TOXICOLOGY TEAM · CSI KSU · 435

ASPIRIN

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Objectives

? Not given):

NOTES EXTRA BOOK IMPORTANT GOLDEN NOTES

Aspirin

Aspirin (ASA)

Pathophysiology

-Peak level = 18-24 hrs.
-Acidemia = non-ionized ASA = cross BBB
-Early stimulates respiratory center
-Increases pulmonary vascular permeability
-Reversible sensorineural hearing loss correlates with ASA concentrations.

What is aspirin used for? It's an NSAID, it is commonly used as an antiplatelet more than anything but it also has multiple functions, like antipyretic, anti-inflammatory and analgesic effect. (a lot of countries use it as a painkiller)

Pharmacokinetics

-Rapidly absorbed from GI tract within 30 minutes.
-Peak levels occur in 2 to 4 hours.
-Two thirds of a therapeutic dose is absorbed in 1 hour.
-Free salicylate and its conjugates are eliminated by renal excretion.

Factors affect peak levels of ASA:

1-Large ingestions
2-Delay gastric emptying
3-Prolonged absorption
All of which will lead to rising serum levels for 12 hours or more

Why is knowing the peak important? When a patient takes 100 pills for example, we cannot measure the actual amount in their blood after one hour, we have to wait until it reaches its peak
Absorption starts after 30 min reach peak level after 2-4h and maybe prolonged for 12h with very large doses

Toxicity in brief

What is the toxicity of aspirin? It usually doesn't not cause bleeding. It causes respiratory alkalosis first because it affects the medullary centers for respiration, it then causes metabolic acidosis (it disrupts krebs cycle so it leads to anaerobic pathway which leads to accumulation of ketones which will cause high anion gap metabolic acidosis) and it causes further respiratory alkalosis. However in children younger than 4 years old their respiratory centers are immature so they don't compensate and they only have metabolic acidosis.so at the beginning respiratory alkalosis is not a compensation for metabolic acidosis bc it starts first.

Elimination:

Elimination of ASA is dose dependant

Therapeutic Dose

1
1
1

At therapeutic salicylate concentrations, elimination follows first order kinetics (which means that it's elimination rate depends on the concentration of the drug, the more the drug the faster the excretion) and excretion is proportional to salicylate concentration

Toxic Dose

0
0
0

When serum salicylate concentrations are greater than 30 mg/dL, however, elimination follows zero order kinetics (which means that its excretion does not depend on the concentration because of the saturation of the receptors هذا هنا وقت التوكسيسيتي) , and the metabolic rate is constant.

When the metabolic pathways become saturated, urinary excretion of salicylic acid determines the half-life, which becomes prolonged and may approach 15 to 30 hours with toxic doses.

Aspirin

Clinical Features:

Clinical symptoms vary according to body response and acuity of overdose

In Children

- Primarily = metabolic acidosis and acidemia
  <4 years old
- If >4 years of age it's just like adult

Presenting signs:
Fever, hyperventilation, and altered mental status with volume depletion, acidosis, and severe hypokalemia. nausea vomiting , abdominal pain, pulmonary edema, renal failure

Poor prognosis = hyperpyrexia

- Chronic higher mortality

In Adults

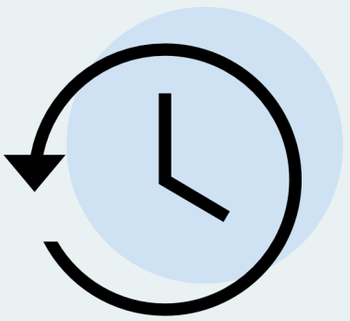
	Acute ingestion (dose)	End-Organ Toxicity
Mild	<150 milligrams /kg	-Tinnitus -Hearing loss -Dizziness -Nausea/vomiting
Moderate	150-300 milligrams /kg	-Tachypnea -Hyperpyrexia -Diaphoresis -Ataxia caused by cerebral edema -Anxiety
Severe	>300 milligrams /kg	-Abnormal mental status -Seizures -Acute lung injury -Renal failure -Cardiac arrhythmias -Shock

Toxic dose of aspirin is 200 to 300 mg/kg, and ingestion of 500 mg/kg is potentially lethal.
Five mL of oil of wintergreen contains 7 g of aspirin and can be deadly to a toddler

Aspirin

Diagnosis:

Do Not use single level !



