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FEATURE ARTICLE

PEER REVIEWED

Recognizing Dangerous Poisonings in Primary Care: Part 2, Antihistamines

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The 5 most common causes of poisoning-related fatalities in the United States are antidepressants, antihistamines, cardiovascular drugs, opioids, and pesticides.[1] Drug poisonings, particularly mild cases, are often exceptionally difficult to recognize. Slightly dilated pupils, mild tachycardia and hypertension, slight fever, and tachypnea are all constitutional symptoms that fit myriad working diagnoses, but autonomic instability is a hallmark of drug poisonings. Motor stiffness and hyperreflexia are frequently seen with a number of drug poisoning syndromes, although not with pesticide poisoning.[2,3]

This 6-part review article series helps sort out some of the more common symptoms, interactions, and therapeutic considerations in the clinical approach to a patient whom you suspect may be experiencing the effects of the most common types of poisoning.

This article, the second in the series, covers antihistamine poisonings. Other articles in the series cover antidepressants, cardiovascular drugs, opioids, and pesticides, and one article specifically covers serotonin syndrome.

Background

The American Association of Poison Control Centers' National Poison Data System (NPDS) annual report for 2011 reported 94,000 antihistamine exposures, representing 3.4% of all reported exposures for 2011.[1] This was a slight decrease in antihistamine exposures from the previous year, but antihistamines retain their ranking as the ninth most common exposure reported to the NPDS.[4]

Antihistamines comprise a large group of pharmacologic agents that can cause a wide variety of clinical symptoms, including agitation, confusion, drowsiness, blurred vision, tachycardia, hypotension, and urinary retention. Antihistamines bind to 1 of 4 identified human receptors: H_1 receptors are found in smooth muscle and endothelial cells and account for acute systemic allergic responses; H_2 receptors are found in the parietal cells of the stomach and are responsible for the secretion of gastric acid; H_3 receptors are located in the central nervous system (CNS) and modulate neurotransmission; and H_4 receptors are located in mast cells, eosinophils, T cells, and dendritic cells and regulate immune responses.[5]

The effects of antihistamines on the H_1 receptor are the primary cause of clinical toxicity. The H_1 antagonists are competitive inhibitors of the histamine receptor and also have an effect on muscarinic receptors and voltage-gated sodium and potassium channels.[6,7] These effects can lead to serious clinical toxicity when overdose occurs.

Traditionally, H_1 antihistamines have been classified into 6 chemical groups: alkylamines, ethanolamines, ethylenediamines, phenothiazines, piperazines, and piperidines. However, a more functional and commonly used system classifies H_1 antihistamines as either first- or

second-generation medications.[5] First-generation medications cross the blood-brain barrier and can cause sedative effects. Second-generation medications that tend to not cross the blood-brain barrier are considered nonsedating and nonimpairing.[8] First-generation H_1 antihistamines are responsible for the majority of antihistamine poisonings.[9]

Clinical manifestations of an antihistamine overdose can vary greatly depending on the chemical group, the dose, and the absorption rate for the medication. An antihistamine ingestion can cause anticholinergic syndrome, seizures, rhabdomyolysis, and cardiac toxicity and may affect other organ systems.[10] Manifestations of toxicity, such as seizures, cardiac arrhythmias, and dyspnea, are common and can be the result of nonanticholinergic mechanisms.[11]

The mnemonic, “Dry as a bone, red as a beet, hot as a hare, mad as a hatter, and blind as a bat,” is a simple way to remember the exaggerated central and peripheral anticholinergic effects commonly seen with antihistamine poisoning.[12] Hot, dry skin and dry mucous membranes result from inhibition of secretions from the salivary and sweat glands.[12] Redness appears due to vasodilation of the peripheral blood vessels resulting in flushing. The central effects of the antihistamine poisoning can occur in addition to the peripheral effects or can occur independently and account for the blindness (more correctly, mydriasis), and the “madness,” which can be manifested by agitation, hallucinations, disorientation, and paranoia, among other symptoms.[13] Overdoses with these medications commonly produce inhibition of the muscarinic receptors in the intestines and bladder wall causing ileus urinary retention, respectively.

Antihistamines can cause a multitude of other peripheral effects. A few of the first-generation antihistamines are known to slow conduction of the cardiac sodium channels, thereby causing cardiovascular effects. These can include sinus tachycardia, ventricular tachycardia, and torsades de pointes; even cardiogenic shock has been reported.[14,15] Decreased cardiac contractility seen in cardiogenic shock can lead to pulmonary edema and hypoxia. The combination of peripheral and central effects, including agitation, delirium, and hyperthermia, can lead to cellular damage, which in turn leads to elevations of creatine phosphokinase levels from rhabdomyolysis. If not treated promptly, this situation can lead to acute kidney failure.[16]

The treatment of antihistamine overdose depends on the clinical manifestations of the overdose. Based on clinical symptoms, a full altered mental status evaluation should be performed to rule out other causes. Activated charcoal should be administered to patients who are cooperative and who are not mentally altered; however, the use of charcoal has been shown to be beneficial only in patients who ingested the medication less than 1 hour before presentation.[12] For suspected overdoes in which the ingestion was more than 1 hour before presentation, care is mainly symptomatic and supportive. Care for all patients who are critically ill should be in a monitored environment where CNS depression, hemodynamic instability, or seizures can be recognized rapidly and addressed.

The general treatment of antihistamine overdose is supportive care with special attention to the presenting symptoms. Anticholinergic-induced agitation and delirium should be treated with the use of chemical and physical restraints.[12] Emergency personnel are privileged to use such methods if the patient is at risk of doing harm to himself or herself, staff, or third parties. The most common parenteral “chemical restrains” in agitated patients remain haloperidol, risperidone, and olanzapine; however, benzodiazepines still are considered first-line treatment for agitation. Haloperidol is not recommended, since it possesses anticholinergic properties that can exacerbate symptoms. Hyperthermia should be treated promptly with common cooling measures such as air-cooling blankets, cold intravenous fluids, and ice packs.[13] Rhabdomyolysis should also be treated aggressively with either sodium chloride, 0.9%, or lactated Ringer solution.

In severe cases, physostigmine, a reversible acetylcholinesterase inhibitor, can be administered to reverse the anticholinergic effects of the overdose. This medication crosses the blood-brain barrier and inhibits acetylcholinesterase activity, thereby increasing acetylcholine levels and reversing the dysphoric effects of the medication. Physostigmine also reverses the peripheral effects of the overdose. Physostigmine reversal should be used with caution and only in patients manifesting severe agitation, delirium, seizures, or hyperthermia. Patients with a significant antihistamine overdose should be admitted for observation or until their clinical symptoms resolve.[17]

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