What the HEC? H⁺ and Electrolyte Cases

Ogden Surgical-Medical Society Conference
May 18, 2017

Disclosures

- Tricida: consultant and travel
- Research support
  - VA CDA-2 IK2CX000537
  - NIH NIDDK u01 DK099933
  - Center on Aging, University of Utah

Objectives

Using a case-based approach, participants will
- Develop an approach to the diagnosis of acid-base and electrolyte disorders
- Analyze results from case studies to inform treatment decisions
Case 1 - warmup

- "Hey, we admitted a 24 F with generalized weakness. Her K was undetectable, bicarb was low and urine pH was high. We think she has an RTA. Can you see her? Thanks a lot!"

141 112 14
< 1.6 16 0.8
103

Do you agree with their diagnosis?

Case 1 - warmup

- Exam: 115/79, HR 79, generalized weakness, hypotonia

<table>
<thead>
<tr>
<th>ABG</th>
<th>Other Labs</th>
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<tbody>
<tr>
<td>pH 7.41</td>
<td>Ca 9.7</td>
</tr>
<tr>
<td>pCO₂ 29</td>
<td>Phos 1.5</td>
</tr>
<tr>
<td>pO₂ 94</td>
<td>Mg 2.0</td>
</tr>
<tr>
<td>HCO₃ 18</td>
<td>TSH 2.5</td>
</tr>
<tr>
<td>BE -5</td>
<td></td>
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</tbody>
</table>

What is the acid-base problem, if any?

Case 1 - warmup

- Problems
  1. Profound hypokalemia
  2. Normal anion gap metabolic acidosis

Urine pH 6.5

Looks like RTA, but K is awfully low. < 20 meq/L suggests renal retention

\[
\text{TTKG} = \frac{\left(\frac{K_u}{\text{Osm}_u}\right)}{\left(\frac{K_s}{\text{Osm}_s}\right)} = \frac{11.7}{290} = 0.004 \approx 0.4\%
\]

24 hour urine K = 17 meq
Case 1 - warmup

Problems
1. Profound hypokalemia
2. Normal anion gap metabolic acidosis

Non-renal potassium loss

K = 5
Cl = 68
UAG = -9

Non-renal cause of acidosis

What is the diagnosis?
1. RTA
2. Hypokalemic periodic paralysis
3. Laxative abuse/diarrhea

Urine pH 6.5? Hypokalemia increases NH₃ production, binds free urine H⁺

Case 2 – Type 1 twice?

“Hey, we admitted a 42 F with DKA. Her K was undetectable, bicarb was low and urine pH was high. Her DKA is resolved but her K and bicarb remain low. We think she has an RTA. Can you see her? Thanks a lot!”

Do you agree with their diagnosis?

ABGs consistently show primary metabolic acidosis

Urine pH ≥ 6.5 on three occasions

Problems
1. Hypokalemia
2. Normal anion gap metabolic acidosis

TTKG = \[
\begin{array}{c}
\frac{43}{290} \\
\frac{343}{2.9}
\end{array}
\]
= 12.5%

24 hour urine K = 118 meq
**Case 2 – Type 1 twice?**

**ABGs consistently show primary metabolic acidosis**

Urine pH ≥ 6.5 on three occasions

**Problems**

1. Hypokalemia  
2. Normal anion gap metabolic acidosis

**Renal potassium loss**

Urinary Na = 48  
K = 43  
Cl = 66

**UAG + 25**

**UAG may underestimate NH₄⁺ excretion if there are nonreabsorbable anions**

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**Case 2 – Type 1 twice?**

**ABGs consistently show primary metabolic acidosis**

Urine pH ≥ 6.5 on three occasions

**Problems**

1. Hypokalemia  
2. Normal anion gap metabolic acidosis

Urine Osmolar Gap  
Na = 92  
K = 37  
Cl = 124  
Osm = 343  
UUN = 201  
Gluc = neg

**Renal potassium loss**

**Urine osmolar gap** = measured urine osm - calculated urine osm

\[ = 2(Na + K) + UUN \text{ (mg/dL)} + \text{ glucose (mg/dL)} \]

\[ = 2.8 \]

**Urine osmolar gap = 343 - 2(92 + 37) \times 201 = 343 - 330 = 13 \text{ meq/L} \]

\[ = 2.8 \]

½ is NH₄⁺ ½ is anion

**UOG < 150 suggests impaired renal NH₄⁺ excretion**
**Case 2 – Type 1 twice?**

- **ABGs consistently show primary metabolic acidosis**
- **Urine pH ≥ 6.5 on three occasions**

