Aspirin toxicity

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Objectives:

- not given

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[Color index : Important | Notes | Extra | Editing file]

introduction:

Aspirin, or acetylsalicylic acid(ASA), is widely consumed for its analgesic, anti-inflammatory, and antiplatelet effects.

(هنا مايستخدمونه كمسكن بكثرة لكن في بريطانيا و امريكا يستخدم كمسكن بكثرة)

Although its therapeutic use is wide, salicylate toxicity is not a benign condition and causes a complex set of life-threatening metabolic derangements with significant morbidity and mortality.

Salicylate containing products:

•Aspirin (most common)

•Topical salicylates

•Oil of wintergreen, willow bark, and bismuth subsalicylate.

(الدكتور تكلم عنه في اكثر من موضع خصوصا انه مشهور عند كبار السن ومنتشر هو اللي يسمونه ابو فاس)

•Ingestion of oil of wintergreen is of particular concern given that 1 mL of 98% solution contains the equivalent salicylate of 1.4 grams of aspirin.

(يعني واحد مل من ابوفاس تساوي 1.4جرام من الاسبيرين وهذا توكسيك)

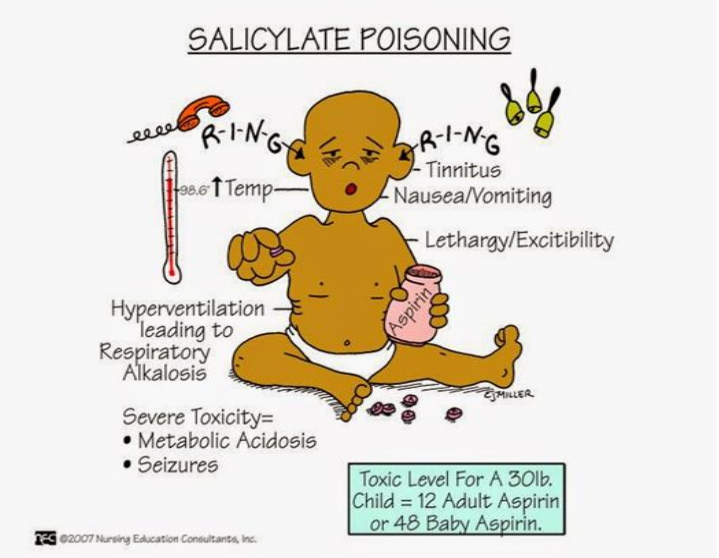
Pathophysiology:

- Unpredictable GI absorption (2-4 hours, but can be longer – up to 12 hours)

الامتصاص غالبا يبدأ بعد 30 دقيقة ويصل للقمة خلال 2 الى 4 فيه حالات يطول الامتصاص فيها اكثر تصل الى 12 ساعة مثل اذا اخذ كمية جدا جدا كبيرة من الاسبيرين بيصير فيه زيادة في فترة الامتصاص .

- In the intestinal wall, liver, and red blood cells, aspirin is hydrolyzed to free salicylic acid, which reversibly binds to albumin.
- Toxicity results primarily from salicylate interference with aerobic metabolism by uncoupling of mitochondrial oxidative phosphorylation
- Inhibition of the Krebs cycle increases production of pyruvic acid and increases its conversion to lactic acid. (علشان كذا يصير عندهم high anion gap metabolic acidosis)
- Metabolic rate increase → metabolic acidosis
- Tissue glycolysis → hypoglycemia and ketosis.

Clinical Features



	clinical	Laboratory
CMV	**Tinnitus, decreased hearing, agitation, somnolence, confusion, seizure, cerebral edema, coma**	**Metabolic acidosis Respiratory alkalosis Transaminitis**
Pulm	**Tachypnea, ARDS, respiratory failure**	**Hypoglycemia coagulopathy**
CV	**Hypotension, CHF, cardiovascular collapse.**	
GI	**Nausea, vomiting, gastritis, hepatitis**	
Renal	**Volume depletion, proteinuria, AK**	

-Why do patients with salicylate intoxication develop respiratory alkalosis?
It starts by direct stimulation of respiratory center → hyperventilation → respiratory alkalosis. Not due to a compensatory response to metabolic acidosis. Then after inhibition of krebs cycle and beginning of metabolic acidosis the continuation of respiratory alkalosis well be as a compensatory mechanism.
-Cerebral and pulmonary edema → secondary to alterations in capillary integrity.
-Uncoupling of oxidative phosphorylation → anaerobic metabolism, lactate production, anion-gap acidosis, 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)

