ACID-BASE CONFERENCE

Lama Nazzal
Case

• 46 yo CM with PMHx of HTN, ETOH abuse presenting thirty minutes after ingesting 50 tablets of full strength ASA (16.25g).

• Patient ingested ASA while ETOH intoxicated in an attempt to have GI upset and stop drinking ETOH.

• Patient complained of tinnitus, no N/V, no diarrhea, no SOB.

• PMhx: HTN

• Social Hx: ETOH abuse 1L of hard liquor/day, Non smoker, no illicits.

• Home meds: lisinopril 5 mg daily
Case

- Vitals in ER: BP: 153/107, HR: 125, RR: 22, Temp: 98.5, Sat: 95% on RA

- Physical Exam:
  - GA: lethargic, responds appropriately to question
  - HEENT: nystagmus, alcoholic smell
  - Lungs: clear, GBAE
  - Heart: tachycardic, nl S1, S2 no murmurs
  - Abd: Soft, non tender, +BS
  - Ext: no edema

- In ER: patient given activated charcoal, librium 50mgx1 dose, valium 10mg IV x1 dose, 3 amps of IV bicarb then started on bicarb gtt at rate of 166ml/hr (3amps of bicarb in 1 L D5W)
Labs:

- WBC: 10.6, Hg: 15.7, Plts: 264
- Na: 141, K: 4.0, Cl: 109, CO2: 26, BUN: 15, Cr: 1.0, Ca: 9.6, Gluc: 113
- INR: 0.96
- 7.459/ 38.6/ 72.9/ 27/+3.4/95% lactate: 1.5
- Urine tox: +ve for benzos
- urinalysis: PH: 6, sp. gr.: 1.02, no ketones, RBCS or WBCs
- Acetaminophen level: <10,
- Salicylate: 54.8 mg/dl
- ETOH: 201 mmol/l
- CXR: normal
# Labs

<table>
<thead>
<tr>
<th>ASA level</th>
<th>PH</th>
<th>PCO2</th>
<th>PaO2</th>
<th>Bicarb</th>
<th>BE</th>
<th>% Sat</th>
<th>Lact acid</th>
<th>Ser CO2</th>
<th>Ser Na</th>
<th>Ser Cl</th>
<th>Ser K</th>
<th>Ser Cr</th>
</tr>
</thead>
<tbody>
<tr>
<td>46.4</td>
<td>7.47</td>
<td>37</td>
<td>64</td>
<td>27</td>
<td>+3.4</td>
<td>93%</td>
<td>1.5</td>
<td>29</td>
<td>142</td>
<td>109</td>
<td>3.7</td>
<td>1.0</td>
</tr>
<tr>
<td>39.5</td>
<td>7.49</td>
<td>37</td>
<td>80</td>
<td>28</td>
<td>+4.2</td>
<td>97%</td>
<td>1.8</td>
<td>32</td>
<td>144</td>
<td>108</td>
<td>3.5</td>
<td>0.9</td>
</tr>
<tr>
<td>34.1</td>
<td>7.51</td>
<td>38</td>
<td>92</td>
<td>30</td>
<td>+6.2</td>
<td>98%</td>
<td>0.9</td>
<td>33</td>
<td>139</td>
<td>102</td>
<td>3.5</td>
<td>0.9</td>
</tr>
<tr>
<td>32.5</td>
<td>7.48</td>
<td>43</td>
<td>113</td>
<td>31.1</td>
<td>+7.3</td>
<td>98%</td>
<td>0.9</td>
<td>34</td>
<td>140</td>
<td>102</td>
<td>3.3</td>
<td>0.8</td>
</tr>
<tr>
<td>24.1</td>
<td>7.44</td>
<td>47</td>
<td>80</td>
<td>32</td>
<td>+7.6</td>
<td>96%</td>
<td>1.4</td>
<td>34</td>
<td>138</td>
<td>101</td>
<td>3.2</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Urine PH: 7.5-8
Case

• Inpatient Meds: Folic acid, thiamine, KCl, MgSO4, Lisinopril, nexium, valium, bicarb gtt 166ml/hr

• After stopping bicarb gtt:

• Na: 137, K: 4.2, Cl:104, CO2: 28, BUN:8, Cr:0.7

• Urine output: 2450ml/24hrs

• Patient transferred to regular floor and discharged home with a follow up in medicine clinic.
ASA OVERDOSE
History

- The salicylates originally were derived from salicin, the active ingredient in willow bark, which Hippocrates used 2500 years ago for treating pain and fever.