**Problems**
1. Hypokalemia
2. Normal anion gap metabolic acidosis

- Renal potassium loss
- Impaired NH₃ excretion

- 24 hour urine citrate < 48 mg

**What is the diagnosis?**

Distal RTA

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**Case 3 – it’s not what you think**

- 21 F with hypokalemic periodic paralysis
- Admitted for generalized weakness

- **ABG**
  - pH: 7.30
  - pCO₂: 25
  - Exp: pCO₂ = 1.5[HCO₃] + 8

- **Urine Labs**
  - pH: 6
  - Na: 5
  - K: 4.7
  - Cl: 7.5

**Problems**
1. Hypokalemia
2. Normal anion gap metabolic acidosis

*What drug exposure causes this picture?*
**Toluene**

- Organic solvent
- Paint thinner, gasoline, glue, etc
- CNS-depressant
- Asphyxia
- Arrhythmia
- Seizures
- Severe cognitive impairment
- Effect in seconds, up to one hour
- Elimination
  - 20-45% lung
  - Renal

**Ways to inhale**

- Sniffing
- Huffing
- Bagging
Toluene

- Treatment
  - Restore volume
  - Replace K, phos as necessary
  - Several days may be required to clear toluene because of high lipid solubility
  - “RTA” resolves after stopping toluene

- Several days may be required to clear toluene because of high lipid solubility


- Mimic type 1 RTA
- Diagnosis challenging

Potential clues:
- Urine anion gap positive
- Urine osmolar gap > 300 mosm/kg

**Glue sniffer’s rash**

**Face paint sign**
86 F ESRD patient presents with tachypnea, confusion, ataxia. Had been taking Lactobacillus and mulberry juice for past three days.

<table>
<thead>
<tr>
<th>Hb</th>
<th>SB</th>
<th>SB</th>
<th>Temp</th>
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<td>103</td>
<td>37</td>
</tr>
<tr>
<td>4.4</td>
<td>&lt; 5</td>
<td>3.4</td>
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</tbody>
</table>


Case 4 - a short story

PMH
ESRD
Gastrojejunostomy

Brain CT: normal
Abd plain film: distended intestinal loops

Exam
180/96
42 breaths/min
36.8°


Case 4 - a short story

<table>
<thead>
<tr>
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<tbody>
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<td>pO₂</td>
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<td>HCO₃</td>
<td>4</td>
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<tr>
<td>BE</td>
<td>-24</td>
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</table>

Anion gap  = ≥ 10
Δ bicarb   = ≥ 19
Δ anion gap = 8 - 12

What A-B disorders does this patient have?
• High anion gap metabolic acidosis
• Normal anion gap metabolic acidosis
• Respiratory alkalosis

**Basic DDX of Anion Gap Metabolic Acidosis**

- Methanol
- Uremia
- Diabetic ketoacidosis
- Paraldehyde
- INH
- Lactic acidosis
- Ethylene glycol
- Salicylates

**Case 4 - a short story**

Anion gap tests normal, unusual for “uremia.”

Remember the history?

**PMH**
- ESRD
- Gastrojejunostomy

Mulberry juice with sugar + honey
Lactobacillus acidophilus
- Short bowel
  - Delivery of carbs to colon
  - Overgrowth of gram + anaerobes
    - Lactobacillus
  - Produce D-lactic acid
  - D-lactate not metabolized by L-LDH

**Case 4 - a short story**

- D-lactate: 6.8 mmol/L (NL < 0.1 mmol/L)
- High carbohydrate load with mulberry juice + Lactobacillus in ESRD patient

**D-lactic acidosis**

- L-Lactic acid: Reabsorbed in prox tubule
- D-Lactic acid: Poorly reabsorbed

  - Urinary Na & K loss: hypokalemia and volume depletion
  - Positive UAG w/ high UOG
  - Δ anion gap < Δ bicarbonate
  - Hyperchloremic acidosis

*Chang et al. Kidney Int 2010.*
D-lactic acidosis

1. Short bowel
   ▪ Jejunoileal bypass
   ▪ Small bowel resection or disease
   ▪ Low levels of D-lactate, increased with high carb diet
   ▪ Episodic acidosis

2. DKA
   ▪ D-lactic acid produced from acetone metabolism

3. Propylene glycol (IV lorazepam)
   ▪ Metabolized to D-lactic acid
   ▪ Osmolal gap + anion gap acidosis
   ▪ IV lorazepam

D-lactic acidosis

- Confusion, ataxia
- Infusion of D-lactic acid in normal subjects does not cause these symptoms
  ▪ Other colon-derived toxin
D-lactic acidosis

Therapy
- Bicarbonate replacement
- Metronidazole, neomycin, vancomycin
  - May precipitate D-lactic acidosis by causing overgrowth of lactobacilli
- Low carbohydrate diet
- DKA treatment
- Propylene glycol: stop infusion

