PLANTS - ACONITINE

Description

In North America includes monkshood *(Aconitum napellus)*, also called aconite, wolfsbane and helmet flower; mountain monkshood *(A. delphinifolium)*, western monkshood *(A. columbianum)*, wolfsbane *(A. lycoctonum)*, and related species. Species used in Chinese and Indian herbal medicine include *A. carmichaeli* (chuanwu) and *A. kusnezoffii* (caowu). Lateral root of *A. carmichaeli* is called fuzi and is less toxic than chuanwu. Genus *Aconitum* contains aconitine, mesaconitine and related alkaloids; concentrations vary from 0.3-2% in fresh tubers, 0.2-1.2% in fresh leaves and 1-2% in seeds. Delphinium and larkspur (genus *Delphinium*) contain aconitine-like alkaloids.

Poisonings have resulted from ingestion of aconitine-containing herbal products or from mistaking leaves for parsley and roots for horseradish or celery. In herbal products, roots are soaked or boiled; alkaloid content of chaunwu and caowu samples has been reported to be 0.6% and 0.4%.

Toxicity

Primary toxic effects include neurotoxicity (numbness, paresthesias) and cardiotoxicity (bradycardia, hypotension, dysrhythmias). Death is related to cardiac toxicity. CNS depression usually does not occur.

Mechanism of Toxicity

Aconitine and related alkaloids are neurotoxins and cardiotoxins, which act on the sodium channels of excitable membranes. Persistent activation of sodium channels prolongs the depolarization and prevents repolarization of membrane. Cardiac toxicity is manifested by enhanced automaticity which together with increased vagal tone and slowed atrial-ventricular conduction leads to dysrhythmias. Progressive muscular weakness is caused by depressed neuromuscular transmission. Aconitine stimulates the medullary centre of brain resulting in bradycardia and hypotension. Hyperventilation may be a central effect.

Toxic Dose

Lethal dose of pure aconitine in an adult is 3-6 mg. Severe poisoning has resulted from ingestion of 0.2 mg of aconitine. One gram of fresh *Aconitum napellus* contains from 2-20 mg of aconitine. Ingestion of 2-4 g of root has proven fatal.

Case Reports

Within 2 hours of ingesting aconite stem and leaves, a 61-year-old developed nausea, diarrhea, generalized discomfort and numbness of extremities. One hour later he developed hypotension (60/37 mmHg) and ventricular dysrhythmias which were refractory to cardioversion and antidysrhythmic therapy for 6 hours. Cerebral edema was diagnosed on day 5; patient died on day 6. Aconitine and related alkaloids were detected in urine.

A 35-year-old drank a broth containing a variety of herbs including roots of *Aconitum carmichaeli* (chuanwu) and *A. kusnezoffii* (caowu), and within 90 minutes developed nausea, weakness and paresthesias of trunk and extremities. Four hours later, patient was alert and oriented with a HR of 73 beats/min and BP 115/70 mmHg. He had minimal proximal muscle weakness in all limbs; reflexes and sensation were normal. Gastric lavage was performed and activated charcoal administered. Patient vomited four times over next 5 hours. ECG showed a ventricular rate of 85 beats/min with frequent multifocal ectopics. Patient remained mildly hypotensive (95/50 mmHg) for about 10 hours. All symptoms gradually subsided by 40 hours post ingestion.

Pharmacokinetics

Limited data. Rapidly absorbed from oral and topical exposure. Onset of symptoms within minutes or delayed up to 2 hours after ingestion (may require 2-3 doses of herbal products before toxicity is seen). Cardiac symptoms usually begin within 6 hours post ingestion but may be delayed up to 24 hours. In severe cases, death has occurred in 1-6 hours (range: minutes to 6 days). Recovery in mild poisoning may be seen within 1.5-2 days; patients with cardiac toxicity from Chinese herbal products have required 7-9 days for recovery. Elimination half-life of aconitine was 3 hours in one patient. Aconitine is detectable in urine in over 90% of patients.