- Salicylates also occur naturally in many plants such as strawberries, almonds, and tomatoes.
Mechanism of action

- Interferes with aerobic metabolism by means of uncoupling of mitochondrial oxidative phosphorylation.

- Interruption of a series of enzyme-mediated mitochondrial functions and increased anaerobic metabolism with cellular conversion of pyruvate to lactate and rapid development of lactic acidosis

- The inefficiency of anaerobic metabolism results in less energy being used to create ATP and release of the energy created during the metabolism of glucose in the electron transport chain as heat, so salicylate poisoned patients may become febrile
Mechanism of action

• The presence of acetasalicylic acid or salicylate molecules probably contributes little to the acidotic state

• Interference with oxidative phosphorylation causes glycogen depletion, gluconeogenesis, and catabolism of proteins and free fatty acids, the end result being low serum glucose levels and central nervous system (CNS) hypoglycemia relative to serum glucose levels
ASA metabolism:

• Salicylic acid (HS) is a weak acid: \( \text{H}^+ + \text{sal}^- \leftrightarrow \text{HS} \)
• \( \text{pH} = 3.0 + \log \left[ \text{sal}^- / [\text{HS}] \right] \) \( \text{pKa: 3} \)
• Uncharged molecules (HS), unlike charged molecules (sal-), can easily move across cellular barriers, including the blood-brain barrier and the epithelium of the renal tubule.
• In an acidic environment like the stomach, more of the drug will be absorbed compared with tissues at a higher pH
• Salicylates also are absorbed readily in the unionized form from the small intestine in therapeutic doses
• Aspirin is thought to cause spasm of the pyloric sphincter
• Salicylate is conjugated with glycine in the liver
• A small amount of aspirin is excreted unchanged in the urine
ASA poisoning symptoms:

• In mild or early poisoning burning in the mouth, lethargy, nausea, vomiting, tinnitus, or dizziness can occur.

• In moderate poisoning all of the above plus tachypnea, hyperpyrexia, sweating, dehydration, loss of coordination, and restlessness, can occur.

• In severe poisoning hallucinations, stupor, convulsions, cerebral edema, oliguria, renal failure, cardiovascular failure, and coma may be seen together with metabolic acidosis.
Clinical presentation:

- **Tinnitus:** it is thought to be secondary to interference with chloride channels in the cochlear hair cells that transmit sound waves

- **GI irritation:** Aspirin, especially enteric-coated formulations, are known to develop concretions and bezoars in the stomach and act as a direct GI irritant leading to nausea, vomiting, and abdominal pain

- **Postmortem examination:** myocardial necrosis suggestive of toxic myocarditis, pulmonary congestion, hemorrhagic gastritis with unabsorbed salicylate and GI ulceration, cerebral edema, and paratonia (extreme muscle rigidity).
Salicylate level

- Should be interpreted in the context of acuity of exposure, clinical condition and serum PH.
- Done nomogram does not predict severity of intoxication.

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**Table 3 | Data from Ontario showing serum salicylate concentrations in selected patients**

<table>
<thead>
<tr>
<th>Category</th>
<th>Total number in category</th>
<th>Number of patients who underwent premortem testing</th>
<th>Mean premortem salicylate concentrations (mg/100 ml)</th>
<th>Number of patients who underwent postmortem testing</th>
<th>Mean postmortem salicylate concentrations (mg/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death prior to medical intervention</td>
<td>16</td>
<td>10</td>
<td>80 (range 34–137)</td>
<td>16</td>
<td>51 (range 17–101)</td>
</tr>
<tr>
<td>Presented with coma</td>
<td>11</td>
<td>10</td>
<td></td>
<td>2</td>
<td>68 and 33</td>
</tr>
<tr>
<td>Presented in ‘alert status’</td>
<td>23</td>
<td>7</td>
<td>97 (range 61–193)</td>
<td>12</td>
<td>66 (range 36–130)</td>
</tr>
</tbody>
</table>
Chronic Salicylate poisoning

- Occurs with lower serum concentrations.
- Does not necessarily require a long-term exposure
- The tissue burden is high and at near steady state
- In acute poisoning the tissue burden is low and/or rising.
Acid/Base disturbances: Resp Alkalosis

- Salicylate toxicity initially creates a pure respiratory alkalosis because of direct stimulatory effects on the respiratory centers of the cerebral medulla.

- Patients may hyperventilate with a normal respiratory rate by increasing tidal volume

- Decrease PCO₂, increased PH and slightly decreased levels of serum HCO₃
Acid/Base disturbances: Mixed disorders

• In toxicity, ASA is incorporated into the mitochondria, uncoupling oxidative phosphorylation, lactic acid accumulates in the serum.