→ Obtain serial serum salicylate concentrations initially every 1 to 2 hours until level declined then every 4-6 hrs

Treatment:

-Very important to maintain it 4.5 even though it is higher than the normal range. The kidney has receptors that sense the concentration of potassium, when potassium is low, the kidney keeps the potassium and excretes the hydrogen ion and this will make the urine more acidic and if the urine is acidic due to this it will disrupt the secretion of aspirin.
-ECG is important to do

Treat dehydration; maintain urine output at 2 to 3 mL/kg/hr.

Correct potassium depletion with goal serum level of 4.5 mEq/L.

Consider activated charcoal (AC); 25 grams every 2 to 4 hours for two to four doses if tolerated. Only if awake alert and stable.

Alkalinize urine with goal urine pH of 7.5 to 8.0. The most IMP in treating aspirin toxicity. why we do it ?To allow the aspirin to be excreted in the urine

Infuse bicarbonate drip: 132 to 150 mEq (three 50-mL ampules) of 7.5% or 8.4% sodium bicarbonate (NaHCO3) in 1 L of dextrose 5% in water (D5W) + 40 mEq of potassium chloride (KCl) running at 2 to 3 mL/kg/hr.

Allow serum pH up to 7.55.

Do not attempt forced diuresis.

Contraindication of charcoal usage:
Altered mental status
Hemodynamically unstable bc it may harm the patient later on or make any intervention difficult

Aspirin

Treatment:

Initiate hemodialysis if any of the following occur:

Altered mental status, coma, seizure	Renal failure
Hepatic failure	Pulmonary edema or respiratory failure Severe acid-base imbalance (pH <7.1 to 7.2)
Deterioration in condition	Failure of urine alkalinization
Rapidly rising salicylate level	Serum salicylate concentration ≥100 mg/dL after acute ingestion
Serum salicylate concentration ≥40 mg/dL after chronic ingestion	Intubation

Administer intravenous (IV) dextrose 0.5 to 1 g/kg IV for any central nervous system (CNS) abnormalities (altered mental status, coma, agitation, seizure)

All the symptoms indicate End organ damage!, so basically the main indication for hemodialysis is end organ damage or failure of alkalization or >100mg in acute ingestion or >40 in chronic

Disposition:

A patient may be discharged from the ED if serial declining salicylate levels.

Hospital admission is required for: pulmonary edema, CNS symptoms, seizures, acidosis, electrolyte disorders, dehydration, renal insufficiency, or increasing serum levels during serial testing.

Overdosed of enteric-coated or modified-release preparations of aspirin should be treated and observed for approximately 24 hours, with serial serum salicylate concentrations.

Consultation with a clinical toxicologist is recommended.

The mortality rate for chronic salicylate intoxication is 25%, compared with a mortality rate of 1% after acute salicylate intoxication.

Bc symptoms aren't very clear in chronic cases and it's hard to diagnose them

With any case of intentional overdose, psychiatric evaluation is essential.

