Complex Acid-Base Disorders

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- Slides available by email
- rcentor@uab.edu
Objectives

- Develop a standardized approach to diagnosing acid-base disorders
- Differential dx of normal gap acidosis
- Differential dx of increased anion gap acidosis
- Understand all the
Case #1

- A 50-year-old man admitted with worsening ascites
- HIV with low CD4, Hep C cirrhosis
- H/O diarrhea (3-5 stools daily) on lactulose, also takes spironolactone, furosemide and propranolol

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<td>135</td>
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<td>12</td>
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Case #1

- Identify acid-base disorder:

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Laboratory data show that the patient actually has a respiratory alkalosis, secondary to pulmonary edema.

Note A-a gradient – room air ABG

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<td>pO₂</td>
<td>63</td>
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Morning Report guesses

- Type IV RTA secondary to spironolactone
- Diarrhea
- Distal RTA secondary to cirrhosis
Teaching Point #1

- You cannot diagnosis acid-base disorders without an ABG
Case #2

- A 38 year-old woman with progressive quadriparesis
- h/o joint pain, stiffness and Raynaud’s

Laboratory data:

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<td></td>
<td>137</td>
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<tr>
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<td>0.9</td>
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Case #2

- A 38 year-old woman with progressive quadriparesis
- h/o joint pain, stiffness and Raynaud’s

**Laboratory data:**

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Normal gap acidosis

- This patient has a gap of 10
- Remember to adjust “normal gap” for the patient’s albumin level
Expected anion gap

- Classic formula
  - 11 – (2.5*[4-serum albumin])
- UAB quick formula
  - Serum albumin * 3
The Differential Diagnosis of Normal Anion Gap Acidosis

- Bicarbonate wasting
- Incomplete buffering
Bicarbonate wasting

- Proximal RTA
  - Fanconi’s syndrome
  - Acetazolamide

- Diarrhea
Incomplete buffering

- CKD Stage III or IV
- Type IV RTA
  - ACE, ARB, aldosterone antagonists
- Distal RTA
  - Urine-bowel connections
Renal Ammonia Handling

1. Glutamine -> alpha ketoglutarate
   - GLN
   - HCO₃⁻
   - NH₄⁺
   - Na⁺
   - NH₃
   - NH₄⁺
   - H⁺

2. Increasing interstitial ammonia
   - Na⁺ K 2Cl cotransporter (loop diuretics)
   - NH₃
   - NH₄⁺
   - H⁺
   - NH₃ accumulation

3. Urine acidified
   - Medullary loop
K+ impact
Additional information in this case.

- Urine pH 7.5
Final Diagnosis

- Sjögren’s syndrome with distal RTA
- Distal RTA causing severe hypokalemia
Teaching Point #2

- Understanding physiology helps us diagnose normal gap acidosis
Case #3

- A 48-year-old female
- s/p ileostomy, now admitted for increased ileal output

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141   112   18   97
4.3   15   0.7
Case #3

- A 48-year-old female
- s/p ileostomy, now admitted for increased ileal output

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<tr>
<td>K⁺</td>
<td>18</td>
</tr>
<tr>
<td>Na⁺</td>
<td>97</td>
</tr>
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</table>
Acid Base Disturbance

- Low bicarbonate with an anion gap of 14
- Patient had a serum albumin of 5.7
- Thus, normal gap
- Presumed diagnosis
  - Normal gap acidosis secondary to increased ileal output
Diarrhea Causing Acidosis

- Diarrhea normally has a basic pH

- Or

- Stool is BASIC!
Diarrhea Causing Acidosis

- Diarrhea normally has a basic pH
- With profound diarrhea (at least 2-3 liters/day), patients may develop an acidosis
- This is more common in the presence of CKD
Analyzing this patient

- Urine sodium 10
- Urine potassium 47
- Urine chloride 72
- The urine anion gap differentiates renal and GI causes
Urine Anion Gap

- UAG = Urine ([Na\(^+\) + K\(^+\)] − [Cl\(^-\)])
- UAG = Urine ([Na\(^+\) + K\(^+\) + NH\(_4^+\)] − [Cl\(^-\)])
- If NH\(_4^+\) = 0
  - UAG + and renal cause
- If NH\(_4^+\) = large
  - UAG − and GI losses
Final thoughts

- Urine anion gap = 10 + 47 – 72 = -15
- Confirms patient has GI losses
Teaching Point #3

- Use the urine anion gap to differentiate between buffering problems and bicarbonate losses
Case #4

- 65-year-old man with h/o chronic constipation
- 3 weeks PTA - exploratory lap - no obstruction
- 5 days PTA - large volume watery diarrhea
### Laboratory values

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<tr>
<th>Parameter</th>
<th>Value 1</th>
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<th>Value 3</th>
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Case #4 - lab values

- Laboratory values

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</table>

![Table of laboratory values](table.png)
Case #4 solved

- The patient has a metabolic alkalosis
- Unexpected with large volume diarrhea
- Diarrhea secondary to lactulose
- Because lactulose acidifies the stool!
Teaching Point #4

- Lactulose works by acidifying the stool and thus could cause a metabolic alkalosis.
- All other diarrhea causes a metabolic acidosis
Case #5

- A 28-year-old man found non-responsive.
The patient did not respond to naloxone.

