Anticholinergic Plants

Introduction

Most plants with anticholinergic properties are from the family Solanaceae, and can be identified from their characteristic flowers. The Solanaceae family is extensively utilized by humans for food and medicine but is often rich in alkaloids that can cause life-threatening toxicity in humans. Plant chemistry is complex and most plants contain multiple chemicals and chemical classes that work independently or additively. Plants causing human toxicity include Atropa belladonna (deadly nightshade), Mandragora officinarum (mandrake), Hyoscyamus niger (henbane), Datura and Brugmansia. Atropa belladonna contains sweet-tasting berries that may be particularly dangerous for children. In addition to poisonous plants, a number of food staples, such as potato, tomato, eggplant and chili pepper belong to the Solanaceae family. Although atropine can be isolated in small quantities from the unripe skin of these "edible" plants, symptoms of toxicity are rare. Alkaloids are nitrogen-containing organic compounds that act as bases and form salts with acids. Alkaloids are generally distributed throughout the plant; therefore all ingested parts may be toxic. However, alkaloid concentrations vary within and among each plant, and victims are unaware of the dosage of chemicals they may ingest. Alkaloids in anticholinergic plants are also called tropane alkaloids and include atropine, hyoscyamine and hyoscine (scopolamine). Tropane alkaloids are found in about 25 genera and 2000 species of plants.

Case Presentation

A 17 year old male was brought in to the Emergency Department by paramedics after being found by police running partially clothed in the street after consuming Angel’s Trumpet. His initial vital signs were a temperature of 100.7°F, blood pressure of 155/78 mmHg, heart rate of 112 beats per minute, respiratory rate of 20 per minute and oxygen saturation of 99% on room air. His examination was significant for dry mucus membranes and his skin was warm and flushed. On neurologic exam, he was awake, but was confused, agitated and answering “I am Batman” to all questions. His ECG demonstrated a sinus tachycardia, but was otherwise normal. Complete blood count and serum electrolytes were within normal limits. He was given an intravenous (IV) antidote and 10 minutes later, his mental status had normalized and his heart rate...
improved. He was subsequently discharged home without further toxicity after 8 hours of observation.

Questions

1) What was the IV antidote this patient was administered? How does it work?
2) What physical exam findings classically occur with anticholinergic syndrome?
3) What treatment is usually required for patients with anticholinergic syndrome?

Epidemiology

The 2004 annual report of the American Association of Poison Control Centers listed 1058 cases of exposure to anticholinergic plants, 456 of these being intentional. One death was reported. 38% of these exposures occurred in children less than 6 years old. The recreational use of these plants, especially *Datura stramonium* (Jimson Weed) is the main source of exposure. Individuals seeking the hallucinatory effects of these plants may use the roots, leaves, and seeds to ingest, smoke, or brew into teas. Jimsonweed parties have become popular among teenagers, so multiple victims are often involved in an exposure. One hundred Jimsonweed seeds contain up to 6 mg atropine; ingestion of this amount can cause significant anticholinergic toxicity and can be fatal in severe cases.

Pathophysiology

Tropane alkaloids competitively inhibit postsynaptic muscarinic acetylcholine receptors producing the classic anticholinergic syndrome. Since nicotinic cholinergic receptors are rarely affected, a more accurate characterization of the syndrome would be antimuscarinic toxicity, but most sources still use the terms “antimuscarinic” and “anticholinergic” interchangeably. The most commonly ingested plants are *Datura* species, known as Jimsonweed (*Datura stramonium*) and moonflowers (*Datura inoxia*); and *Brugmansia* species, generally known as Angel’s Trumpet. Jimsonweed seeds contain the highest relative concentrations of tropane alkaloids, the equivalent of 0.1 mg of atropine per seed. The lethal dose of atropine is reported to be in the range of 10 mg, but is highly dependent on other factors. *Datura inoxia* contains the largest amount of scopolamine of any plant (3.85 mg/g in the leaves). Scopolamine’s tertiary amine structure and toxic effects are similar to those of atropine, permitting rapid penetration into the central nervous system (CNS). In therapeutic doses, scopolamine antagonizes muscarinic receptors; however, at higher doses, it can also antagonize nicotinic receptors at the neuromuscular junction leading to flaccid paralysis. The lethal dose of scopolamine has been reported to be 2-4 mg. In case reports of patients ingesting either *D. inoxia* or *D. stramonium*, there were no significant differences in clinical manifestations because these plants contain atropine, scopolamine, or both. Solanine, another chemical found in certain plants of the Solanaceae family, inhibits the enzyme cholinesterase in vitro; however, clinical symptoms of cholinergic toxicity generally do not occur with these exposures. Most symptomatic patients develop nausea, vomiting, diarrhea and abdominal pain, beginning 2-24 hours after ingestion and lasting up to several days. Occasionally, central nervous system toxicity such as hallucinations and
delirium occur with exposure to solanine-containing plants. Solanine toxicity is rarely encountered in humans. Green potatoes are most commonly associated with symptoms.

Clinical Presentation

Various species contain different concentrations of tropane alkaloids, but clinical manifestations are usually similar. Onset of symptoms generally occurs within 1-4 hours of ingestion. If the plant is smoked or consumed as a tea, symptoms may occur more rapidly. The duration of effects may last from hours to days. Anticholinergic findings suggestive of poisoning include hyperthermia, dry mouth, tachycardia, blurred vision, flushed dry skin, absent bowel sounds, urinary retention, agitation, hallucinations, lethargy, mumbling speech, undressing behavior (generally due to hyperthermia) and repetitive picking behavior. Blurred vision and photophobia may be due to mydriasis and paralysis of accomodation. Seizures, paralysis, respiratory depression, and coma may ensue in severe cases. Anticholinergic effects may delay gastric emptying, resulting in a prolonged duration of action. Patients may be amnesic to events that occur during poisoning.

