

Methamphetamine Toxicity

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Introduction

Methamphetamine is a highly addictive psychostimulant drug that is a derivative of amphetamine. Methamphetamine can produce euphoria and stimulant effects like those from other stimulants such as cocaine. In addition, methamphetamine is easily synthesized from inexpensive and readily obtainable chemicals. These characteristics have led to widespread and rampant abuse worldwide, currently estimated at 33 million users based on the 2016 United Nations Office on Drugs and Crime World Drug Report. In the United States, there were greater than 150,000 emergency department visits for toxicity from methamphetamine in 2011 based on data from the Substance Abuse and Mental Health Services Administration. The Drug Enforcement Agency estimated there were 439,000 past-month methamphetamine users in 2011.^{[1][2][3]}

Etiology

Methamphetamine is a Schedule II stimulant under the Controlled Substances Act, which means that it has a high potential for abuse and limited medical use. Methamphetamine hydrochloride is FDA-approved for long-term treatment of attention-deficit hyperactivity disorder (ADHD) with and short-term treatment of exogenous obesity. With regard to prescribed methamphetamine, in 2011 6.4 (11%) of children 4–17 years old had at some point in their lives been diagnosed with attention deficit hyperactivity disorder (ADHD), and 3.5 million were taking an ADHD medication. Illicit use of these prescribed medications among young adults without ADHD is an increasing problem. Methamphetamine used illegally may be snorted, ingested, injected, or smoked. A dangerous form of methamphetamine ingestion, “parachuting,” in which drugs are wrapped in toilet paper or plastic wrap to delay absorption, is becoming more commonplace.^[4]

Epidemiology

Methamphetamine was initially synthesized in the early 1900s and used unregulated as a nasal decongestant, to enhance alertness, and for weight loss. It was used extensively by myriad armed forces in World War II, the Korean War, and Vietnam War. Initially Japan experienced a high prevalence of abuse in the 1950s, followed by the United States in the 1960s. The street name “crank” refers to biker gangs’ transport of methamphetamine hidden in their motorcycle crankcase. The southwestern and west

coast states (including Hawaii) reported the highest prevalence of abuse from the 1970s to 1990s. Over the past decade, all regions of the United States have experienced a significant increase in the number of persons using the drug and emergency department visits. In the USA, methamphetamine abusers are predominantly white males in their 30s and 40s. More recently, epidemic abuse has been described in adolescents. Methamphetamine abusers tend to be mendacious and mistrustful of health care professionals when describing their drug history.[4][5][6]

Pathophysiology

Methamphetamine promotes the release of monoamine neurotransmitters dopamine, serotonin, and norepinephrine within central (CNS) and peripheral nerve endings. It also blocks re-uptake of dopamine similar to cocaine, and it may act as a false transmitter. This explains its euphoric effects in the CNS and sympathomimetic effects such as tachycardia and hypertension.[7]

Toxicokinetics

For oral administration, peak methamphetamine concentrations are seen in 2-4 hours; snorting, smoking, and injecting peak concentrations occur within minutes. Elimination half-life ranges from 6-15 hours. Methamphetamine is metabolized via the cytochrome P450 complex to active amphetamine, and p-OH-amphetamine and norephedrine, which are both inactive. The rate of excretion into the urine is enhanced as pH falls. Urine toxicology screening may be positive up to 4 days after use.

History and Physical

Acute and long-term methamphetamine use may lead to abnormal findings on examination of the following systems: cardiovascular, CNS, gastrointestinal, renal, skin, and dental. Tachycardia and hypertension are frequently observed, and atrial and ventricular dysrhythmias may occur. Chest pain from cardiac ischemia and infarction, acute aortic dissection or an aneurysm has been associated with methamphetamine abuse. Hypotension may be observed with methamphetamine overdose with profound depletion of catecholamines. Acute and chronic cardiomyopathy results directly from methamphetamine cardiac toxicity and indirectly from chronic hypertension and ischemia; intravenous use may result in endocarditis; patients may present with dyspnea, edema, and other signs of acute congestive heart failure (CHF) exacerbation. [8] Acute noncardiogenic pulmonary edema and pulmonary hypertension may result from acute and chronic use, as well as from adulterants introduced during intravenous use such as talc or cornstarch.

Severe abdominal pain may result from acute mesenteric vasoconstriction; methamphetamine has also been associated with the formation of ulcers and ischemic colitis. Renal failure may occur from rhabdomyolysis, necrotizing angitis, acute interstitial nephritis or tubular necrosis.

