia

- low H+, high pH
- result of increased HCO₃ or decreased PCO2
Acidemia

Consequences:

- Cardiovascular
- Respiratory
- Metabolic
- Cerebral

Adrogué, H, et al. Management of Life-Threatening Acid-Base Disorders First of Two Parts. NEJM 1998; 338 (1): 26-34
Alkalemia

Consequences:

- Cardiovascular
- Respiratory
- Metabolic
- Cerebral

PRIMARY ACID-BASE DISTURBANCES

\[ \text{pH} \]

- pH < 7.4
  - ↑pCO₂ (>40 mmHg)
    - Respiratory Acidosis
  - ↓HCO₃ (<24 mEq/L)
    - Metabolic Acidosis

- pH > 7.4
  - ↓pCO₂ (<40 mmHg)
    - Respiratory Alkalosis
  - ↑HCO₃ (>24 mEq/L)
    - Metabolic Alkalosis

Respiratory acidosis

- Primary change: increased PCO2
- Increase in PCO2 due to alveolar hypoventilation or impairment of respiration
- Compensation: enhanced renal H+ secretion (occurs over 3-5 days) resulting in increased plasma HCO$_3^-$
Respiratory Acidosis

Respiratory center depression

- Drug-induced
  - Anesthetics
  - Barbituates
  - Benzodiazepines
  - Opiates
  - Parenteral or enteral nutrition (if excessive carbohydrates)
- Sleep apnea
- Obesity
- CNS disease (stroke, infection)
Respiratory Acidosis

- Neuromuscular disorders:
  - myasthenia gravis, Guillain-Barré syndrome, hypokalemia, myopathy

- Upper airway obstruction

- Pulmonary disease:
  - COPD
  - Asthma
  - Pulmonary edema
  - Pneumothorax
  - Pneumonia

- Mechanical ventilation
Respiratory Acidosis

Treatment

- Correct underlying disorders

- Hold or discontinue any respiratory depressant drugs

- Improve ventilation/respiration

- Reverse effects of respiratory depressants if present:
  - Opiates: Naloxone 0.4-2 mg SQ/IV/IM q 2-3 min prn (should see response within 10 minutes)
  - Benzodiazepines: Flumazenil 0.2 mg IV q1 min prn (max 5 doses per series, may repeat series at 20 minute intervals)
Respiratory Acidosis

- ABG every 2-5 hours initially
- ABG every 12-24 hours as pH improves
- Basic Metabolic Panel
- Respiratory status
Metabolic Acidosis

- Primary change: decreased $\text{HCO}_3^-$
- Decrease in plasma $\text{HCO}_3^-$ due to $\text{HCO}_3^-$ loss or accumulation of acid
- Compensation: fall in PCO2 resulting from alveolar hyperventilation
Diagnostics

Anion Gap

- $[\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])$
- Normal: 10-14
- High AG indicates overproduction of acid or presence of renal failure
- Low AG signifies hypoalbuminemia, halide intoxication, multiple myeloma
GAP Metabolic Acidosis

- Lactic Acidosis
- Ketoacidosis
- Endstage Renal Failure
- Methanol ingestion
- Ethylene Glycol ingestion
- Salicylates
GAP Metabolic Acidosis

**M**ethanol

**U**remic acid

**D**iabetic Ketoacidosis

**P**ropylene glycol

**I** (Infection, Iron, Isoniazid)

**L**actic acidosis

**E**thylene glycol

**S**alicylates
GAP Metabolic Acidosis

- Methanol
- Uremia
- Lactic Acidosis
- Ethylene glycol
- Propylene Glycol
- Aspirin
- Ketoacidosis
Lactic Acidosis

Risk factors

- hypoxia
  - hypotension
  - sepsis
  - cardiovascular shock
  - anemia
  - ischemia
  - diabetes

- leukemia

Lactic Acidosis

Drug Induced:

- APAP
- catecholamines
- NRTIs (ddI, d4T, ddC)
- Ibuprofen
- Iron overdose
- Isoniazid overdose
- Linezolid
- Metformin
- Neuroleptic malignant syndrome
- Nitroprusside (secondary to cyanide toxicity)

Lactic Acidosis

Drug Induced cont.

