

Practical Clinical Toxicology

Toxicity of CNS Stimulants

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Introduction:

- Central nervous system (CNS) stimulants represent a diverse group of chemically & pharmacological dissimilar compounds.
- There are many CNS stimulants including: amphetamine, theophylline, caffeine, cocaine, strychnine, & camphore .
- They may cause acute or chronic toxicity due to drug abuse.

Amphetamine:

Toxicity of Amphetamines (amphetamine & amphetamine-like drugs) may result from:

- **Prescribed medications:** combination of dextroamphetamine & amphetamine (brand name: Adderall) & dextroamphetamine (brand name: Dexedrine) are approved for the treatment of attention deficit hyperactivity disorder (ADHD) & also for narcolepsy (a neurological condition marked by severe daytime drowsiness).
- **Street drug abuse:** recreational "street" amphetamine, is another cause of toxicity.

Mechanism of toxicity:

- Amphetamine induces CNS stimulation, mainly by causing release of catecholamines into central synaptic spaces & inhibiting their reuptake into nerve endings.
- Both CNS & peripheral nervous system (PNS) are stimulated due to sympathomimetic effects of catecholamines.
- A problem that frequently encountered by amphetamine users is tolerance to the anorexiant & euphoric actions.

- Because of tolerance to the anorexiant & euphoric actions, users may need to increase the dose, sometimes approaching several hundred milligrams daily.
- Toxic psychosis may appear after months of continued use.

Characteristics of poisoning:

- Clinical manifestations of acute & chronic amphetamine toxicity are listed in Table 1.
- The clinical effects of amphetamines are largely related to the stimulation of central & peripheral adrenergic receptors.
- Compared to cocaine, amphetamines are less likely to cause seizures, dysrhythmias, & myocardial ischemia.

- Tachycardia & hypertension are the most common manifestations of cardiovascular toxicity.
- Visual & tactile hallucinations, as well as psychoses, are common.
- Other sympathetic findings include mydriasis, diaphoresis, & hyperthermia.
- Rhabdomyolysis from amphetamine toxicity usually results from agitation & hyperthermia.

- Direct CNS effects may result in seizures.
- Euphoria may account for the widespread abuse potential of amphetamine.
- Death from amphetamine toxicity most commonly results from hyperthermia, dysrhythmias, & intracerebral hemorrhage.
- Chronic methamphetamine use has been linked to characteristic oral pathology known as “meth mouth”.
(Figure 1)



Figure 1. Meth Mouth

- Meth mouth is a condition that is characterized by extensive & severe tooth decay, & has been linked to poor hygiene, bruxism, & xerostomia associated with methamphetamine use.
- The lethal dose of amphetamine varies. The acute lethal dose in adults has been reported at 20 to 25 mg/kg. Death from as little as 1.5 mg/kg in adult has also been noted.

Table 1. Clinical manifestations of acute & chronic amphetamine toxicity

Clinical Manifestations of Amphetamine Toxicity	
Acute	Mydriasis
Cardiovascular system	Tremor
Hypertension	Nausea
Tachycardia	Other organ system manifestations
Dysrhythmias	Rhabdomyolysis
Myocardial ischemia	Muscle rigidity
Aortic dissection	Acute lung injury
Vasospasm	Ischemic colitis
Central nervous system	Laboratory abnormalities
Hyperthermia	Leukocytosis
Agitation	Hyperglycemia
Seizures	Hyponatremia
Intracerebral hemorrhage	Elevated CPK
Headache	Elevated liver enzymes
Euphoria	Myoglobinuri
Anorexia	
Bruxism	Chronic
Choreoathetoid movements	Vasculitis
Hyperreflexia	Cardiomyopathy
Paranoid psychosis	Pulmonary hypertension
Other sympathetic symptoms	Aortic and mitral regurgitation
Diaphoresis	Permanent damage to dopaminergic and serotonergic neurons
Tachypnea	

Management:

- Hyperthermia requires immediate interventions to achieve cooling. Therapeutic approach to a patient with amphetamine toxicity is summarized in Table 2.
- Because agitation & resistance against physical restraint may lead to rhabdomyolysis & continued heat generation, intravenous chemical sedation should be instituted immediately.
- The most appropriate choice of sedation is benzodiazepines because they have a high therapeutic index & good anticonvulsant activity.

- Antipsychotics, particularly potent dopamine antagonists such as haloperidol & droperidol, are frequently recommended by others for amphetamine-induced delirium.
- Antipsychotics may lower the seizure threshold, may cause acute dystonia & cardiac dysrhythmias.
- Patients with acute renal failure, acidemia, & hyperkalemia will likely require urgent hemodialysis.

Table 2. Management of patients with amphetamine toxicity

Management of Patients with Amphetamine Toxicity

Agitation

Benzodiazepines (usually adequate for the cardiovascular manifestations)

Diazepam 10 mg (or equivalent) IV, repeat rapidly until the patient is calm (cumulative dose may be as high as 100 mg of diazepam)

Seizures

Benzodiazepines

Barbiturates

Propofol

Hyperthermia

External cooling

Control agitation rapidly

Gastric decontamination and elimination

Activated charcoal for recent oral ingestions

Hypertension

Control agitation first

α -Adrenergic receptor antagonist (phentolamine)

Vasodilator (nitroprusside, nitroglycerin or possibly nicardipine)

Delirium or hallucinations with abnormal vital signs

If agitated: benzodiazepines

Delirium or hallucinations with normal vital signs

Consider risk/benefit of haloperidol or droperidol

Case study:

A 16-year-old girl was taken to the emergency room an hour after confessing to her mother that she had ingested a large handful of what supposed mescaline tablets. Instead, she actually consumed an unknown amount of amphetamine. Gastric lavage was performed immediately and the victim admitted. Shortly , she became agitated, and experienced auditory hallucinations and insomnia that persisted for 2 days. She was discharged on the third day after showing constant improvement.

Two days later, she began to experiencing auditory hallucinations. She also claimed to have appointed by God as a church elder.

She was readmitted to the hospital where she was treated with haloperidol, flurazepam, & chropromazine. Approximately 8 to 10 days later, she no longer experienced psychotic symptoms, and was discharged on the 14th hospital day.

*Thank
you*