• Hyperventilation is a true compensatory mechanism in addition to the byproduct of central medullary stimulation.

• Resulting in decrease in the pCO2, marked decline in HCO3 and a decrease in serum pH.
Acid/Base disturbances: Metabolic acidosis

- As the ability to compensate for the acidosis is overwhelmed, pH drops; lactic acid accumulates, and serum bicarbonate is consumed.

- Unmeasured anions: lactate, salicylate (and its metabolites), and ketoacids

- At this stage of ASA poisoning (pH < 7.4, low pCO2 and low serum bicarbonate) pts are dangerously unstable, likely to decompensate hemodynamically and will begin to demonstrate other symptoms of end-organ injury.
Endotracheal Intubation

- ASA poisoned pt who have depressed mental status (2/2 salicylate-induced cerebral hypoglycemia or acidosis or coingestants) requiring ET intubation and mechanical ventilation

- This poses a clinical problem because positive pressure ventilation is unlikely to maintain the minute ventilation required in seriously salicylate-poisoned patients.

- Result is hemodynamic instability and worsening of acid–base status.

- Patients who require endotracheal intubation for airway protection and maintenance should be hemodialyzed simultaneously to remove salicylate and the accumulated organic acids.
Treatment

• There is no antidote for salicylate poisoning.

• Goal of treatment:
  ➢ prevent further GI absorption of the drug,
  ➢ prevent its entry into the CNS
  ➢ Enhance removal of drug from CNS
  ➢ increase elimination of the drug from the body
Treatment: Gastric decontamination

- Activated charcoal is effective for decreasing ASA absorption and is recommended for ASA poisoning

- Multidose activated charcoal similarly has been shown to reduce absorption of aspirin but this has not improved morbidity or mortality rate

- It is reasonable to consider gastric lavage with a large-bore endogastric tube (36 French or larger) if there is no likelihood of airway compromise
Enhanced elimination

• Treatment of salicylate intoxication is directed toward increasing **systemic** pH by the administration of sodium bicarbonate.

• \[ \text{pH} = 3.0 + \log \frac{[\text{sal}^{-}]}{[\text{HS}]} \]

• Salicylate anions are “trapped” in the blood, since charged molecules do not easily diffuse across the blood-brain barrier into the CNS.

• Through the same theory, increasing urine PH will increase substantially the elimination of salicylic acid.

• No randomized controlled studies for the use of sodium bicarb.
Enhanced elimination

- Three ampules 150 mL total volume of sodium bicarbonate (containing 43 mEq of sodium each) into one liter of D5W, the resulting solution should have 132 mEq of sodium, started at rate of 1-2ml/mg/hr

- A total of 40 mEq of KCl per liter of solution

- Goal urine output of 1 to 2 mL/kg/hr.

- For enhanced excretion of salicylate by raising urine pH and GFR
Hemoperfusion

- Hemoperfusion is not recommended for the treatment of salicylate poisoning.

- Unlike hemodialysis, fluid, electrolyte and acid base corrections cannot be performed.

- In hemoperfusion, blood is pumped through a cartridge containing activated charcoal encased in a thin porous membrane.

- Thrombocytopenia, leukopenia and hypocalcemia may occur with this technique but charcoal emboli are less likely with current cartridges.
Hemodialysis

- Low molecular weight of ASA: 138 Da and acetylsalicylic acid: 180Da, low apparent volume of distribution 0.2 l/kg

- 90% protein binding at therapeutic doses, but at higher serum levels total free salicylate increases.

- Hemodialysis is more efficacious at toxic levels because more free salicylates.

- HD with blood flow rate of 350–400 ml/min for at least 3.5–4 h with biocompatible hemodialysis membranes with larger surface areas.

- Decision for a second HD session depending on salicylate levels, clinical signs and symptoms, and response to continuing urinary alkalinization.
Hemodialysis indication

Table 4 | Findings that should prompt consideration of hemodialysis

- Markedly elevated serum concentrations (>100 mg/100 ml), even without clinical findings
- Serum concentrations in or above therapeutic range and
  - CNS dysfunction (e.g. delirium, lethargy, seizures, coma) with no other explanation
  - Renal failure
  - Pulmonary edema/hypoxia
  - Severe acid-base or electrolyte imbalance with no other explanation
CVVHD

- CVVHDF may have a useful role in the management of patients with severe salicylate poisoning, when hemodialysis is unavailable or the patient is hemodynamically unstable.

- No data on optimal blood flow rates, ultrafiltration and dialysate flow rates necessary to maximize elimination.
References


THANK YOU