Psychostimulant poisoning

Dan McCormack, Emergency/Toxicology Registrar, The Canberra Hospital, and Nicholas A Buckley, Department of Clinical Pharmacology and Toxicology, Australian National University Medical School, Canberra

Summary

Psychostimulants are sympathomimetic activators of the central nervous system. Licit examples include caffeine, decongestants, methylphenidate, dexamphetamine and some drugs for weight loss. While these have the potential for abuse, the major problem in Australia is illicit use of amphetamines, ecstasy (3,4-methylenedioxymethamphetamine) and cocaine. These substances are taken to produce feelings of euphoria and well-being, increased energy and alertness. Potential problems with toxicity range from tachycardia and hypervigilance to seizures, psychosis and serotonin syndrome. Management is primarily directed at reversing the excitation of the central nervous system by sedation with benzodiazepines, but more specific treatments are occasionally indicated.

Key words: amphetamines, drug abuse, overdose.

Introduction

In the 2004 national drug survey, over 9% of Australians over the age of 14 years had tried amphetamine/methamphetamine, 7.5% had tried ecstasy and nearly 5% had tried cocaine. From this survey, it is estimated that over half a million people used ecstasy at least once in 2004, and a similar number had used amphetamines. In contrast, only 1% had used cocaine in the previous year.1 These drugs have a long history of use and abuse. Cocaine was first isolated in 1860, amphetamines were first synthesised in 1887, ecstasy was first patented in 1914, and methamphetamines were produced in 1919. Each drug has had a variety of licit indications at various times. Methamphetamine was prescribed for a range of conditions including depression and obesity. Amphetamines were used as decongestants (Benzedrine) and have been given to soldiers to increase energy and alertness. They are still used for disorders like narcolepsy and attention deficit hyperactivity disorder, while cocaine is still in limited use as a topical anaesthetic. Even ecstasy has been used as an adjunct to psychotherapy in the USA.

Current patterns of use and abuse

The predominant amphetamine available during the 1980s was amphetamine sulphate. Introduction of legislative controls over the precursor materials has meant that in recent times over 90% of amphetamines seized have been methamphetamines. Methamphetamines are produced by reduction of ephedrine or pseudoephedrine, found in decongestants and other household products, making them relatively simple drugs to produce. Ecstasy is 3,4-methylenedioxymethamphetamine (MDMA) and is mostly smuggled into Australia because of the lack of local expertise in production, although local production may be increasing. Cocaine is purified from a plant and is imported.

Formulations and cost

Amphetamines and ecstasy are commonly taken as tablets. The tablets can also be crushed and injected. Ecstasy costs between $30 and $50 a tablet. There are several different kinds of methamphetamines available (see box). ‘Speed’ is methamphetamine powder, generally manufactured in Australia, and is usually low quality. ‘Pills’ are tablets of methamphetamine produced in Australia which are often sold as ecstasy. ‘Base’ is an oily, damp powder that is made in Australia and is generally of high purity. ‘Ice’ or ‘crystal meth’ is high quality methamphetamine crystals, generally imported from Asia. Methamphetamines can be smoked, injected or swallowed. The cost of methamphetamine varies in different parts of Australia and with its form, from $50 for a ‘point’ (0.1 g) of crystal to $55 for a gram of speed.2 Cocoine can be snorted, smoked or injected. It costs approximately $200/g.

- ‘speed’ methamphetamine powder
- ‘pills’ methamphetamine tablets
- ‘base’ oily damp methamphetamine powder
- ‘ice’ or ‘crystal meth’ methamphetamine crystals
- ecstasy 3,4-methylenedioxymethamphetamine (MDMA)
and hypertension, hypervigilance, dilated pupils, rapid speech, exaggerated 'fight or flight' response. Signs include tachycardia and psychological effects that psychostimulants elicit are an and circumstances. The common adverse acute physiological are rare and partly dependent on individual susceptibility events that precipitate a hospital visit. Serious complications The majority of ecstasy users do not experience adverse Clinical presentations

The majority of ecstasy users do not experience adverse events that precipitate a hospital visit. Serious complications are rare and partly dependent on individual susceptibility and circumstances. The common adverse acute physiological and psychological effects that psychostimulants elicit are an exaggerated 'fight or flight' response. Signs include tachycardia and hypertension, hypervigilance, dilated pupils, rapid speech, clenched jaw and bruxism, diaphoresis, peripheral vasoconstriction and being generally restless with repetitive movements. More serious acute sequelae can be grouped by the affected organ systems:

- central nervous system – haemorrhagic and non-haemorrhagic stroke, seizures, coma, cerebral vasculitis
- cardiovascular – hypertension, arrhythmias, cardiac ischaemia (coca ine in particular) and aortic dissection
- psychiatric – aggression, delirium, paranoid psychosis
- respiratory – non-cardiogenic pulmonary oedema, pulmonary hypertension
- gastrointestinal – diarrhoea, mesenteric ischaemia, hepatotoxicity
- renal – acute renal failure
- musculoskeletal – rhabdomyolysis
- other – serotonin toxicity, hyperthermia, syndrome of inappropriate antidiuretic hormone, obstetric complications, urinary retention.

