Emergency management of drug abuse in South Africa

Drug abuse remains both a global scourge and a significant social and medical problem in South Africa.

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Primary practice and emergency department practitioners have the dual responsibility of managing the acute medical complications associated with illicit drug abuse and managing the day-to-day problems associated with such abuse.

Because many drugs of abuse are illegal, there are little accurate data on drug use in South Africa. The simplest classification of these drugs is into 'uppers' (such as cocaine and methamphetamine), those taken for sedation or narcosis, i.e. the 'downers' (besides alcohol, the opioid group including heroin) and the hallucinogens, i.e. the 'round and rounders' (such as lysergic acid diethylamide or LSD). This article does not deal with alcohol abuse.

Drugs are abused for their complex effects on mood, perceived enhancement of pleasurable sensations, and physiological endurance. These include 3,4 methylenedioxymethamphetamine (MDMA or ecstasy), gamma-hydroxybutyrate (GHB) and ketamine. The US National Institute on Drug Abuse (NIDA) in its *Community Alert on Club Drugs*, defined 'club drugs' as ecstasy, gamma-hydroxybutyrate (GHB), ketamine, flunitrazepam (Rohypnol), methamphetamine, and lysergic acid diethylamide (LSD).[1] Emergency present- ations are often complicated by the fact that the drug is mixed with inert bulking agents (such as flour or chalk), toxic industrial agents and other drugs. Drug concentrations also vary widely.

National surveys of cannabis use between 2000 and 2005 showed rates of use among adolescents from 2% to 9% and among adults of 2%, cocaine/crack (0.3%), Mandrax or sedatives (0.3%), club drugs or amphetamine-type stimulants (0.2%), opiates (0.1%) and hallucinogens (0.1%).

The primary substances of abuse at admission to South African drug treatment centres over the same period was cannabis (16.9%), methamphetamine (tik) (12.8%), crack cocaine (9.6%), cannabis and Mandrax (3.4%), heroin/opiates (9.2%), and prescription and OTC drugs (2.6%). There has been an increase in admissions for the treatment of substance abuse. While the prevalence of illicit drug use in South Africa is relatively low compared with the USA (20% of American youths aged 16 - 23 having ever used one or more club drugs) and Australia, the problem is steadily increasing.[2]

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Designer drugs

This remains a truly complex arena – a multitude of illegally synthesised compounds, often analogous to existing drugs, manufactured in efforts to find new markets, and to circumvent various countries' drug laws. Some examples include:

- alpha methylfentanyl – or 'china white' on the heroin market
- phenethylamine based – such as bromo-dragonfly
- methoxyketamine
- piperazine based – such as trifluoromethylphenylpiperazine
- an entactogen such as 3,4-methylenedioxy-N-methylcathinone
- stimulants such as methadrone and also methylenedioxypyrovalerone
- sedatives such as gamma-butyrolactone, both a precursor to and substitute for GHB.

This review presents a system-based approach (as elucidated by Devlin and Henry[3]) highlighting suggestive histories and certain acute system signs or complications.

Clinical presentations and management

Respiratory complications[3]

Crack cocaine is the drug most commonly associated with respiratory complications that require hospital admission. Smoking this drug can lead to severe thermal injury of the pharynx and airways. However, cough, haemoptysis, pneumothorax, pneumomediastinum, pneumopericardium and haemothorax are the main acute complications of inhaling crack cocaine vapour and should be considered whenever present without an obvious history of trauma. For enhanced absorption and effect, users commonly inhale deeply and then perform a Valsalva manoeuvre. The rise in intra-alveolar pressure, in addition to barotrauma caused by vigorous coughing, can cause both alveolar rupture and air dissection in the peribronchiolar connective tissue. Cocaine

and cannabis smoking as well as intravenous methylphenidate abuse have been associated with severe bullous emphysema, one complication of which is pneumothorax. Management of these complications follows conventional lines.[4]

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The main subacute pulmonary complications of cocaine use include pulmonary oedema, 'crack lung', interstitial pneumonitis and bronchiolitis obliterans with organising pneumonia. Cocaine-associated pulmonary oedema may not be recognised immediately in young patients. Treatment with diuretics, nitrates and oxygen followed by mechanical ventilation, if necessary, usually produces rapid improvement. If the presentation is asthmatic, consider cocaine or heroin inhalation.

