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Acute effects of drugs of abuse

John P Thompson MRCP(UK), Senior Lecturer in Clinical Pharmacology
National Poisons Information Service (Cardiff Centre), Academic Centre, Llandough Hospital, University of Wales College of Medicine, Cardiff

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The terms ‘recreational drugs’ and ‘drugs of abuse’ are, to some extent, societal. Substances known to be toxic (eg ethanol) may be legal and culturally accepted in some countries but illegal in others. Similarly, therapeutic use of heroin (diamorphine) as an analgesic or a cannabinoid as an antiemetic is deemed legal and acceptable.

Drugs of abuse are widely available. Data from the British and Scottish crime surveys suggest that 22% of 16–29 year olds have used cannabis within the previous 12 months but that opiate use is much rarer.^{1,2} Exact quantification of acute drug abuse deaths remains difficult due to the methods of classification, but several hundred people die acutely from drugs of abuse each year in England and Wales and the number is rising for heroin.³

Adverse effects of drugs of abuse

The adverse effects of drugs of abuse are both acute and chronic. Adverse effects on the user include risks associated both with the drug itself and with the route of administration. Intravenous drug abusers in particular are at increased risk.⁴ Drugs are often administered in secluded places where even transient respiratory depression may prove fatal. Infections associated with drug misuse include viral hepatitis, HIV, bacterial endocarditis, typically affecting the right side of the heart, and local infections at the site of injection.

Societal effects of drug abuse include those from the effect of crime undertaken to support an illegal and potentially expensive activity, and also indirectly due to the spread of infection into the wider community. Many treatment strategies for drug abusers (eg needle exchange schemes) focus upon harm reduction rather than an attempt to end misuse completely. Even these schemes are not without their own problems – methadone, prescribed as a heroin substitute, is now a regular cause of death.⁵

For overdose from drugs of abuse, the mainstay of treatment remains good supportive care. The importance of obtaining an accurate history and in maintaining airway, breathing and circulation cannot be overemphasised.

Key Points

Abuse of drugs is common

The diagnosis of drug abuse should be considered in patients with decreased consciousness

The diagnosis of drug abuse should be considered in agitated patients

Treatment is generally supportive and symptomatic

Harm may arise from both the route of administration and the drug itself

Street drugs are not pure products

Consider associated infectious diseases

Anticipate withdrawal syndromes

KEY WORDS: cannabis, cocaine, drugs of abuse, ecstasy, gamma hydroxybutyrate (GHB), heroin, lysergic acid diethylamide (LSD), overdose, poisoning

Heroin (diacetylmorphine, diamorphine)

Heroin is an opioid analgesic. Street heroin is an impure substance; it may typically contain around 40% active ingredient, having been diluted (cut) with other substances including sugars or talc. However, the concentration may vary greatly, which contributes to accidental overdoses. It is injected intravenously ('main lining'), intramuscularly, or subcutaneously (skin-popping), or smoked.

Heroin is rapidly converted to morphine. Unwanted effects include nausea, vomiting and respiratory depression. With regular use, abusers develop tolerance to some of these effects and require increased doses to maintain the same 'high'. Physical and psychological dependence develops. Withdrawal features include drug craving, anxiety, agitation, myalgia, vomiting, diarrhoea, yawning and rhinorrhoea.

Accidental overdose may occur due to a change in purity of the heroin or because users have lost tolerance – as may occur on release from prison. Respiratory depression occurs with bradypnoea and this is the commonest cause of death in overdose. Features of opioid overdose (Table 1) are potentiated by co-ingestion of alcohol and other central nervous system depressants.

Treatment of overdose

If there is coma or respiratory depression, naloxone, a specific opioid antagonist, should be given, preferably intravenously, in an amount sufficient to improve respiration and the level of consciousness. Typical doses are 400 µg to 2 mg for an adult, or 10 µg/kg for a child. Naloxone is a competitive antagonist and large doses may be required in a seriously poisoned patient. It should be administered with care because naloxone may precipitate an acute withdrawal crisis in addicts. Naloxone has a shorter half life (1–2 hours) than morphine (3–4 hours) and patients require careful monitoring as the effects of naloxone wear off faster than those of the opiate. Some patients require continued naloxone administra-

Table 1. Features of acute opioid overdose.

