ANTIHISTAMIN TOXICITY
5TH STAGE 2021-2022

LECTURER SALIM DAWOD

the most common modern antihistamine, diphenhydramine, was first synthesized. Shortly after, in 1947, orphenadrine was synthesized and used for the treatment of Parkinson disease. With the turn of the decade, antihistamine use became more prevalent, and pediatric deaths increased. A comparison to atropine poisoning and the similar pharmacologic properties between atropine and antihistmaines was soon realized`

The specific concern of antihistamine toxicity is not due to their competitive H1-receptor binding and sedation but due to their anticholinergic effect. Toxic exposure causes varying degrees of symptoms with differing implications. This activity describes antihistamine toxicity and highlights the role of the interprofessional team in its management

The specific concern of antihistamine toxicity is not a result of their competitive H1-receptor binding and sedation but due to their anticholinergic effect. Toxic exposure causes varying degrees of symptoms with differing implications. Treatment for antihistamine exposure can range from close monitoring and supportive therapy to rapid pharmacologic intervention

Etiology

Antihistamine toxicity occurs almost exclusively via oral ingestion. Other forms can include intravenous (IV), intramuscular, and topical, but these forms are rare in households.

Epidemiology

The risk for antihistamine toxicity results from ingestion of unintentional toxic doses or attempted suicide mostly occurs in two categories: pediatric patients or the elderly. In the former group, antihistamines can be commonly excessively administrated due to their therapeutic sedative properties and worldwide availability. The elderly are more susceptible to their anticholinergic and sedative properties

Pathophysiology

The pathophysiology of antihistamine toxicity varies as the drug has a wide range of therapeutic and toxic effects. Most commonly, ingestion of H1 antihistamines (such as diphenhydramine) manifests with hallucinations or antimuscarinic effects. Rapid IV administration of antihistaminic medications often results in the hallucinogenic effect., this presents with vasodilation and reddening of the skin, anhidrosis and lack of sweat production, hyperthermia due to decreased sweat production, mydriasis causing blurred vision, hallucination, delirium, and urinary retention due to reduced detrusor contraction. Furthermore, diphenhydramine has been shown to potentiate opioid receptors, modulate serotonin function, and enhance dopamine concentration

Toxicokinetics

Oral ingestion of antihistamines is the primary cause of toxicity.. Within two hours of ingestion, the peak serum concentration is reached, and the maximum antihistaminic effect occurs several hours later. Outside of ingestion, there are some rare incidences of topical exposure causing anticholinergic toxicity. With the peak therapeutic concentration being 0.06 mg/L, many patients with anticholinergic symptoms will have concentrations above the therapeutic levels. Antihistamines, in general, are highly lipid-soluble with approximately 98% binding to a protein and their volume of distribution ranging from 0.5-30 L/kg. The metabolism of antihistamines is mainly via the hepatic route, except for fexofenadine, levocetirizine, and cetirizine which are renally excreted and eliminated

History and Physical

The patient history will often be obtained from parents or supervising adults as patients may be obtunded or too young to communicate. Important history findings would include co-administration of other anticholinergic medications such as tricyclic antidepressants, atropine, and scopolamine, as the unintentional mixture of medications may increase antimuscarinic toxicity

Physical exam findings will be divided by organ systems. Neurological symptoms, especially with first-generation H1 antihistaminics, can be found two hours post-ingestion and can manifest as drowsiness, hallucinations, and in pediatric populations, may present as ataxia and irritability. At any point following ingestion, seizures may occur, but they typically occur within the first one to two hours. Visual disturbances may manifest as mydriasis, blurred vision, and diplopia

Cardiovascular findings include tachycardia and both hypertension and hypotension. The binding of sodium and calcium channels may prolong QRS complexes and QT intervals, respectively, as well as the appearance of a Brugada-like syndrome. Lastly, with agitation, irritability, and seizures, some reports of rhabdomyolysis have been r supervising adults as patients may be obtunded or too young to communicate. Important history findings would include co-administration of other anticholinergic medications such as tricyclic antidepressants, atropine, and scopolamine, as the unintentional mixture of medications may increase antimuscarinic toxicity

Evaluation

Initially, ECG, temperature, heart rate, respiratory rate, and blood pressure should be assessed. Further diagnostic testing can be useful, although unreliable in some aspects of antihistaminic toxicity. Many common over-the-counter antihistamines produce false negatives for amphetamines. Methadone and phencyclidine in urinary drug screens and may lead practitioners down the wrong diagnostic pathways. Extensive testing such as gas chromatography/mass spectroscopy (GC/MS) or liquid chromatography/mass spectroscopy (LC/MS) can be reliable in determining antihistamine concentrations but are not commonly ordered due to the long diagnostic time. Creatinine and blood urea nitrogen (BUN) should be assessed to evaluate kidney function, as well as beta-hCG or other serum pregnancy tests

Treatment / Management

Proper guidelines exist to guide out-of-hospital management. For diphenhydramine and dimenhydrinate, any ingestion under 7.5 mg/kg in children under the age of 6 and less than 300 mg or 7.5 mg/kg for adults and older children, at-home observation is appropriate. If these prove inadequate, prompt evaluation to the closest emergency department is needed. Initially, management should include constant cardiac monitoring and initiation of IV access. Activated charcoal (AC) administration may be indicated, especially if the patient presents shortly after the substance's ingestion. It may be tempting to initiate attempts to increase renal elimination, but due to antihistaminic extensive protein binding and a large volume of distribution, these attempts will be in vain

Prognosis

Depending on the amount ingested, the prognosis can vary greatly, but typically with rapid emergency department admission and close cardiac monitoring, the prognosis of toxic antihistaminic ingestion is very good.

Go to:

Complications

- Arrhythmias
- Respiratory failure
- Coma
- Rhabdomyolysis
- Hyperthermia
- Seizure

Outcomes

The outcomes of patients with antihistamine toxicity depend on many factors such as underlying medical conditions, the amount of drug ingested, and any coingestants. The majority of patients do recover fully and are discharged. However, the elderly and children can suffer multiorgan failure from a high dose. First-generation antihistamines like diphenhydramine are more sedating than most other antihistamines. Also, there are reports that this agent is known to cause arrhythmias and seizures