Summary

Pathophysiology	Pharmacokinetics	Toxicity	Diagnosis and treatment
-ASA = early stimulate respiratory center (non-ionized ASA=cross BBB) -ASA = increased pulmonary vascular permeability -Reversible sensorineural hearing loss correlates ASA concentrations.	-Peak levels occur in 2 to 4 hours. -Rapid GI absorption, renal excretion. -Salicylate elimination: 1- at <u>therapeutic</u> concentrations --> **first** order kinetics 2- **<30 mg\dL -> zero** order kinetics	-Toxic dose of aspirin is 200 to 300 mg/kg, and ingestion of 500 mg/kg is potentially lethal -Toxicity in Children (<4 years): -Primarily = metabolic acidosis and acidemia -hypokalemia -Chronic higher mortality -Toxicity in adults (depends on dose): 1-Mild: <150 mg/kg, tinnitus 2-Moderate: 150-300 mg/kg, hyperpyrexia 3-Severe: >300 mg/kg, Shock, seizures and renal failure (start dialysis)	-Diagnosis: Don't use single level (Obtain serial serum salicylate concentrations) -Treatment: **1-** Treat dehydration **2-** Correct potassium depletion with goal serum level of 4.5 mEq/L.´ **3-** Alkalinize urine with goal urine pH of 7.5 to 8.0. **4-** Infuse bicarbonate drip **5-** Allow serum pH up to 7.55 -When to Initiate hemodialysis?Basically the main indication for hemodialysis is end organ damage or failure of alkalization or >100mg in acute ingestion or >40 in chronic

How Toxic is your knowledge

1)Which of the following is an expected acid-base pattern found a few hours after significant acute ingestion of salicylates.
A. Acute respiratory alkalosis and alkalemia
B. Acute respiratory acidosis and acidemia
C. Respiratory alkalosis, metabolic acidosis , alkalima
D. Metabolic acidosis, and respiratory alkalosis, acidemia

2)Which of the following is toxic dose of aspirin?
A. 2550 mg/kg
B. 50100 mg/kg
C. 75100 mg/kg
D. 200300 mg/kg

3) Which one of the following is a presentation of severe salicylate toxicity?
A. Tinnitus
B. Vertigo
C. Lethargy
D. Hyperthermia

4) A 30-year-old maid has taken a large overdose of aspirin. Which of the following set of clinical signs and symptoms are likely to be present in this patient?
A- Tinnitus, hyperpnoea, agitation
B- Hypothermia and metabolic acidosis
C- Hyperthermia and respiratory acidosis
D- Tinnitus, hypopnea and hypothermia

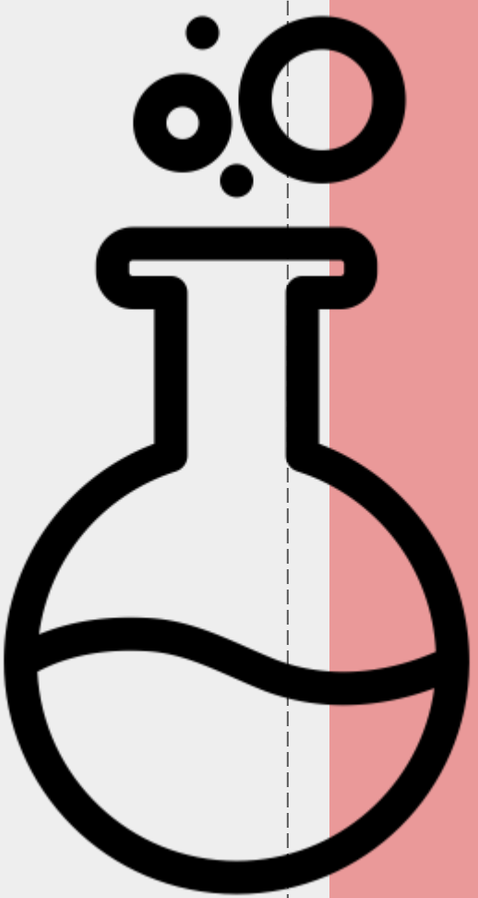
5)Which of the following is the appropriate management in severe aspirin poisoning?
A- Activated charcoal
B-Gastric lavage
C-Hemodialysis
D- Urine acidification

6)In which of the following organs the major proportion of salicylate is metabolized?
A. The lungs
B. The liver
C. The kidney
D. The skin

7) In poisoning with salicylates, hemodialysis is indicated in which of the following conditions?
A. Pulmonary edema
B. Hyperthermia
C. Excessive vomiting
D. Severe abdominal pain

1-D
2-D
3-D
4-A
5-C
6-B
7-A

Thank you and good luck!



Very Toxic but you are gonna do it!

A+ is yours (:

- Email us at:

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