D-lactic acidosis

- Tough diagnosis

Consider in
1. Short bowel patients
2. Long-term IV lorazepam use in the ICU

Case 5 – I’m not in shock

- 31 F seen in ER obtunded

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<tr>
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<tr>
<td>pO₂</td>
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<tr>
<td>HCO₃</td>
<td>7</td>
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<tr>
<td>BE</td>
<td>-19</td>
</tr>
<tr>
<td>Lactate</td>
<td>17</td>
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</table>

Acid-base disorders?
1. High anion gap metabolic acidosis due to lactic acid
2. Non-anion gap metabolic acidosis
3. Respiratory alkalosis (exp pCO₂ = 21)
Case 5 – I’m not in shock

- Patient not in shock; no other cause of lactic acidosis.
- Serum lactate 1.4 when ABG lactate was 8.
- Since lactate is normal, what is the cause of high anion gap acidosis?

Ethylene glycol: 380 mg/dL

Calc Osm = 2 (Na) + BUN (mg/dL) + glucose (mg/dL) + EG (mg/dL)

Calc Osm = 2(147) + 20 + 84 + 380 = 367

\[ \text{Meas Osm} = 378 \]

\[ \text{Osm gap} = 11 \]

Methanol: < 5
Case 5 – I’m not in shock

- Ethylene glycol poisoning with a “lactate gap”
- Diagnosis could have been easily missed
- Complete workup of high anion gap acidosis

Case 6 – last shot

- 40 M presents to ED seeking alcohol rehab. He has been “living on store bought alcohol.”
PMH
EtOH pancreatitis

Exam
Not intoxicated
115/78
115 beats/min

ABG
- pH 7.44
- pCO₂ 35
- pO₂ 79
- BE 0

Other Labs
- FENa 2.1%
- Serum Osm 348
- Calc Osm 288
- Tox Neg
- EtOH Neg

Cr 1.0
2 months before

Three main problems
- High anion gap = 23
- Acute renal failure
- Hyponatremia

Is this ethylene glycol or methanol poisoning?
- EG & Methanol undetectable

Osmolar gap
- No metabolic acidosis, but high anion gap
- Acute renal failure
Case 6 – last shot

- Dialysis considered
- Saline overnight
- Labs normalized
  - BUN/Cr 37/2.6

Presumptive diagnosis?

Isopropanol

- Cleaning agent
- Deicer
- Composes 70% of rubbing alcohol
- Upset stomach
- Hypotension
- Altered mentation, coma
  - Cross-tolerance in chronic alcoholism
- Toxicity caused by isopropanol (not metabolite)

Should you treat with fomepizole?
Isopropanol

Clues to the diagnosis

- Fruity breath
- Hyperosmolality (isopropanol & acetone)
- Absence of metabolic acidosis
- Ketones in blood/urine
  - Not b-hydroxybutyrate

Isopropanol

- Conflicting data regarding toxicities at certain blood levels

- Fatality rare: airway compromise, CV depression/shock

Isopropanol

Treatment

- Supportive
- HD
  - Hypotension requiring pressors
  - Respiratory failure
  - Coma
  - > 200 mg/dL (unclear)
Isopropanol

- Why the acute renal failure in this case?
  - Acetone $\rightarrow$ false elevation of serum Cr
    - However, BUN was high
  - Rhabdomyolysis can occur
    - CK normal in this patient
  - Unclear, but rapidly improved with volume

Case 7 - pyromaniac

- 40 M seen in clinic after pancreatitis

<table>
<thead>
<tr>
<th>141</th>
<th>103</th>
<th>29</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>3</td>
<td>29</td>
</tr>
<tr>
<td>23</td>
<td>9</td>
<td>1.7</td>
</tr>
</tbody>
</table>

40 yo M
Improving, but has poor appetite, malaise, abdominal pain.

PMH
Congenital NDI
Familial polycythemia
Gout
Rheumatoid arthritis
Obstructive uropathy
Recurrent pancreatitis
Case 7 - pyromaniac

Meds
- Probenecid
- Amiloride/HCTZ
- Doxazosin
- Nitrofurantoin
- Finasteride
- Colchicine
- Methotrexate
- Acetaminophen
- KCl
- MVI

Exam
97°
Lying 118/72, 114 beats/min
Standing 109/71, 133 beats/min
JVP 2cm below sternal angle
2+ edema

Exam

<table>
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<td>pCO₂</td>
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<td>pO₂</td>
<td>88</td>
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<tr>
<td>HCO₃⁻</td>
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</tr>
</tbody>
</table>

