Lecture 11

Aspirin

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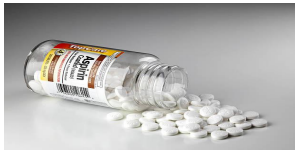
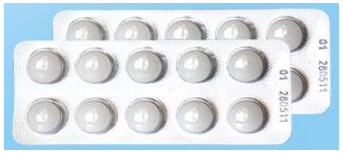
Color Index : Important , doctor`s note

Editing File

Perspective





- The incidence of aspirin (acetylsalicylic acid [ASA]) overdose and related childhood deaths has **decreased** significantly in recent years.

- **Reasons:** include pediatricians' preference for acetaminophen preparations, the Food and Drug Administration's mandate limiting 36 tablets of baby aspirin to each bottle, and the use of child-resistant caps[1].

- Unfortunately, the severity of this poisoning may be underestimated because of the **lack of familiarity** with the clinical picture.

- Salicylate toxicity can cause metabolic acidosis, seizure, hyperthermia, pulmonary edema, cerebral edema, renal failure, and death.

1: in KSA, instead of giving the patient a bottle with 60 tablets of aspirin, they give him (شريطة) with 36 tablets. Why? Because sometimes the child may think of it as a candy jar and start to eat it.

Principles of Disease

- Salicylic acid is a weak acid that at normal serum pH is mostly **ionized**, therefore will not cross the blood-brain barrier or the renal tubules (for reabsorption).
- As the blood becomes more acidemic, a more **non**ionized form develops, allowing salicylate to enter the brain and be reabsorbed by the kidneys (decreasing renal excretion).
- Treatment is logically geared toward keeping salicylate in the **ionized** form.
- Chronic excessive use of salicylates (chronic ingestion) is seen primarily in the **elderly** and is associated with a higher clinical toxicity for a given serum salicylate level.

-Aspirin doesn't cause acidosis in normal situation because it is a weak acid.

-ionized = not crossing the BBB = No toxicity

-Acidemic blood = nonionized = cross the BBB = toxicity

-How you treat it?
Alkalization (we will try to ionized it)

-Geriatric with aging process will decrease the renal clearance +there will be more drug drug interaction

-Highest mortality?
chronic use of aspirin

Pharmacokinetics

- Salts of salicylic acid are rapidly absorbed intact from the gastrointestinal tract, with **appreciable serum concentrations occurring within 30 minutes**.

- Two thirds of a therapeutic dose is absorbed in 1 hour, and **peak levels occur in 2 to 4 hours**.

- **Large ingestions** frequently delay gastric emptying, and **ingestions of enteric capsules** may **cause a prolonged absorption with rising serum levels for 12 hours or more.**

- Onset = 30 mins
- Peak = 2-4 h
- Enteric capsule = 12 h
- If a patient come to the ED after 15 minutes of taking aspirin, the lap results will be –ve. We have to wait at least 30 minutes (the aspirin will reach the blood within 30 mins)
- We have to ask the patient about the type of the aspirin, if it was enteric capsule it will slowly release and prolong the absorption.

Pathophysiology

1. **Direct stimulation of respiratory center →** hyperventilation and **respiratory alkalosis**.
2. **Stimulation of chemoreceptor trigger zone** → vomiting.
3. **Uncoupling of oxidative phosphorylation** → anaerobic metabolism, lacate production, anion-gap acidosis, and hyperthermia.
4. **Increased fatty acid metabolism → metabolic acidosis** (ketones)
5. **Ototoxicity** → tinnitus and hearing loss correlate with salicylate level

6. **Platelets permanently lose their ability to aggregate at therapeutic aspirin doses.** Bleeding is rare in overdose.

7. **Cerebral and pulmonary edema →** secondary to alterations in capillary integrity.

- What will see in the arterial blood gas test?
We will see a two mixed pathologies (they are not compensated for each other)
1-Respiratory alkalosis 2-high anion-gap metabolic acidosis
Why? Because the aspirin works on both respiratory center and increasing the fatty acid metabolism
- one of the commonest presentation in the elderly is ototoxicity

Clinical Features

Acute ingestion :

- Early symptoms include N/V, tinnitus, hearing loss, lethargy, hyperventilation, and hyperthermia.
- **The classic presentation of mild to moderate toxicity is** a mixed acid- base picture with a respiratory alkalosis, wide anion-gap metabolic acidosis, and (possibly) a metabolic alkalosis (from dehydration).
    - ○Blood gases early on often show a respiratory alkalosis with pH > 7.5.
    - ○Less respiratory alkalosis (and therefore greater overall acidosis) is seen in children.
- **Severe intoxication** results in profound metabolic acidosis, marked hyperthermia, cerebral edema (coma and seizure), hypoglycemia, pulmonary edema, cardiovascular collapse.
- **So , patient with respiratory alkalosis and increased anion-gap metabolic acidosis? *Think salicylate toxicity.***

Severe= end organ failure
Mild or moderate= GI symptoms, ototoxicity

Cerebral edema comes with confusion, headache, loss of consciousness and coma.
Pulmonary edema comes with SOB and cough.

