

Methamphetamine abuse: a growing worldwide problem

Olson KR.

California Poison Control System, University of California, San Francisco

Methamphetamine and related drugs are responsible for an increasing number of admissions to emergency departments. In the US, the leading causes of drug abuse related ED visits in 2005 were cocaine, heroin, and methamphetamine (1). Amphetamine-like drugs share a common chemical backbone with various substitutions that impart different pharmacokinetic and clinical consequences (2,3). The substituted amphetamine methylenedioxymethamphetamine (MDMA, or “ecstasy”) now accounts for almost 10% of amphetamine-related ED visits (1).

Methamphetamine use has reached Asia, with reports of use and/or trafficking from Taiwan, China, North Korea, Japan, and Thailand (4,5).

Methamphetamine may be ingested, smoked, injected intravenously, or nasally insufflated (“snorted”). Crystalline methamphetamine hydrochloride (“ice”) is often smoked in a glass pipe or vial (6). Onset of clinical effects is most rapid with intravenous injection or smoking, otherwise peak effects after ingestion occur after 1-3 hours. Ingestion of the drug in a plastic bag or other container may delay its onset for several hours (7,8). The half-life (6-15 hours) and duration of effect depend on the urine pH as methamphetamine, a weak base, is reabsorbed in alkaline urine. The volume of distribution is 3.5-5 L/kg, reflecting its diffuse distribution into tissues. Postmortem redistribution can give falsely elevated levels, especially from heart blood. (9)

Methamphetamine and related drugs act largely by stimulating the release of neurotransmitters such as dopamine (DA), norepinephrine (NE) and serotonin (5-HT). Varying the chemical substitutions on the phenylethylamine structure may influence the relative effect on DA, NE or 5-HT (10). In addition, other neuroendocrine functions may be affected; for example, MDMA appears to have significant effects on the 5-HT_{2A} receptor, as well as causing an increase in antidiuretic hormone (ADH) contributing to hyponatremia (11).

Typical clinical effects of acute methamphetamine intoxication include central nervous system (CNS) stimulation with euphoria, anxiety, agitation, psychosis (12) and seizures (13). Cardiovascular effects include tachycardia and hypertension, and on rare occasion acute myocardial infarction, stroke or aortic dissection. Agitation, seizures and increased muscle activity, as well as enhanced serotonin effect, can lead to hyperthermia and rhabdomyolysis, which in turn can cause acute renal failure. Severe hyperthermia can cause hypotension, disseminated coagulopathy, and brain damage (14).

Hyponatremia is an unusual complication of MDMA abuse, and may result from a combination of excessive water intake and enhanced ADH. It appears to be more common in women compared to men (11). It can result in confusion, coma, seizures and brain damage.

Sequelae of chronic amphetamine abuse include psychosis (15,16), depression (upon withdrawal of the drug), and cardiomyopathy (17). CNS vasculitis may contribute to stroke in chronic users

(18). Parkinson's disease may be more common among chronic high-dose users (19,20). A common finding in patients with chronic methamphetamine use is severe tooth decay and fractures, apparently due to bruxism and dry mouth.

Treatment of acute methamphetamine intoxication includes assessment of the airway, breathing and circulation (ABCs) and control of agitation, seizures, abnormal blood pressure or pulse, and rapid lowering of elevated body temperature (21). Agitation is best treated with benzodiazepines; dopamine-blocking sedatives such as haloperidol or chlorpromazine are also effective although they may lower the seizure threshold. Seizures should be treated with benzodiazepines followed by barbiturates (eg, phenobarbital) or propofol. Hypertension and tachycardia may be treated with a combination of vasodilators and beta- adrenergic blockers; use of nonselective beta blockers without a vasodilator might paradoxically raise the blood pressure due to blockade of beta-2 mediated vasodilation leading to unopposed alpha-adrenergic effect. Severe hyperthermia needs immediate management, and is most rapidly treated with neuromuscular paralysis and intubation under sedation. Other temperature-lowering techniques include application of tepid water or mist and fanning to encourage evaporative cooling (14). Severe hyponatremia with coma or seizures should be treated with hypertonic (3%) saline; otherwise, gradual normalization of the sodium level with supplemental intravenous normal saline is preferred (22).

References: 1. DAWN 2005: National Estimates of Drug-Related Emergency Department Visits. U.S. Department of Health & Human Services. <http://DAWNinfo.samhsa.gov> 2. Craner JC et al: Fatalities caused by the MDMA-related drug paramethoxyamphetamine (PMA). *J Anal Toxicol* 2001; 25:645. 3. Lin DL et al: Recent paramethoxy methamphetamine (PMMA) deaths in Taiwan. *J Anal Toxicol* 2007; 31:109. 4. Farrell M and Mardsen J: Methamphetamine: drug use and psychoses becomes a major public health issue in the Asia Pacific region. *Addiction* 2002; 97:771. 5. Matsumoto T et al: Methamphetamine in Japan: the consequences of methamphetamine abuse as a function of route of exposure. *Addiction* 2002; 97:809. 6. Fulde GWO and Wodak A: Ice: cool drug or real problem? *Med J Australia* 2007; 186:334. 7. Hendrickson RG et al: "Parachuting" meth: a novel delivery method for methamphetamine and delayed- onset toxicity from "body-stuffing". *Clin Toxicol* 2006; 44:379. 8. Takekawa K et al: Methamphetamine body packer: acute poisoning death due to massive leaking of methamphetamine. *J Forensic Sci* 2007; 52:1219. 9. Baselt RC: d-Methamphetamine. In Disposition of Toxic Drugs and Chemicals in Man, 5th Ed. Chemical Toxicology Institute, Foster City California. 10. Lynton RC and Albertson TE: Amphetamines and Designer Drugs. In Medical Toxicology, 3rd Edition (Dart RC, editor), Lippincott 2004. 11. Rosenson Jet al: Patterns of ecstasy-associated hyponatremia in California. *Ann Emerg Med.* 2007 Feb;49(2):164. 12. Dore G and Sweeting M: Drug-induced psychosis associated with crystalline methamphetamine. *Australasian Psychiatry* 2006; 14:86. 13. Prosser JM et al: A 14-year-old girl with agitation and hyperthermia. *Pediatr Emerg Care* 2006; 22:676. 14. Rusyniak DE and Sprague JE: Toxin-induced hyperthermic syndromes. *Med Clin North Am* 2005; 89:1277. 15. Barr AM et al: The need for speed: an update on methamphetamine addiction. *J Psychiatr Neurosci* 2006; 31:301. 16. McKetin R et al: The prevalence of psychotic symptoms among methamphetamine users. *Addiction* 2005; 101:1473. 17. Yeo KK et al: The association of methamphetamine use and cardiomyopathy in young patients. *Am J Med* 2007; 120:165. 18. Ohta K et al: Delayed ischemic

stroke associated with methamphetamine use. J Emerg Med 2005; 28:165. 19. Hanson GR et al: The methamphetamine experience: a NIDA partnership. Neuropharmacol 2004; 47:92. 20. Garwood et al: Amphetamine exposure is elevated in Parkinson's disease. Neurotoxicol 2006; 27:1003. 21. Ruha AM and Yarema MC: Pharmacologic treatment of acute pediatric methamphetamine toxicity. Pediatr Emerg Care 2006; 22:782. 22. Albertson TE: Amphetamines. In Poisoning & Drug Overdose, 5th Edition (Olson KR, Ed), McGraw-Hill, 2007.