- Propylene glycol
- Propofol
- Salicylate overdose (mixed disorder: metabolic acidosis with respiratory alkalosis)
- Streptozocin
- Sorbitol and Xylitol
- Theophylline overdose

Lactic Acidosis

Treatment

- Optimize hemodynamics
  - MAP
  - HR
  - CVP

- O$_2$ delivery
  - Hb
  - Arterial O$_2$ saturation
  - Central venous O$_2$ saturation

Lactic Acidosis

**Treatment**
- pH correction
  - Sodium Bicarbonate
    - $V_d$ 50% body weight
  - THAM
    - Tromethamine (mL of 0.3 M solution) = body weight (kg) x base deficit (mEq/L) x 1.1
- HD
  - Continuous HD preferred, controlled studies needed

Acetaminophen Overdose

- Stage III
- Liver failure
- Decreased lactate clearance

**Treatment**
- Standard APAP overdose treatment and supportive care
Metformin

- **Mechanism**
  - Increased serum levels of metformin
  - Interference with oxidative phosphorylation
  - Suppression of hepatic gluconeogenesis

- **Treatment**
  - Supportive Care
  - Hemodialysis

- Contraindicated with renal dysfunction?

Propylene Glycol

- d-Lactate and l-lactate are normal products of metabolism

- May occur with or without oxidative phosphorylation impairment

Propylene Glycol

- diazepam
- digoxin
- esmolol
- etomidate
- hydralazine
- lorazepam
- MVI injection
- nitroglycerine
- pentobarbital
- phenobarbital
- phenytoin
- trimethoprim/sulfamethoxazole

Propylene Glycol

Treatment

- Discontinue drug
- Optimize hemodynamics
- \( \text{O}_2 \) delivery
- pH correction
Aspirin Overdose

- Interference with oxidative phosphorylation
- Hyperlactatemia is usually minimal
- Commonly presents as a mixed disorder
- Treatment:
  - Activated charcoal
  - Sodium bicarbonate to pH greater than 7.45
  - HD in patients with renal failure

Propofol Infusion Syndrome

- Interference with oxidative phosphorylation

- Lactic acidosis can be seen with prolonged high-dose infusion (>5 mcg/kg/min for > 48 h)

Treatment:
- Discontinuation
- Supportive Measures

Diabetic Ketoacidosis

- Diabetes Mellitus
  - Infection
  - Myocardial infarction
  - Gestational Diabetes
  - Initial presentation/insufficient insulin

- Breakdown of fatty acids/production of ketones

- Treatment
  - Insulin
  - Fluid/electrolytes
  - Sodium bicarbonate for pH < 7.1
Gap Metabolic Acidosis

Treatment

- Increased AG Acidosis: treat underlying disorder

- Renal Failure
  - Hold or discontinue any suspected drugs
  - Consider oral alkali therapy if no improvement in acidosis within 1-3 days or if symptomatic
Gap Metabolic Acidosis

**Monitoring**

- Hemodynamics
- $O_2$ delivery
- Basic Metabolic Panel
- Lactic Acid
Acid-Base

Uh-oh, my audience has fallen into a PowerPoint coma.

The only thing I can do now is put them in funny poses and leave.

It looks like his finger hit brain.
Non-Gap Metabolic Acidosis

Risk Factors

- Cirrhosis
- CHF
- Diabetes
- renal dysfunction
- ECF volume depletion
- cholestyramine + aldosterone antagonists
- cumulative dose of amphotericin B > 2-3 g
Non-Gap Metabolic Acidosis

- Renal $\text{HCO}_3^-$ loss
  - Carbonic Anhydrase Inhibitors
  - Renal Tubular Acidosis (RTA)
- Gastrointestinal $\text{HCO}_3^-$ loss
  - Diarrhea
  - Pancreatic, biliary or small bowel fistulas or drainage
  - Cholestyramine, laxative abuse
- Dilutional (rapid administration of IV fluids)
# Non-Gap Metabolic Acidosis