Chronic ingestion :

- Symptoms of toxicity overlap with those of acute ingestion, but are **slower** in onset and often **nonspecific**.
- Patients often present with confusion, dehydration, and metabolic acidosis.
- **Neurologic symptoms are common**, including confusion, hallucinations, agitation, coma.
- Pulmonary edema, cerebral edema, seizures, and renal failure occur more frequently compared to acute ingestions.

neurologic symptoms + end organ failure

Diagnostic Strategies

- Based on history, physical examination, and acid-base findings.
- **A toxic dose** of aspirin is 200 to 300 mg/kg, and ingestion of 500 mg/kg is potentially **lethal**.
- **Maintain high level of suspicion in patients with:**
  - Unexplained respiratory alkalosis
  - Mixed metabolic disorders
  - Metabolic acidosis
  - Elderly with altered mental status (common)
  - Patients with hearing complaints
- **Key labs:** Salicylate level, ABG, electrolytes

Why do we ask for electrolytes? To know if there is hypokalemia or not

Initial Evaluation

-**After the primary survey**, a general physical examination is conducted to assess vital signs (including oxyhemoglobin saturation and a counted respiratory rate and reliable temperature).Tachycardic, high temperature, oxygen is decreased, rr is high.

-Chest auscultation may provide evidence of pulmonary edema(crackles), and mental status may suggest CNS toxicity.

-Early arterial blood gas determinations in symptomatic patients rapidly assess acid-base and compensatory status.

-A serum salicylate concentration should be measured with a second sample obtained **2 hours** later.

-If the second concentration is greater than the first, serial concentrations should be obtained to monitor continued absorption, which may be prolonged.

-**Urine ferric chloride test** will **confirm exposure, but not toxicity.**

-The Done nomogram should **NOT** be used as salicylate toxicity correlates poorly with serum concentrations.

When do we measure for a second salicylate level?
After 2 hours If the first sample was –ve. Why? Because the aspirin peak is within 2-4 hours
How do we know if the patient is improved or not? We check for salicylate level
We check it every 2 hours

How to diagnose aspirin toxicity?
ABG, salicylate level, electrolytes
Urine ferric chloride + the done nomogram
(should NOT be used for aspirin toxicity)

Management

- **Specific treatment of salicylate toxicity has two main objectives:**
  - (1) to correct fluid deficits and acid-base abnormalities.
  - (2) Increase excretion.
- **Supportive and symptomatic care :**
  - Avoid CNS/respiratory depressants, which may decrease the respiratory alkalosis and thereby worsen the acidemia.
  - If intubated, match the preintubation Pco2[2].
- **IV hydration** (**not** forced diuresis) to maintain renal perfusion.

- The common mistakes: give him sedative medication (CNS suppression) --> coma
High RR --> (respiratory suppression) --> respiratory arrest
[2:] the doctor said this information is advanced and "they may not ask about it in our exam"
Usually RR (16-20) and with aspirin it reach 40-50 (above 30)
This will lead to Respiratory alkalosis (hyperventilation)
So If we intubate the patient, it will return the RR to the normal interval. BUT in aspirin toxicity we should not do intubation unless we are checking for Pco2 beforehand.why?
Because the patient will have respiratory acidosis --> arrest

- Be generous with fluid but don't give him lasix
- Patient is **dehydrated** so don't give him lasix
- Increase the renal perfusion and function
+helps with the excretion
- Which type of fluid do we give him?
D5 normal saline or D5 ringer lactate
- we give him fluid because he's dehydrated
- we give him D5 because he has hypoglycemia

- **Sodium bicarbonate therapy:**
  - 1–2 mEq/kg IV bolus, followed by drip.
  - Goal is **urinary alkalinization** to pH 7.5–8.0.
- **Correct hypokalemia:** **"important"**
  - Results from **intracellular shifts** and body losses.
  - **Urinary alkalinization will not occur unless hypokalemia is corrected.**
- **Obtain basic metabolic panel** (Electrolytes + blood gases) **and salicylate levels every 2 hours**. Monitor salicylate levels until levels have declined to near therapeutic concentration.

treatment: Iv fluid - urinary alkalinization - hypokalemia correction

Hemodialysis is indicated for patients with the following: (end organ failure)

1)Level > 100 mg/dL **(acute ingestions)**, Level > 40 mg/dL **(chronic ingestions)** accompanied by clinical signs of severe intoxication.

2)Altered mental status.

3)Renal failure/anuria.

4)Severe persistent acid-base disturbance.

5)Pulmonary edema.

6)Failure to respond to intensive treatment.

Box 149-2 Treatment of Acute Salicylate Poisoning

Treat dehydration; maintain urine output at 2-3 mL/kg/hr with 5% dextrose (D_5) in lactated Ringer's solution or normal saline.
Correct potassium depletion.
Alkalinize urine.
- Obtain baseline arterial blood gas values.
- If pH is <7.4, administer sodium bicarbonate to obtain pH of 7.4 (50 mL bicarbonate increases serum pH by 0.1 in an adult).
- Infuse intravenous fluids: D_5 with bicarbonate 100-150 mEq/L.
- Monitor serum pH; do not cause systemic alkalosis.
- Do not attempt forced diuresis.

Monitor for dialysis indications.
- Coma, seizure
- Renal, hepatic, or pulmonary failure
- Pulmonary edema
- Severe acid-base imbalance
- Deterioration in condition
- Serum salicylate concentration ≥ 100 mg/dL after acute ingestion
- Serum salicylate concentration ≥ 40 mg/dL after chronic ingestion