Tricyclic Antidepressant (TCA) Overdose

California Poison Control 1-800-876-4766

Pediatric considerations

Low toxicity threshold of TCAs

Therapeutic doses range from 2-4 mg/kg/d

Toxicity is observed at doses of 10-20 mg/kg

Ingestion of only two 50-mg tablets in a 10-kg toddler can be sufficient to produce symptoms of toxicity

Pharmakinetics

Absorbed rapidly from GI tract in the alkaline small intestine

Anticholinergic effects of TCAs may impair gastric emptying and delay peak serum levels up to 12 hours after ingestion

Extremely lipophilic, resulting in a large volume of distribution (10-50 L/kg)

Tissue levels of TCAs far exceed those found in plasma; levels are 40 times greater in the brain and 5 times greater in the myocardium

Toxicologic Properties

Muscarinic acetylcholine receptor blockade, causing a variety of anticholinergic effects (See History) that characterize the early stages of intoxication

Inhibition of central and peripheral neurotransmitter (norepinephrine, serotonin) reuptake

By blocking norepinephrine reuptake, an initial transient hyperadrenergic state is followed by eventual catecholamine depletion

Alpha-adrenergic receptor blockade, causing peripheral vasodilation and subsequent hypotension, and slowing of sodium flux through fast channels of the myocardium, causing an anesthetic effect on the myocardium (quinidine-like effect)

Direct myocardial toxicity, in combination with catecholamine depletion, and alpha-adrenergic blockade can produce profound cardiovascular dysfunction

History

May present as a known ingestion

If the history of ingestion is not known, symptoms may be attributed to other medical conditions or toxins

Symptoms can progress rapidly

When toxicity is serious, it usually becomes apparent in the first hour after overdose

Anticholinergic effects: Dry mouth, Flushed skin, Blurred Vision, Urinary retention, Constipation, Dizziness, Emesis

Physical Signs

Anticholinergic effects: Altered mental status (agitation, confusion, lethargy), Resting sinus tachycardia, Dry mucous membranes, Mydriasis (pupil dilation), Fever

Cardiac effects: Hypertension (early and transient, should not be treated), Tachycardia, Orthostasis and hypotension, Arrhythmias (including

ventricular tachycardia and ventricular fibrillation, most serious consequence)/ECG changes (prolonged QRS, QT and PR intervals)

Central nervous system effects: Coma, Seizure, Myoclonic twitches/tremor, Hyperreflexia

Pulmonary effects: Hypoventilation resulting from CNS depression

Gastrointestinal tract effects - Decreased or absent bowel sounds

Lab Studies

Rapid bedside glucose level determination

Serum pH, electrolytes, calcium, magnesium, and phosphorus levels

Screen for anion-gap acidosis present in co-ingestions or lactic acidosis resulting from impaired perfusion

Identify metabolic disturbances that may exacerbate or potentiate TCA toxicity (ie, hypocalcemia may worsen myocardial depression or potentiate seizures or arrhythmias)

Urine toxicologic screening and serum salicylate and acetaminophen levels to screen for co-ingestions

Urine pregnancy test when indicated

Tricyclic levels are expensive, time consuming, and rarely helpful in the acute setting. They correlate poorly with severity of disease and prognosis

Other Tests

The single most important test to guide therapy and prognosis remains the 12-lead surface ECG. Important ECG changes include the following:

Prolongation of the QRS complex: Blockage of fast sodium channels slows phase 0 depolarization of the action potential. Ventricular depolarization is delayed, leading to a prolonged QRS interval. Patients with QRS intervals longer than 100 milliseconds are at risk for seizures, and patients with QRS intervals longer than 160 milliseconds are at risk for arrhythmias. QRS interval is evaluated best using the limb leads

R wave in aVR (SA Node) more than 3 mm: TCAs may have a greater selectivity and toxicity to the distal conduction system of the right side of the heart. The reason is unknown, but the effect can be observed as an exaggerated height of the R wave in aVR. Recent data suggest that this finding may be more predictive of seizure and arrhythmia than prolongation of the QRS complex

R/S ratio more than 0.7 in aVR

QT interval prolongation

Sinus tachycardia, usually secondary to peripheral anticholinergic effects

Arrhythmias

Medical Care

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Careful attention to airway, breathing, circulatory, and neurologic parameters are of utmost importance because of the risk of rapid deterioration

Anticipate airway compromise resulting from possible rapid deterioration of neurologic and cardiovascular functions

Secure the airway if gastric lavage and/or charcoal administration are to be performed in a patient with a decreasing level of consciousness

Gastric lavage

Should be limited to serious toxicity presenting soon after the ingestion has occurred. The patient should be without any sign of airway compromise, or the airway should already be secured

Activated Charcoal

1 g/kg PO/NG

Should be administered in patients with serious toxicity

Unless the patient's airway is intact or protected, administration of activated charcoal is contraindicated

Cardiotoxicity

Alkalization and sodium loading has been shown to be effective in the treatment of TCA-induced conduction disturbances, ventricular arrhythmias, and hypotension

Sodium bicarbonate attenuates TCA cardiotoxicity via several mechanisms:

Alkalinization of blood to a pH of 7.45-7.55 appears to uncouple TCA from myocardial sodium channels

Sodium increases extracellular sodium concentration and, thus, improves the gradient across the channel

Ventricular arrhythmia refractory to sodium bicarbonate may require treatment with lidocaine, magnesium sulfate, or both

Patients with hypotension refractory to fluid resuscitation and sodium bicarbonate may require vasopressor support

Direct acting alpha-agonists (eg, norepinephrine, phenylephrine) are indicated when significant hypotension persists despite adequate volume replacement (as monitored by central venous pressure or pulmonary capillary wedge pressure)

Dopamine may not be as effective because its action is mediated by the release of endogenous catecholamines that may be depleted during TCA toxicity

Use of dopamine or dobutamine alone may result in unopposed beta-adrenergic activity resulting from TCA-induced alpha blockade and, therefore, may worsen hypotension

Central nervous system toxicity

Most TCA-induced seizures should be treated aggressively

Acidosis produced by the vigorous muscle contraction, hypoxia, and hypercarbia that result from seizures may increase the concentration of the free drug, thereby augmenting cardiovascular toxicity

Benzodiazepines remain the agents of choice in treating seizures

Phenobarbital may be used as a long-acting anticonvulsant

Benzodiazepines are also the treatment of choice for the extreme agitation or delirium that occasionally are observed because of the anticholinergic effects of TCAs

Prognosis

More than 98% of patients survive with few or no sequelae

Keys to intact survival are early recognition and aggressive therapy with careful attention to the airway, ventilation, and hemodynamics

Sodium loading and alkalinization are, by far, the most important medical therapies