Anion gap = 29
Δ bicarb = 15
Δ anion gap = 17

What A-B disorders?
- High anion gap met. acidosis
- Respiratory alkalosis

More Labs
- Serum Osm 307
- Calc Osm 298
- Lactate 6.6
- Ketones Neg
- EtOH Neg
- Toxic alcohols Neg
- Acetaminophen 38 μg/mL
- Salicylate Neg

Acetaminophen metabolism

Depletion of glutathione
Gamma-glutamyl cycle

- Glutathione synthetase (GGT)
- G-glutamyl cysteine
- G-glutamyl cyclotransferase
- 5-oxoproline (pyroglutamic acid)
- Glutamate

Urine pyroglutamic acid (5-oxoproline)
- >40,000 ug/mg Cr (<70)

Case 7 - pyromaniac
Glutathione synthesis involves multiple enzymes:
- g-glutamyl cysteine synthetase
- g-glutamylcyclotransferase
- g-glutamyl amino acid
- glycin
- 5-oxoproline (pyroglutamic acid)
- 5-oxoprolinase

Anion gap metabolic acidosis:
- Since excreted in urine, UAG can be positive
- Treatment is largely supportive
  - Stop acetaminophen
  - Usually something else going on (sepsis, etc)
- HD used in case reports
- NAC, theoretically beneficial

Cute Dimples – Anion gap acidosis:
- Cyanide, citrate
- Uremia
- Toluene
- Ethylene glycol
- Diabetic ketoacidosis
- Isoniazid, Iron
- Methanol
- Pyroglutamic acid, propylene glycol, paraldehyde
- Lactic acid, D & L
- Ethanol Ketoacidosis
- Salicylates, starvation ketoacidosis, sodium thiosulfate
Case 8 – a sticky situation

“I have a 29 year old who came to the ER with burning pain in her feet. We were about to send her home, but then the labs came back. Thanks a lot!”

<table>
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<tr>
<th>141</th>
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<th>9</th>
<th>86</th>
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</thead>
<tbody>
<tr>
<td>3.9</td>
<td>25</td>
<td>0.6</td>
<td></td>
</tr>
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</table>

Case 8 – a sticky situation

“I have a 29 yo Hispanic woman who came to the ER with burning pain in her feet. We were about to send her home, but then her labs came back.”

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<td>0.6</td>
<td>Ca 9.7</td>
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AG

<table>
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<tr>
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<td>pCO2</td>
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<td>pO2</td>
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<td>HCO3</td>
<td>22</td>
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<tr>
<td>BE</td>
<td>-1</td>
</tr>
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</table>

Problems:
1. Hyperchloremia
2. Negative anion gap

Case 8 – a sticky situation

Normal tests
- CBC
- LFT
- P, Mg
- Manganese
- Heavy metals
- Ceruloplasmin
- CSF studies including VDRL, ACE
- Glutamic acid decarboxylase Ab
- Urine arsenic, thallium, mercury, iodine
- Hexosaminidase A
- Beta-HCG
- Ro & La Ab
- B12, folate
- ANA
- TSH
- UA + culture
- CK
Case 8 – a sticky situation

- 3 years later
  - Spastic diplegia
  - Distal neuropathic pain & sensory loss
  - Walks with stiff-legged antalgic gait using a clawed cane

Problems:
1. Hyperchloremia
2. Negative anion gap
3. Irreversible neurotoxicity

What is the diagnosis?

Bromism


BROMODERMA
Case 8 – a sticky situation

Serum bromide: 170 mg/dL (21 mmol/L)

Chloride by chlorometer: 107 & 109 meq/L

Bromide

- Anticonvulsant and sedative
- Substitutes for chloride in nerves/kidney

10-50 mg/dL: sedation

75-150mg/dL: therapeutic range for seizure control

>150mg/dL: debilitating toxicity

>300mg/dL: may be fatal

Social History:

- From Mexico, in US for 3 years
- No EtOH, tobacco, drugs
- Takes Maca (herbal supplement)
- Works in a furniture factory gluing styrofoam chair seats, does not use protective equipment
- Another worker started “walking funny.”
Case 8 – a sticky situation

What is Maca?

- 1-2 mg bromide/capsule

Maca Magic
Maca Magic Powder 1500 mg
1005 mg / 1.1 lbs Powder / Item #030012

*4.8 / 5

Over 35% OFF
$19.99

ADD TO CART

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Case 8 – a sticky situation

Occupational exposure?

- 1-bromopropane was a solvent used in the glue

- Other workers had elevated bromide levels

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Case 8 – a sticky situation

1-bromopropane

- Solvent introduced to replace chlorofluorocarbons
  - Banned because these deplete ozone

- Used in dry cleaning

- Carcinogen