Diagnosis

Diagnosis of plant-induced anticholinergic toxicity is usually based on a history of exposure and the presence of typical features such as dilated pupils, dry mouth, flushed skin and a rapid pulse. Positive identification of the plant should be attempted whenever possible, but timely identification of the plant is often difficult and common plant names often refer to more than one species. Communication with a regional poison center or local agricultural authority is highly recommended to confirm the botanical name. Assays of serum levels are unavailable for most plant toxins, and generally provide little clinical utility. A reversal of symptoms following a trial of physostigmine may help to confirm the presence of anticholinergic toxicity (see below).

Sympathomimetic poisoning with agents such as cocaine and methamphetamine can look very similar on physical examination to anticholinergic poisoning. Dry mouth, tachycardia, decreased bowel sounds and agitation are all characteristic of both syndromes. Although antimuscarinic agents may be associated with hyperthermia, the degree of temperature elevation is often mild (except in the presence of convulsions) as opposed to sympathomimetics in which severe temperature elevations can be present. Diaphoresis is usually present and often excessive with sympathomimetic poisoning but can be conspicuously absent, even in the axillae, of those with antimuscarinic toxicity. While patients with both syndromes can have altered level of consciousness, those with sympathomimetic poisoning are more often violent, requiring physical restraint. Finally, vital sign abnormalities (such as elevations in pulse and temperature) and altered mental status found with anticholinergic toxicity may also be seen with a variety of infections, including meningoencephalitis.

Treatment
Treatment of anticholinergic plant exposure consists primarily of decontamination and supportive care. Mild cases of anticholinergic intoxication may be treated solely by discontinuing the offending agent. However, more serious cases may need to be hospitalized for more prolonged monitoring and observation. Activated charcoal can bind tropane alkaloids and may be administered if patients present within 1-2 hours of ingestion and bowel sounds are present. Gastric lavage may be considered in massive ingestions presenting within one hour after exposure; however, this is rarely the case. Treatment is primarily supportive care, to maintain hydration and to treat hyperthermia with external cooling. Foley catheterization is often needed for urinary retention. Benzodiazepines can be used for agitation or seizures.

Physostigmine is a carbamate that inhibits the enzyme cholinesterase within the body, resulting in elevated acetylcholine concentrations at nerve end plates. This rise in acetylcholine concentrations can overcome cholinergic receptor blockade at both central and peripheral nerve terminals, and reverse many anticholinergic effects. Physostigmine can be considered for two main instances in the treatment of severe anticholinergic intoxication. First, physostigmine can be used to support the clinical diagnosis of anticholinergic poisoning. A patient may present without a clear history of anticholinergic plant or medication exposure, but may display the classic physical examination findings listed above. A “diagnostic challenge” with a bolus dose of physostigmine may reverse those signs and symptoms of toxicity, especially in the central nervous system, thus confirming the diagnosis and avoiding a more extensive and time-consuming work up for altered mental status. Secondly, physostigmine can be considered for cases of anticholinergic poisoning with features refractory to conventional management, such as intractable seizures or prolonged agitation. All patients receiving physostigmine should be placed on a cardiac monitor with pulse oximetry, and the drug should be administered in slow, graduated doses by a bedside physician. Physostigmine is dosed in 0.5-1.0 mg increments every 5-10 minutes up to a maximum of 2.0 mg. Atropine should be available at bedside for any patient receiving physostigmine since bradycardia can occur. Patients exposed to tricyclic antidepressants and patients with cardiac conduction delays, such as a widened QRS interval, should not receive physostigmine.

**Discussion of case questions**

1) What was the IV antidote this patient was administered? How does it work? Physostigmine is the antidote for anticholinergic syndrome. It inhibits acetylcholinesterase, the enzyme that degrades acetylcholine, thereby increasing the concentrations of acetylcholine and overcoming the competitive inhibition at nerve terminals.

2) What physical exam findings are classic with anticholinergic syndrome? Physical exam findings suggesting anticholinergic poisoning include hyperthermia, dry mouth, tachycardia, mydriasis, flushed dry skin, absent bowel sounds, urinary retention, agitation, hallucinations, lethargy, mumbling speech, undressing behavior (generally due to hyperthermia) and repetitive picking behavior. Blurred vision and photophobia may be due to mydriasis and paralysis of accommodation. Seizures, paralysis, respiratory depression, and coma may occur in severe
toxicity. Anticholinergic effects delay gastric emptying, resulting in a prolonged duration of action.

3) What treatment is usually required for patients with anticholinergic syndrome? Treatment primarily consists of supportive care. Hypotension generally responds to isotonic fluid administration. Agitation, psychosis, or seizures are treated with benzodiazepines such as diazepam or lorazepam. Cooling via evaporative methods is generally sufficient if hyperthermia is present. Physostigmine can reverse the peripheral or central anticholinergic syndrome if clinically indicated.

**Consultation assistance**

Consultation with a specialist in poison information or with a medical toxicologist can be obtained free of charge by calling the California Poison Control System at 1-800-222-1222.

This issue of CALL US... was written by Alicia Minns, MD.

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*The views expressed in this newsletter are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.*

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The California Poison Control System is operated by the School of Pharmacy, University of California, San Francisco. (callus@calpoison.org)