Clinical Effects

- **Topical**: Pruritus, erythema, vesicles. Dermatitis has been reported from occupational exposure. Possible systemic effects.

- **Ingestion**:
  General: Symptoms generally begin with numbness and paresthesias in mouth and tongue. Nausea, vomiting, generalized paresthesias and muscle weakness may develop. Hypotension, bradycardia and ventricular ectopics are common. In serious cases, cardiac symptoms worsen. Death is primarily due to cardiac tachydysrhythmias and possibly respiratory paralysis. CNS depression usually does not occur.
  HEENT: Burning or paresthesia of mouth, lips, tongue and face are seen early (common). Increased salivation. Miosis (may be seen early). Diplopia, blurred vision, yellow-green scotomata, lacrimation. Chewing a root may cause lip, tongue and mouth swelling.
  CVS: Hypotension, chest pain or tightness, palpitations. Dysrhythmias can include bradycardia, supraventricular tachycardia, heart block, junctional rhythm, bi-directional tachycardia, ventricular ectopics, ventricular tachycardia or fibrillation (can be refractory), and torsades de pointes. Shock may develop. Cardiac arrest has occurred.
  Respiratory: Dyspnea, hyperventilation, respiratory paralysis leading to failure; possible pulmonary edema.
  Neurologic: Paresthesias in extremities (common,

generally resolve within 24 hours). Agitation (common), headache, dizziness, ataxia, lethargy, coma (rare) and seizures (rare).
GI: Nausea (common), severe vomiting, diarrhea, abdominal pain.
Fluids/Lytes/Acid-Base: Dehydration, hypokalemia from vomiting and diarrhea.
Musculoskeletal: Muscle weakness (common).
Other: Chills, sweating.

Treatment

1. **Topical**: Wash skin thoroughly with soap and water. Observe for systemic symptoms. **See** Ingestion.

2. **Ocular**: Flush eyes with a gentle stream of tepid water for 5 minutes. Obtain ophthalmologic opinion if irritation persists.

3. **Ingestion**: *Asymptomatic* patients should have continuous cardiac monitoring and monitoring of vital signs for at least 6 hours. ECG should be performed on admission and prior to discharge. *Symptomatic* patients should be monitored until resolution of symptoms.

4. Administer activated charcoal in cases of recent ingestion.

5. Protect airway and assist ventilation as needed.

6. Maintain fluid and electrolyte balance.

7. Monitor vital signs and ECG.

8. Symptomatic bradycardia may be treated with atropine. Electrical pacing may be required.

9. Hypotension unresponsive to IV fluids may be treated with vasopressors.

10. Cardiac dysrhythmias have been reported to be difficult to treat. Direct current cardioversion is often ineffective. No antidysrhythmic agent has been consistently effective. Lidocaine has been unsuccessful in a number of patients, while flecainide, amiodarone and IV magnesium have been useful in some patients.

11. Charcoal hemoperfusion has been used in patients with refractory dysrhythmias; there are no data on efficacy of alkaloid removal.

Key Points

- ✓ Primary toxic effects include numbness, paresthesias, bradycardia, hypotension and dysrhythmias. Death is related to cardiac toxicity.
- ✓ Rapidly absorbed from oral and topical exposure.
- ✓ Onset of symptoms within minutes or delayed up to 2 hours after ingestion. Cardiac symptoms usually begin within 6 hours but may be delayed up to 24 hours.
- ✓ In severe cases, death has occurred in 1-6 hours (range: minutes to 6 days).
- ✓ *Asymptomatic* patients should have continuous cardiac monitoring and monitoring of vital signs for at least 6 hours. ECG should be performed on admission and prior to discharge. *Symptomatic* patients should be monitored until resolution of symptoms.
- ✓ Treatment is primarily symptomatic and supportive.