Respiratory depression caused by morphine or heroin overdose is usually recognised by most clinicians. Management is straightforward. Ensure a patent airway and administer oxygen followed by naloxone (remembering its short half-life) and continued respiratory support if necessary. Respiratory depression and hypostatic pneumonia may occur in gamma GHB intoxication, for which there is no effective antidote, so these patients may require intubation and mechanical ventilation.[3]

Cardiovascular complications

Cocaine is the most common cause of chest pain in young adults presenting to emergency departments. In the USA it is the cause of 25% of myocardial infarctions (MIs) in people under 45 years of age.[5] Cocaine also promotes platelet aggregation and thrombus formation, accelerates atherosclerosis and produces left ventricular hypertrophy.[3] Widespread vasoconstriction (coronary and peripheral) causes increased myocardial oxygen demand, and the sympathomimetic activity causes tachycardia and hypertension. Myocardial ischaemia and infarction may occur in 6% of cases. Always consider cocaine use in a young otherwise healthy patient presenting with an acute coronary syndrome. Electrocardiogram (ECG) interpretation might be challenging.[3]

Management remains according to standard ACLS principles, with oxygen, aspirin (unless at risk of subarachnoid haemorrhage), benzodiazepines and sublingual nitrates. The debate of proactive co-administration of sublingual nitrates and benzodiazepines remains active. The clinical reality is that these patients remain prone to seizures due to their cocaine usage, which provides a rationale for the prophylactic use of benzodiazepines. Most clinicians would agree that benzodiazepines should be considered for all patients with cocaine-induced chest pain who are anxious, tachycardic or hypertensive. In contrast, a clear consensus exists against the use of beta-blockers, which potentiate cocaine-induced chest pain via unopposed alpha-adrenergic stimulation. Given the difficulty in definitively diagnosing cocaine-induced MI, thrombolysis is rarely used. The infarction is often due to coronary spasm rather than thrombosis and is associated with very low mortality.[3,5]

Cocaine has also been associated with hypotension, cardiac arrhythmias and sudden death if taken in large quantities.[6] Other substances associated with cardiac arrhythmias and sudden death include MDMA or ecstasy and amphetamines, thought to be linked to sympathetic hyperstimulation. In many young victims of sudden death, it is possible that death may be due to undiagnosed conduction defects precipitated by drug abuse. MDMA can prolong the QT interval while methadone, often sold on the illicit market, or used in heroin rehabilitation programmes, can cause long QT syndrome and torsades de pointes.[3,7,8]

The risk of immediate death is 18 - 25 times greater for cocaine co-ingested with alcohol than for cocaine alone.

Neurological complications

Illicit drug use (especially GHB and opioids, often in combination with benzodiazepines or alcohol) can cause coma. Also consider the inhalation of volatile substances in unconscious patients. Respiratory depression, aspiration, rhabdomyolysis and other complications may follow, depending on the depth and duration of central nervous system depression. Management is supportive. Naloxone may be used if opioid toxicity is apparent or suspected. Because of the risk of provoking convulsions, flumazenil is not recommended for reversal of benzodiazepine toxicity, and physostigmine does not have a recommended role in reversing GHB toxicity. Ketamine toxicity rarely causes coma, and the ED doctor usually sees

Table 1. Common toxidromes in illicit drug use

Toxidrome	Features	Drugs implicated
Adrenergic	Hypertension, tachycardia, mydriasis, diaphoresis, agitation, dry mucus membranes	Amphetamines, cocaine, ephedrine, phencyclidine
Sedative	Stupor and coma, confusion, slurred speech, apnoea	Barbiturates, benzodiazepines, ethanol, opiates
Hallucinogenic	Hallucinations, psychosis, panic, fever, hyperthermia	Amphetamines, cannabinoids, cocaine
Narcotic	Altered mental status, slow shallow breaths, miosis, bradycardia, hypotension, hypothermia, decreased bowel sounds	Opiates
Epileptogenic	Hyperthermia, hyperrreflexia, tremors, seizures	Cocaine, phencyclidine

Adapted from Devlin and Henry.[3]

a confused patient reporting euphoria, numbness, 'out of body' sensations, disorientation and panic attacks.

If faced with seizures not immediately due to previously diagnosed epilepsy, consider cocaine, amphetamines (including MDMA), withdrawal states (opioids, GHB, benzodiazepines and ethanol), and cerebral hypoxia. Control is with benzodiazepines as per standard protocols. Hallucinations can follow consumption of LSD, certain mushrooms, amphetamines, or even cocaine. With cocaine, hallucinations may be a relatively isolated unwanted effect or may be part of cocaine-excited delirium. They also occur in withdrawal states, most notably that of alcohol, but also of benzodiazepines, GHB and opioids.[3]

Acute hyponatraemia has caused a number of deaths in association with MDMA abuse. MDMA causes excess antidiuretic hormone (ADH) production and thus a reduced renal response to water loading, so that excess fluid ingestion following MDMA consumption leads to dilutional hyponatraemia and cerebral oedema. The most common presentation is neurological, with confusion, delirium, convulsions or coma. Severe cerebral or even pulmonary oedema may also occur. The most important aspect of management is fluid restriction. Most patients will produce a diuresis within hours as levels of MDMA fall and normal ADH production resumes.[9]

Stimulant drugs such as cocaine and amphetamines have also been associated with cerebrovascular events. The likelihood of haemorrhagic stroke is more common with amphetamines, while thrombotic stroke is more common with cocaine.[10]