- Slow respiration
- Central nervous system depression
- Miosis
- Aspiration pneumonia
- Hypotension
- Tachycardia
- Non-cardiac pulmonary oedema
- Rhabdomyolysis
- Hallucinations

tion via an infusion pump. Administering two-thirds of the 'wake up' dose per hour is a reasonable initial estimate of the dose required, but it is not a substitute for regular careful monitoring of these patients. Failure to respond to adequate doses of naloxone suggests that an opiate is not the cause of the decreased level of consciousness and other causes should be sought. Patients should be observed for at least six hours after administration of the last dose of naloxone. Mechanical ventilation may be required in the presence of pulmonary oedema. Advice should be given to patients regarding their drug abuse habit and may include advice regarding safer routes of administration.

Cocaine (benzoyl-methylecgonine)

Cocaine may be snorted, smoked or injected. Crack cocaine (freebase) is generally taken by inhaling the vapour after a crystal (rock) has been heated.

Table 2. Features of acute cocaine overdose.⁶

- Agitation
- Delirium
- Tachycardia
- Hypertension
- Cardiac arrhythmia
- Chest pain
- Myocardial infarction
- Sweating
- Convulsions
- Hyperpyrexia
- Metabolic acidosis

Cocaine is a natural alkaloid which, in addition to its anaesthetic action of blocking fast sodium channels, inhibits neuronal reuptake of dopamine and catecholamines. It also increases platelet aggregation and has an effect on the vascular epithelium. Chronic use may result in perforation of the nasal septum due to local vasoconstriction and cerebrospinal fluid (CSF) rhinorrhoea. Pulmonary granulomas, oedema, pneumothorax and pneumomediastinum have also been described.

Treatment of toxicity

Features of acute cocaine overdose are shown in Table 2. Treatment is supportive. Convulsions should be controlled using a benzodiazepine (eg diazepam), which also lessens agitation. Hypertension and tachycardia often settle once diazepam has been administered, but if hypertension persists nitrates and calcium channel blockers are alternative therapies. Beta-blockers should be avoided as unopposed alpha stimulation may worsen coronary artery spasm and peripheral vasoconstriction. Metabolic acidosis should be corrected using sodium bicarbonate. Dantrolene may be administered to hyperthermic patients who fail to respond to conventional cooling measures and diazepam.

Ecstasy (3,4-methylenedioxy-methamphetamine (MDMA))

Ecstasy is a semisynthetic amphetamine, particularly popular on the 'dance scene', with thousands of tablets consumed weekly. Its toxicity seems unpredictable and some deaths have occurred following ingestion of amounts previously consumed uneventfully. A typical ecstasy tablet may contain 30–150 mg, but tablet analysis reveals that contaminants or other products are frequently present.

Ecstasy intoxication (Table 3)

The acute toxicity of ecstasy is due to effects on the adrenergic and serotonin (5HT) systems, centrally and peripherally. Typically, effects will occur within one hour and may last up to six hours after a single tablet. Larger ingestions

Table 3. Features of acute ecstasy intoxication.

Moderate doses	Higher doses
Agitation	Delirium
Anxiety	Nystagmus
Insomnia	Tremor
Dry mouth	Coma
Dilated pupils	Hyperreflexia
Hypertension	Convulsions
	Hyperpyrexia
	Rhabdomyolysis
	Adult respiratory distress syndrome
	Hypertension followed by hypotension

may produce pharmacological effects for up to 48 hours.

Early deaths are due to cardiac arrhythmias which may be either supraventricular or ventricular. Late deaths occur due to hyperthermia and a syndrome resembling neuroleptic malignant syndrome or hepatic failure. Fatal intracerebral haemorrhage, hepatic failure and myocardial infarctions have been reported. Hyponatraemia occurs due to inappropriate antidiuretic hormone secretion and generally responds to limiting fluid intake.

Case reports suggest that there may be changes in mood and cognition in regular users. Chronic administration of ecstasy produces damage to serotonergic neurones in animal models⁷ and human data suggest users have lower CSF concentrations of 5-hydroxyindoleacetic acid than controls.

Treatment of intoxication

Treatment of ecstasy intoxication is symptomatic and supportive. An ECG should be obtained, and blood taken to monitor renal and liver function, creatine kinase and acidosis, and in severe cases to exclude disseminated intravascular coagulation. For moderate poisoning, blood pressure and temperature should be monitored for at least 12 hours, and agitation and convulsions controlled using a benzodiazepine. Hypertension may be treated using a nitrate or calcium antagonist, and hypotension with intravenous fluids. In severe cases, dopamine may be required once fluid replacement has been under-

taken. If the rectal temperature exceeds 39°C, active cooling with a fan or tepid water is required and dantrolene may need to be administered to decrease heat production from overactive muscles. If these measures fail to control the hyperpyrexia, mechanical ventilation with muscle paralyzing agents may be necessary. Cyproheptadine, a 5HT antagonist, may also be used.