Skin findings include delusions of parasitosis, and chronic skin-picking may result in neurotic excoriations and prurigo nodularis ("speed bumps"). Injectors frequently present with abscess and cellulitis, which they often blame on a "spider bite." Dental examination usually reveals severe caries, especially of the maxillary teeth "meth mouth." This results from maxillary artery vasoconstriction, xerostomia, and poor hygiene. Methamphetamine use during pregnancy can be fatal to the mother and

fetus from placental vasoconstriction resulting in spontaneous abortion. Methamphetamine is secreted in breast milk.

Evaluation

An electrocardiogram should be performed to assess for myocardial ischemia and tachydysrhythmia. Complete blood count, comprehensive chemistry panel, troponin, B-type natriuretic peptide (BNP), creatine kinase (CK), and urinalysis are helpful tests to obtain for patients presenting with acute methamphetamine toxicity. Methamphetamine users are rarely forthcoming about their most recent drug use, and a urine toxicology screen is extremely helpful, as the differential diagnoses for sympathomimetic signs and symptoms is quite wide. Computed tomography of the head for acute headache or altered mental status may be necessary to rule out hemorrhage. A chest radiograph is essential for those patients presenting with chest pain or dyspnea.[9][10]

Treatment / Management

Benzodiazepines represent first-line treatment for methamphetamine toxicity but frequently require repeated and escalated dosing to achieve the effect. Methamphetamine users may be resistant to benzodiazepine treatment. Antipsychotics, such as haloperidol and olanzapine, are also useful in the management of agitation. Combination treatment with benzodiazepines and antipsychotics has been shown to be more efficacious than monotherapy. [11] Diphenhydramine is often added to enhance sedation and as prophylaxis against dystonia and akathisia. A common example of this is the “B-52” with its combination of haloperidol (5 mg), diphenhydramine (50 mg), and lorazepam (2 mg).[3][9]

For concomitant tachycardia and hypertension that does not respond to sedation, the combined beta/alpha-blocker labetalol is preferred based on a systematic review from 2015. [12] For tachycardia without hypertension, the beta 1-blocker metoprolol is preferred. Both labetalol and metoprolol have the added advantage of being lipophilic, with CNS penetration and antagonism of excess monoamines causing agitation. Despite the unfortunate persistence of dogma carried over from a small number (n=7) of cocaine cases, there have been no cases of “unopposed alpha stimulation” reported with beta-blocker use and treatment of methamphetamine toxicity. For severe hypertension without tachycardia, nitroprusside is recommended as it is easily titrated to effect and has a half-life of minutes.

Administration of copious intravenous crystalloid is also recommended to enhance urinary elimination and prevent acute renal failure. Calcium channel blockers may be used but do not directly treat the hyperadrenergic state induced by methamphetamine, and their reduction of tachycardia and blood pressure is much less predictable than beta-blockers.

Differential Diagnosis

- Acute MI
- Hypertensive crisis
- Hallucinogen toxicity
- Hyperthyroidism, Thyroid storm
- Cocaine toxicity

- Seizures
- Subarachnoid hemorrhage
- Ischemic stroke

Complications

- Hypertension
- Intracranial hemorrhage
- Seizures
- Ischemic stroke
- Coma
- Hyperthermia
- Heart failure
- Arrhythmias

Enhancing Healthcare Team Outcomes

Methamphetamine toxicity is best managed by a team of healthcare professionals that include a social worker, addiction nurse, cardiologist, internist, and a mental health counselor. Once a diagnosis of methamphetamine toxicity is made, the patient should be referred to a psychiatrist or a drug addiction center. Patients need to be educated about the potentially life-threatening adverse effects of this illicit agent. Unfortunately, addiction to methamphetamine is one of the most difficult to cure as there is no agent that can prevent abstinence. The majority of patients continue to abuse the drug until they run afoul of the legal system.[13][14](Level V)

Outcomes

Methamphetamine toxicity is a real serious social problem. The addiction is very difficult to stop, and as yet there is no pharmacological agent that can help patients abstain from this illicit agent. Despite referral to addiction clinics, relapses into addiction are common. When the drug is forcibly withdrawn while the individual is incarcerated or in hospital, withdrawal reactions are very common and often require sedatives or anti-anxiety agents. Deaths from methamphetamine toxicity are common and include arrhythmias, intracranial hemorrhage, and cardiogenic shock. Use of methamphetamine during pregnancy has also been linked to preterm birth and intrauterine growth restriction. The majority of patients come from a subculture that is involved in the manufacture of the drug, and until that environment is changed, the cycle of addiction will continue. [15][16][17](Level V)

Questions

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Figures



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