## Renal Tubular Acidosis (RTA)

<table>
<thead>
<tr>
<th>Proximal RTA (Type II)</th>
<th>Distal RTA (Type I)</th>
<th>Hyperkalemia-associated Distal RTA (Type IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetazolamide</td>
<td>Amphotericin B</td>
<td>Aldosterone deficiency or resistance</td>
</tr>
<tr>
<td>Sulfamethoxazole</td>
<td>Cisplatin</td>
<td>Heparin</td>
</tr>
<tr>
<td>Topiramate</td>
<td></td>
<td>ACEIs and ARBs</td>
</tr>
<tr>
<td>AMGs</td>
<td></td>
<td>Amiloride</td>
</tr>
<tr>
<td>Arginine</td>
<td></td>
<td>Lithium</td>
</tr>
<tr>
<td>Cidofovir</td>
<td></td>
<td>Trimethoprim</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td></td>
<td>Triamterene</td>
</tr>
<tr>
<td>Tetracycline (expired)</td>
<td></td>
<td>Foscarnet</td>
</tr>
<tr>
<td>Streptozotocin</td>
<td></td>
<td>Tacrolimus</td>
</tr>
</tbody>
</table>
Non-Gap Metabolic Acidosis

**Treatment**

pH < 7.1

- Discontinue any suspected drugs
- IV fluids
- Calculate bicarbonate deficit
  \[ (0.5L/kg \times \text{Weight (kg)} \times [\text{HCO}_3^-]_{\text{desired}} - [\text{HCO}_3^-]_{\text{observed}} \]
- Give 30-50% of calculated dose over 30 minutes to several hours
- Reassess need for additional replacement with ABG 30 minutes after end of infusion (target pH 7.15-7.20, plasma bicarbonate 8-10 mEq/L)
- Hemodialysis if renal failure present or insufficient response
Non-Gap Metabolic Acidosis

Treatment

- Proximal RTA
  - 10-25 mEq alkali/kg/24 hr in 3 divided doses
  - prefer potassium citrate or potassium/sodium citrate combination
Non-Gap Metabolic Acidosis

Treatment

- Distal RTA
  - 1-2 mEq alkali/kg/24 hr in 3 divided doses
  - sodium bicarbonate preferred
  - titrate to serum $\text{HCO}_3^-$ 20-24 mEq/L
Non-Gap Metabolic Acidosis

Treatment

- Hyperkalemic Distal RTA
  - reduce serum potassium using following order of intervention
    - Kayexylate 15-30 g po 1-4x/d ± dietary potassium restriction
  - Addition of furosemide 60-80 mg po daily
  - Addition of fludrocortisone 0.1-0.2 mg po daily (monitor for s/sx of fluid retention)
## Alkali Therapy

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>mEq Alkali</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shohl’s solution (sodium citrate/citric acid)</td>
<td>Bicitra</td>
<td>1 mEq Na/ml = 1 mEq bicarbonate/mL</td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
<td>Various</td>
<td>325 mg tablet = 3.9 mEq bicarbonate/tablet</td>
</tr>
<tr>
<td></td>
<td></td>
<td>650 mg tab = 7.8 mEq bicarbonate/tablet</td>
</tr>
<tr>
<td>Potassium citrate</td>
<td>Urocit-K</td>
<td>5 mEq citrate/tablet</td>
</tr>
<tr>
<td>Potassium bicarbonate/Potassium citrate</td>
<td>K-Lyte</td>
<td>25 mEq bicarbonate/tablet</td>
</tr>
<tr>
<td></td>
<td>K-Lyte DS</td>
<td>50 mEq bicarbonate/tablet</td>
</tr>
<tr>
<td>Potassium citrate/Citric acid</td>
<td>Polycitra-K</td>
<td>2 mEq K/ml = 2 mEq bicarbonate/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30 mEq bicarbonate/packet</td>
</tr>
<tr>
<td>Sodium citrate/potassium citrate/citric acid</td>
<td>Polycitra</td>
<td>1 mEq K/mL, 1 mEq Na/mL = 2 mEq bicarbonate/mL</td>
</tr>
</tbody>
</table>
Non-Gap Metabolic Acidosis

Treatment

- pH > 7.1
  - Discontinue any suspected drugs
  - IV fluids
  - Hemodialysis if renal failure or insufficient response
Non-Gap Metabolic Acidosis

**Monitoring**

- ABG
- Basic Metabolic Panel (especially K+)
- Ins and outs
Acid-Base
Respiratory Alkalosis

- Primary change: decreased PCO2
- Decreased PCO2 resulting from hyperventilation
- Compensation: small decrease in NH4+ excretion leading to decreased plasma HCO3 with plasma pH (usually) in normal range
Respiratory Alkalosis