LSD (lysergic acid diethylamide)

Lysergic acid diethylamide (LSD) is usually ingested as microdots (stamps), tablets or capsules. It is a potent agonist at 5HT_{1A} receptors and also at post-synaptic 5HT₂ receptors. Acute effects at 'normal doses' include confusion, agitation, visual hallucinations, dilated pupils, mild hypertension and occasionally raised temperature. It has a low acute toxicity, but in overdose may cause metabolic acidosis, coma and respiratory arrest. Anxiety, depersonalisation, paranoia and hyperacusis occur. Whilst illusions are common, frank hallucinations are rare. Patients usually recover in a few hours, although occasionally hallucinations last up to two days and psychotic states somewhat longer. Neuroleptic malignant syndrome is sometimes observed. Chronic reactions are described with LSD. These include flashbacks, severe depression, prolonged psychotic reactions and exacerbations of pre-existing mental illness. Tolerance is said to occur rapidly, with dose escalation required to achieve the same effect.

Acute adverse effects are generally

short-lived; they generally occur within two hours and peak within four hours, with recovery usually complete within 8–12 hours.

Treatment of intoxication

Treatment is symptomatic and supportive. Gastric decontamination is not indicated as absorption occurs rapidly. Patients should be reassured and nursed in a dim, quiet environment with external stimuli minimised. Benzodiazepines (eg diazepam) are the treatment of choice for sedation. Phenothiazines should be avoided as cardiovascular collapse has been reported.

GHB (gamma hydroxybutyrate)

Gamma hydroxybutyrate (GHB) was originally developed as an anaesthetic agent but fell from favour due to dysphoric effects on recovery. It is now marketed as a body building agent and psychedelic drug. It may be purchased as a powder, capsules or liquid. Some abusers manufacture GHB from gamma butyrolactone using alkalis; the resulting impure product may be highly alkaline and cause mucosal burns.

Although features of intoxication (Table 4) are related to the dose taken, there is considerable interindividual variability. Clinical effects are potentiated by ethanol, benzodiazepines and other central nervous system depressants. Typically, effects will occur within one hour of ingestion or within a few minutes of intravenous administration. Unconscious patients who are not intubated

Table 4. Features of gamma hydroxybutyrate (GHB) intoxication.

Mild	Moderate/severe
Euphoria	Bradycardia
Nausea	Hypotension
Drowsiness	Respiratory depression
Headache	Respiratory arrest
Ataxia	
Confusion	
Agitation	
Hypothermia	

generally recover consciousness within 2–3 hours. In addition to the clinical findings listed, hypernatraemia, hypokalaemia, hyperglycaemia and metabolic acidosis also occur. Chronic abusers may develop withdrawal symptoms, including tremor, confusion, agitation, insomnia, nausea and vomiting.

Treatment of intoxication

Asymptomatic patients should be observed for at least two hours. Naloxone may reverse some of the effects of GHB, and should be considered if there is coma or respiratory depression. A benzodiazepine (eg diazepam) may be administered for withdrawal symptoms or if convulsions occur. Severe bradycardia may respond to atropine.

Cannabis

Cannabis is widely used in the UK, being taken to produce a state of relaxed euphoria. It is usually smoked, though it may also be ingested. Specific cannabinoid receptors have now been identified. Acute toxicological deaths from cannabis use are rare, though accidents may occur due to impaired psychomotor performance.⁸

Acutely, cannabis causes impaired co-ordination, euphoria, anxiety, hypotension, tachycardia, impaired judgement, conjunctival injection, tachycardia, dry mouth and appetite stimulation ('the munchies').

Long-term use

Concern exists over the effects of long-term use of cannabis. Psychological effects of heavy use include hallucinations, and an association with psychosis is well described. Smoking cannabis is likely to cause similar problems to smoking tobacco: chronic obstructive airways disease, lung carcinomas and cardiovascular disease. It is a matter for debate whether cannabis causes chronic psychiatric illness or merely unmasks a pre-existing condition.

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