Laboratory data:

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<td>71</td>
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<td></td>
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<td>25</td>
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Axiom

- Gaps > 25 are usually explainable
- Aggressively seek an explanation when > 25
- Else use clinical judgment
The Differential Diagnosis of Elevated Anion Gap Metabolic Acidosis

- Ketoacidosis
- Ingestion
- Lactic acidosis
- Uremia
Differential Diagnosis of Ketoacidosis

- Diabetic ketoacidosis
- Alcoholic ketoacidosis (10% have negative ketones)
- Starvation ketosis (generally smaller gap)
Ingestions & increased anion gap

- Ethylene glycol and methanol
- Salicylates
- INH - rarely seen
- Iron
- Acetaminophen (oxoproline) - mostly in elderly malnourished women
Lactic acidosis

- Type A – dying tissue
- Type B – tumor secretion
- Medications
  - metformin
  - nucleoside reverse transcriptase inhibitor
  - linezolid
  - Propylene glycol
- D-lactic acidosis
Uremia

- Increased phosphate levels
More equations for complex problems

- Winter’s equation
- Delta gap
The Winter’s Equation

- \( pCO_2 = 1.5 \times (HCO_3^-) + 8 \pm 2 \)
- Uses calculated bicarb from ABG

Delta Gap

- Delta gap = (observed – expected) anion gap
- Here the observed anion gap is 25 and the expected anion gap is 12; therefore, the delta gap is 13
Use of the Delta Gap

- One adds the delta to the observed bicarbonate.
- This estimates bicarbonate prior to the elevated anion gap.
- In this case the patient started out with a normal bicarbonate of 27.
Further Evaluation

- Normal lactate
- Serum and urine ketones negative
- Measured osms = 354
- Calculated osms = 303
- Osm gap = 51
Calcium Oxalate Crystals
Final Diagnosis
Ethylene Glycol

- Classically treated with dialysis and IV alcohol
- New medication – fomepizole
- Often can obviate dialysis
- Now generic ~$500 per dose
Teaching Point #5

- Anion gaps of 25 or greater deserve a thorough evaluation
- The Winter’s equation helps us determine the appropriate respiratory response
- We can use the Delta gap to diagnose a “double” metabolic abnormality
**Case #6**

- 62-year-old man, alcoholic, CAP
- Transferred after 4 days (on respirator)
- On 10 mg/h of IV Ativan

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<tr>
<th>Parameter</th>
<th>Value</th>
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Case #6 - solution

- Increased anion gap - 25
- Respiratory acidosis
- Serum osms = 364
- D-lactic acid is markedly increased
Propylene glycol toxicity

- Propylene glycol is used to dissolve several IV drugs
- Lorazepam (Ativan) - most important
  - Diazepam
  - Trimethroprim-sulfamethoxazole
- Propylene glycol -> lactate and acetate
- Increased osm gap -> increased AG -> AKI
Teaching Point #6

- To avoid propylene glycol toxicity
  - Limit IV lorazepam to under 7 mg/hr
  - If you must go above
  - Check serum osms q12
  - When osm gap increases find another option
Case #7

- 41-year-old woman, s/p bariatric surgery (100# wt loss), presents “feeling drunk”
- Chronic diarrhea - short gut syndrome
- Mild gait instability

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<td>82</td>
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Double metabolic acidosis

- Anion gap = 17
- Expected gap = 8 \( (2.5 \times 3) \)
- Expected \( \text{HCO}_3^- = 8 + 9 = 17 \)

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<td>Alb</td>
<td>2.5</td>
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Case #7 double acidosis

- Winter’s equation:
  - $5 \times 1.5 = 8 + 8 = 16$
  - Use calc $\text{HCO}_3^-$, not measured $\text{HCO}_3^-$
  - Therefore no respiratory problem

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Case #7 - diagnosis

- Lactic acid 2.4 (0.7-2.1), neg salicylate
- normal osm gap
- D-Lactic acid 6.62 (0.0-0.25)
- Pt gave history of recurrent symptoms - always after a high carbohydrate meal
A 58-year-old schizophrenic male was brought to the hospital because of strange behavior after “overdose”

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Evaluating a mixed acid-base disorder

- Elevated anion gap = 35
- Delta Gap = 35 – 12 = 23
- Revealed bicarbonate = 23 + 14 = 37
- Anion gap acidosis & metabolic alkalosis
Continued Evaluation

- $pCO_2 = 15$ therefore, primary respiratory alkalosis
- triple disorder of an elevated anion gap acidosis, metabolic alkalosis, and a respiratory alkalosis
- Alka-seltzer overdose.
Teaching point #8

- A systematic approach to electrolyte panels and ABGs allow us to diagnose “triple” acid-base disorders
Metabolic acidosis - Rx

- Acute
  - Increased anion gap
  - Normal gap
- Chronic Kidney disease
Acute increased anion gap

- Experts differ on need for bicarbonate
- Most suggest definitely treating pH < 7.0
- No good data
- Do not treat if underlying disorder will correct quickly
Always treat

Goal bicarbonate 22

Estimate deficit:

- \((22 - \text{pt’s bicarb}) \times \text{TBW}\)
- \(\text{TBW} \sim 0.5 \text{ wt in kg}\)

Add bicarbonate \((50 \text{ mEq/amp})\) to D5/W = usually 2 or 3 amps
Recent studies suggest
- Correcting acidosis delays progression
- Perhaps giving bicarb prior to acidosis will also delay progression

- One tablet with each meal – 650 mg = 7.7 mEq
- Or 1 tbsp sodium citrate solution twice daily
Summary

- Reviewed importance of ABG
- Differential diagnosis of normal gap acidosis
- Differential diagnosis of increased gap acidosis
- Possibly expanded knowledge of iatrogenic acid base disorders
Slides available by email

rcentor@uab.edu