- Hypoxemia:
  - Pulmonary disease
  - Anemia
  - Heart failure
  - High altitude

- Respiratory center stimulation

- Pulmonary disease: pneumonia, edema, emboli, interstitial fibrosis

- Mechanical hyperventilation
Respiratory Alkalosis

Respiratory center stimulation

- Drug-induced:
  - Salicylates (mixed metabolic acidosis and respiratory alkalosis)
  - Progesterone
  - Theophylline overdose
  - Catecholamines
- Pregnancy
- Psycogenic
- CNS disorders
- Liver failure
- Gram-negative sepsis

Respiratory Alkalosis

**Treatment**

- Identify and correct underlying disorders

- Hold or discontinue any suspected drugs

- Initiate oxygen therapy in patients with severe hypoxemia (pO2 < 40 mmHg) or change ventilator settings as needed

- Treat theophylline and salicylate overdoses appropriately

Respiratory Alkalosis

**Monitoring**

- Arterial Blood Gas
- Basic Metabolic Panel
- Respiratory status
Metabolic Alkalosis

- Primary change: increased HCO$_3$$_3$
- Increase in plasma HCO$_3$$_3$ due to H$^+$ loss or HCO$_3$$_3$ gain
- Compensation: rise in PCO2 resulting from decreased alveolar ventilation
Metabolic Alkalosis

- ECF volume contraction, normotension, hypokalemia, secondary hyperaldosteronism

- ECF volume expansion, hypertension, hypokalemia, mineralcorticoid excess
Metabolic Alkalosis

Volume Contraction

- Drug-induced
  - nonreabsorbable anions (ampicillin, nafcillin, penicillin, ticarcillin)
  - Diuretics
  - Gentamicin
  - Laxative abuse
  - Co-administration of sodium polystyrene sulfonate and AlOH or MagOH
Metabolic Alkalosis

Volume Contraction

- GI: vomiting, gastric aspiration, villous adenoma
- Edematous states
- Mg or K depletion
- Recovery from lactic acidosis or ketoacidosis
- Post-hypercapnic states
Metabolic Alkalosis

Volume Expansion

- Drug-induced:
  - Fludrocortisone
  - Glycyrrhizic acid (black licorice, chewing tobacco)
Metabolic Alkalosis

Volume Expansion

- Renal artery stenosis
- Hypertension
- Renin-secreting tumor
- Primary aldosterism
- Adrenal enzyme defects
- Cushing’s syndrome
- Liddle’s syndrome
Metabolic Alkalosis

Treatment

- Correct underlying disorder, hold or discontinue any suspected drugs
- If ECF volume contracted:
  - NS at appropriate rate for degree of volume depletion
- Replace potassium as needed
- If ECF volume overload:
  - If no renal insufficiency: Acetazolamide: 250-375 daily or BID
  - If ARF or ESRD: hemodialysis or peritoneal dialysis (reduced bicarbonate bath)
Metabolic Alkalosis

Treatment

- If severe alkalemia (pH > 7.7) with ECF volume excess or renal failure:
  - Calculate HCl dose required:
    - Males: \[0.5 \text{L/kg} \times \text{weight (kg)} \times [103 \text{ mEq/L-observed serum chloride}]\]
    - Females: \[0.6 \text{L/kg} \times \text{weight (kg)} \times [103 \text{ mEq/L-observed serum chloride}]\]
  - Administer dose HCl in D5W or NS via central vein at rate of 10-25 mEq/hr

- Hypoaldosteronism: spironolactone or amiloride
Metabolic Alkalosis

Monitoring

- Arterial Blood Gas
- Respiratory Status
- Basic Metabolic Panel
Conclusion

- Verify disorder
- Hold or discontinue any suspected drugs
- Supportive Care
- Correct pH if disorder severe
- Monitor
Questions

THAT’S MY PLAN. I’D LIKE TO THANK ALL OF YOU FOR YOUR UTTER APATHY.

THE END

A FEW OF YOU STAYED AWAKE, AND I THINK I GOT SOME ACCIDENTAL EYE CONTACT ONCE WHEN THE A.C. MADE A NOISE.

IN CONCLUSION, I HATE MY JOB, I HATE MY CO-WORKERS, AND I HOPE FERAL CATS EAT EVERY ONE OF YOU.

ARE YOU TAKING QUESTIONS?