Differential diagnosis

- Sepsis
- CNS infection
- Withdrawal syndromes (like opioid or alcohol withdrawal)
- Alcoholic or diabetic ketoacidosis
- Sympathomimetics toxicity

Diagnosis

severity grading of Salicylate toxicity in adults

	Mild	Moderate	Severe
Acute ingestion (dose)	**<150 Mg/Kg**	**150-300 Mg/Kg**	**>300 Mg/Kg**
End-organ toxicity	**Tinnitus Hearing loss Dizziness Nausea/vomiting**	**TAchypnea Hyperpyrexia Diaphoresis Ataxia Anxiety**	**Abnormal mental status Seizures Acute lung injury Renal failure Arrhythmias Shock**

(الدكتور ركز على الدوز لكل وحدة يعني اقل من 150 يعتبر خفيف وبين 150 و300 يعتبر متوسط وفوق 300 يعتبر شديد وفي الاخيرة ركز على انه يسبب (cardiac arrhythmias, shock and death)وايضا قرا اعراض كل واحدة منهم فاعرفوها كلها. الدكتور اعطى مثال على طفل وزنه 15 وقال كم يحتاج يشرب من ابوفاس (Oil of wintergreen) فضرب 15 ضرب 300 علشان نطلع التوكسيك دوز اولا فطلع الناتج 4500 ثم نقسمها على 1.4 (لان 1 مل Oil of wintergreen يساوي 1.4 جرام من الاسبيرين) فيطلع الناتج 3 مل وهذا يعني ان الطفل الصغير يحتاج يشرب 3مل بس من ابوفاس وتسبب في وفاته).

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

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.

- 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.
- Fever indicate severe life-threatening toxicity

Management

اول شيء نطبق (A,B,C) بعدين لازم نتاكد ان مافيه (COINGESTION) وخصوصا البارا سيتامول يقول دايما اذا جاك واحد ماخذ اسبيرين قس البارا سيتامول مباشرة حتى لو ما قال لك.

Specific treatment of salicylate toxicity has two main objectives:

1-Correct fluid deficits and acid-base abnormalities (because of vomiting Gi upset diarrhea and excessive sweating that cause dehydration)

2-Increase excretion

- Intubation is indicated for patients with refractory shock, pulmonary or cerebral edema, or other manifestations of severe salicylate poisoning.

- Electrolyte values are helpful to guide replacement and to assess renal function necessary to excrete salicylates.

•Serum salicylate levels measurement should be repeated every two hours until they are decreasing to measure the effectiveness of treatment and to guide the decision for dialysis.

Activated Charcoal ? no evidence of benefit

Intravenous Fluids: أول شيء نعطيهم نورمل سلاين

- Correct Potassium depletion.
- Maintain urine output of 2 to 3 mL/kg/hr.
- Avoid excessive fluid administration (why ?) (because of pulmonary edema)
- Should contain dextrose, and the serum glucose level should be frequently monitored to prevent hypoglycemia.

Urine Alkalinization:

Advisable in patients with:

- Salicylate levels greater than 35 mg/dL
- Significant acid-base disturbance
- Increasing salicylate levels

Urine pH of 7.5 to 8.0 is necessary to increase excretion. Sodium bicarbonate (1-2 mEq/kg) can be administered during 1 to 2 hours. (how ?)
(we give 3 ampoule (150-200 mEq) + 1L d5w each hour)

Potassium depletion must be corrected (why ?)
(in order to alkalize the urine we need H/K pump to work)
(وظيفة الهيدروجين بوتاسيوم بمب انها تمسك الهيدروجين في الجسم وتطلع البوتاسيوم، فاذا ماكان فيه بوتاسيوم بالجسم هذي البمب لن تعمل ولن يتحول اليورين الى قلوي)

Forced diuresis? (harmful) (ولم يعد يستخدم)

- *Forced diuresis does not significantly increase salicylate excretion and may potentiate cerebral and pulmonary edema*

Hemodialysis ? (when to do)

- Coma, seizure, Altered mental status.
- Renal, hepatic, or pulmonary failure
- Pulmonary edema
- Severe persistent acid-base imbalance
- Deterioration in condition
- Serum salicylate concentration ≥ 100 mg/dL after acute ingestion
- Serum salicylate concentration ≥ 40 mg/dL after chronic ingestion
- Rapidly rising serum salicylate level
- Failure to respond to conservative or intensive treatment

Summary of the 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

Disposition

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

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

MCQs

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 alkalima

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

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