MDMA and amphetamines can cause serotonin toxicity. This is particularly likely if they are taken in conjunction with monoamine oxidase inhibitors including moclobemide. Extreme dehydration and water intoxication have been associated with MDMA toxicity. Dehydration is due to a lack of awareness of thirst in the setting of extreme physical activity. Water intoxication can be a consequence of increased antidiuretic hormone secretion and drinking too much water (to prevent dehydration), leading to complications associated with hyponatraemia. Cardiac ischaemia can occur with any of these drugs, but is particularly associated with cocaine. It is due to a combination of increased myocardial demand, coronary vasoconstri ction, and increased thromboxane A\textsubscript{2} activity and thrombus formation. The risk of a myocardial infarction is 24 times greater in the first hour after cocaine ingestion, even in persons otherwise of low risk.

**Assessment**

A history of the ingested substances needs to take into account possible substitutions or the addition of other substances to illicit tablets. Past history should focus on medication (due to concerns about potentiating drug interactions), psychiatric history and other risk factors for serious adverse effects (for example cardiovascular disease or epilepsy). Alternative medical diagnoses need to be considered.

A full set of physical observations is important, particularly temperature, blood pressure and pulse. Relevant investigations include an electrocardiogram (ECG), serum electrolytes, liver function tests and creatine kinase concentration. Screening for drugs of abuse in the urine may confirm exposure to particular drugs, but is not useful in acute management which is based on the detection and prevention of complications.

**Management**

While some patients can just be observed, others will need management of specific complications.
Psychiatric complications

Psychiatric sequelae need to be managed in a calm, non-confrontational manner, as for any agitated, potentially aggressive disorder. Either oral or intravenous sedation may be needed if further assessment is required and the patient is unco-operative. The primary aim is to ensure that the patient is not a risk to themselves or the staff. Benzodiazepines are preferred and have the added benefit of decreasing the likelihood of seizures. Antipsychotics such as haloperidol may be useful for patients with severe psychosis. ‘Chemical sedation’ should only be given in a monitored environment where rapid intervention is possible in the event of respiratory compromise or hypotension.

Depressive symptoms can occur in the days following stimulant use. These may progress to overt depressive illness possibly warranting antidepressants. Suicidal ideation and suicide attempts may occur.

Cardiovascular complications

Hypertension associated with amphetamine and cocaine abuse is mostly transient and will not require specific management. Benzodiazepines will generally provide adequate control of blood pressure in the agitated patient. Severe hypertension in the setting of possible neurovascular pathology may require vasodilators such as phentolamine or hydralazine.

If cardiac chest pain is suspected in someone who has taken cocaine it should be treated with aspirin, oxygen and nitrates. Beta blockers are contraindicated as unopposed alpha-receptor stimulation can worsen vasoconstriction and increase blood pressure. Most cocaine-related chest pains do not result in infarction and the risk of subsequent ischaemic events without further drug abuse is relatively low. Standard chest pain protocols including monitoring cardiac enzymes and ECGs can be followed. If there are confounding factors then a semi-urgent exercise stress test should be organised.

Neurological complications

An acute neurological deterioration such as a severe headache, seizures, localising signs or ongoing confusion requires a CT scan of the brain to exclude haemorrhagic or non-haemorrhagic stroke and traumatic injury secondary to the confused state. Seizures can be controlled in the first instance with benzodiazepines and then phenoobarbitone if persistent or recurrent. Phenytoin has no role in the treatment of drug-induced seizures.

Serotonin syndrome

The diagnosis of serotonin toxicity is based on clinical findings – in particular clonus and hyperreflexia. Treatment is essentially supportive, with intravenous hydration and close monitoring. Severe serotonergic crises with marked hyperthermia and development of pyramidal rigidity require admission to intensive care for active cooling, paralysis and ventilation to prevent development of rhabdomyolysis and disseminated intravascular coagulation. There are case reports of moderate to severe serotonin syndrome being treated with cyproheptadine 4–8 mg three times a day, in addition to supportive measures.

Chronic sequelae

The most commonly repeated findings in studies of MDMA, methamphetamine and cocaine use have been problems in the area of learning and memory. There is both animal and human evidence of neurotoxicity, but the evidence as to whether this is reactive but reversible, or permanent and irreversible in humans is inconclusive.

References


Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 115)

7. The most common substance found in ecstasy tablets currently available in Australia, other than 3,4 methylenedioxymethamphetamine (MDMA), is methamphetamine.
8. Cocaine use increases the risk of myocardial infarction in otherwise healthy people.
9. Chest pain following cocaine use is managed with beta blockers.