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Hyperthermic complications

Cocaine use can cause hallucinations, agitation and hyperthermia, requiring prompt management. In addition, cocaine-excited delirium is an important but unusual complication of cocaine use and considered to be an entity separate from cocaine toxicity. It is characterised by hyperthermia with profuse sweating, followed by agitated and paranoid behaviour (with dilated pupils), progressing to collapse (often accompanied by respiratory arrest) and death.[3]

The hyperthermic complications of MDMA use are well known – exertional hyperpyrexia and serotonin syndrome, although the two may overlap. In exertional hyperpyrexia, the circumstances in which the drug is taken are important in the development of this complication. It is generally found following prolonged dancing. Patients may present collapsed, hypotensive and tachycardic, with hyperpyrexia without rigidity. Subsequent multi-organ failure may occur. Management should focus on fluid replacement to support cardiac output and facilitate thermoregulation, rapid cooling and intensive care support. Hyperthermia affects skeletal muscle by reducing the calcium requirement for excitation-contraction coupling and establishing a cycle of heat production secondary to muscle contraction. This is the rationale behind using dantrolene to aid cooling of

these patients, although there is no well-proven benefit.[3]

Serotonin syndrome, in contrast, is characterised by rapid onset of markedly increased muscle tone with shivering, tremors and hyperreflexia. Contraction of opposing muscle groups tends to generate heat at a greater rate than can be lost by vasodilatation and sweating, leading to hyperpyrexia and cardiovascular instability. In addition, the patient may be confused and have diarrhoea. Mortality is reported as 10 - 15%. Patients on monoamine oxidase inhibitors and selective serotonin re-uptake inhibitors are at particular risk. Management of severe cases is by immediate paralysis accompanied by sedation and ventilation.[3]

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Hepatic and metabolic complications

MDMA is a significant cause of drug-induced liver failure. Patients present with acute hepatitis, sometimes progressing to encephalopathy, and should be managed supportively.[3]

Non-traumatic rhabdomyolysis is also a complication common to many drugs of abuse, either as a result of pressure necrosis of muscle in unconscious patients or excessive muscle contraction. There is frequently asymptomatic muscle swelling and tenderness. Check urine for large amounts of haemoglobin and myoglobin. Ultrasonography can reveal hyperechoic regions of pressure necrosis.

Management is usually fluid and electrolyte monitoring, with fluid replacement. Alkalinisation of urine is sometimes recommended to reduce the risk of myoglobinuric renal failure, but may delay the excretion of amphetamines.[11]

Polysubstance abuse

Be aware of the common toxidromes associated with drugs of abuse as this might assist with a more rapid clinical diagnosis (Table 1). Many drug complications mimic other medical conditions and polysubstance use is also quite common. It is therefore helpful to have the result of a rapid urine test to confirm clinical suspicions and guide management decisions. However, these tests only confirm the presence of a substance in urine, indicating consumption of the drug during the previous 24 - 72 hours, and don't usually give any indication of blood levels or of the relationship of the drug to the clinical effects observed. Interaction with alcohol must also be considered, especially in cases of cocaine abuse. Alcohol causes hepatic metabolism of cocaine to an ethyl homologue cocaethylene that has a plasma half-life 3 - 5 times longer than that (30 - 60 minutes) of cocaine. The risk of immediate death is 18 - 25 times greater for cocaine co-ingested with alcohol than for cocaine alone.[3,10,12]

References available at www.cmej.org.za

In a nutshell

- The simplest classification of drugs of abuse is into 'uppers' (such as cocaine and methamphetamine), those taken for sedation or narcosis, i.e. the 'downers' (besides alcohol, the opioid group including heroin) and the hallucinogens, i.e. the 'round and rounders' (such as lysergic acid diethylamide or LSD).
- Consider drugs of abuse when faced with non-traumatic respiratory complications, non-epileptic seizures and otherwise unexplained cardiac or neurological symptom complexes in young adults.
- Crack cocaine is the drug most commonly associated with respiratory complications that require hospital admission.
- The main subacute pulmonary complications of cocaine use include pulmonary oedema, 'crack lung', interstitial pneumonitis and bronchiolitis obliterans with organising pneumonia.
- Cocaine is the most common cause of chest pain in young adults presenting to emergency departments.
- Cocaine has also been associated with hypotension, cardiac arrhythmias and sudden death if taken in large quantities.
- Acute hyponatraemia has caused a number of deaths in association with MDMA abuse.
- Stimulant drugs such as cocaine and amphetamines have also been associated with cerebrovascular events.
- Cocaine use can cause hallucinations, agitation and hyperthermia, requiring prompt management.
- The hyperthermic complications of MDMA use are exertional hyperpyrexia and serotonin syndrome, which may overlap.
- Serotonin syndrome is characterised by rapid onset of markedly increased muscle tone with shivering, tremors and hyperreflexia.
- MDMA is a significant cause of drug-induced liver failure and patients present with acute hepatitis, sometimes progressing to encephalopathy.
- Many drug complications mimic other medical conditions and polysubstance use is also quite common.

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