The intensive care management of common and uncommon drugs of misuse

With an ever-expanding field of illicit drugs available, doctors working in the acute specialties will inevitably be involved in the management of the serious and life-threatening side effects of drug misuse, as outlined in this article.

The 2009–10 British Crime Survey estimated that 8.6% of adults (almost 3 million people) within the UK had used illicit drugs within the last year, with 3.1% (almost 1 million people) using a Class A drug (Home Office Statistics Unit, 2010). With approximately 1 in 3 people aged 16 to 59 years admitting to using an illicit drug in the past it is almost inevitable that the intensive care physician will at some point be involved in the management of the more severe side effects of illicit drug use. In its 2008–9 annual report the National Poisons Information Service (2009) identified increased activity associated with a number of illicit drugs, both common and uncommon (*Table 1*), and these drugs form the main focus of this review.

General supportive measures for all overdoses

The initial assessment of the unconscious poisoned patient is often complicated by the lack of a reliable history, the possibility of co-ingestion with other drugs and alcohol, and the need to exclude other causes of coma. It is paramount to obtain as accurate a history as possible from any available sources, e.g. paramedics or acquaintances (this may be fraught with potential error or withheld information, compounded by fear of reprise by the police). Specimen tablets are often the key to guidance of therapy (if available). Initial management should follow an airway, breathing, circulation (ABC) approach with simultaneous clinical examination to help identify the substance involved.

Initial resuscitation and stabilization

All patients must be approached with full advanced trauma life support management. A full primary survey should be performed and, once done, a secondary survey with specific therapy for the ingested agent can then be considered. Patients may be comatose, but it must not be assumed that this all relates to the ingested substance. Other injuries must be sought and excluded at all costs.

Endotracheal intubation and ventilatory support may be required to provide definitive airway protection and adequate minute ventilation in patients with a reduced Glasgow Coma Score or inadequate spontaneous ventilation. A Glasgow Coma Score of 8 or less will require intubation. Venous access should be established and the circulation assessed. Clinical observation of pulse, blood pressure and urine output should be used to guide fluid resuscitation; invasive monitoring may be required. Assessment of pupils, temperature and cardiac rhythm may guide diagnosis. Arterial blood lactate level is often taken as a marker of poor cardiac output states (shock) but should be interpreted with care, especially if a patient is post seizure. In this setting, the patient may have a significantly raised blood lactate level not necessarily relating to drugs ingested or to a poor cardiac output. Venous oxygen saturation has similar shortcomings post seizure. In the absence of seizures, the findings of a metabolic acidosis, a high anion gap and a high lactate level are worrying, as it is likely that the patient's cardiac output has been poor for some time, or that it is the drug itself directly causing the metabolic acidosis.

The use of naloxone and/or flumazenil is controversial and should be carefully considered in light of patient presentation and likely causative substance (Hoffman and Goldfrank, 1995).

Table 1. Drugs and their common street names

Drug	Street names
Cocaine	Powder: coke, charlie, C, white, percy, snow, toot
	Crack: rocks, wash, stones, pebbles, base, freebase
MDMA, or 3,4-methylenedioxymethamphetamine	Ecstacy, pills, brownies, Mitsubishis, Rolexs, dolphins, XTC
Benzylpiperazine (BZP)	Party pills, fast lane, silver bullet, smileys, happy pills, bolts extra strength, pep, pep love, pep twisted, pep stoned, A2, legal e, legal x, frenzy, nemesis, ESP, cosmic kelly, charlie, the good stuff, exodus, rapture, charge, blast, euphoria
Gamma-hydroxybutyrate (GHB)	Liquid ecstasy, GBL, 1,4-BD
Gamma-butyrolactone (GBL)	GHB, liquid ecstasy, 1,4-BD
Mephedrone	Meph, MC, MCAT, m-cat, 4-MMC, miaow, meow meow, bubbles, bounce, charge, drone, white magic

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Naloxone is a competitive antagonist at the opioid receptor, and is indicated for the reversal of CNS and respiratory depression caused by pure opiate overdose. The recommended dose is 0.4–2 mg, titrated to the patient's respiratory rate. The likelihood of precipitating acute opioid withdrawal should be borne in mind. This dose may be repeated every 2–3 minutes until full reversal is achieved or to a maximum of 10 mg. Although the effects of sudden opiate withdrawal are not considered life-threatening (e.g. agitation, nausea, vomiting, diarrhoea), caution should be exercised if polydrug intoxication is suspected. Naloxone may precipitate vomiting in a patient whose CNS suppression is incompletely reversed because of the effects of a second drug leading to the risk of aspiration. Naloxone is also contraindicated in the presence of combined opioid and cocaine toxicity (see section on cocaine).

Flumazenil is a competitive benzodiazepine antagonist which is only indicated for the reversal of acute benzodiazepine-induced sedation, at a dose of 0.2–0.5 mg in 30-second increments up to a total of 3 mg. Flumazenil should be used with extreme caution in patients suspected of being benzodiazepine dependent; sudden withdrawal may precipitate seizures and autonomic dysfunction that is more dangerous and difficult to manage than the primary effects of benzodiazepine overdose. Flumazenil should not be given in the context of polydrug overdose because of possible difficulty in the management of withdrawal seizures in the presence of a benzodiazepine antagonist.

Investigations

Initial investigations should include blood glucose, electrocardiogram, basic biochemistry, osmolar and anion gap, arterial blood gases and urinalysis. A qualitative toxicology screen (urine) and quantitative drug concentrations (serum) should also be requested – these tests are not useful in the acute setting, but are necessary to ultimately identify causative agents.

Ongoing management

If the patient is received within 1 hour of ingestion of the drug activated charcoal can be used (this reduces absorption by up to 60%). Activated charcoal molecules contain thousands of micropores on their surface providing a huge contact surface area with which to bind chemicals. When charcoal meets with ingested substances they attach, become trapped and adsorbed. If over 1 hour has passed after ingestion a significant proportion of the compound will already have been absorbed into the bloodstream, rendering charcoal useless as a first-line therapy. Activated charcoal can only act on ingested agent still contained within the lumen of the gastrointestinal tract.

Gastric lavage is only effective immediately after swallowing a toxic substance (within about 30 minutes) and has no effect beyond the stomach, unlike activated charcoal.

Patients with severe drug toxicity are likely to require ongoing management within intensive care, so early referral is prudent. Reference to online information services (e.g. Toxbase; www.toxbase.org/) can be invaluable in the management of specific drug poisoning.

Cocaine

Epidemiology

In 2007, the United Nations Office on Drugs and Crime (2009) estimated the worldwide annual prevalence of cocaine use as 15.6–20.8 million people, equivalent to 0.4–0.5% of the population aged 15–64 years. The UK is estimated to have ~1 million cocaine users, making it Europe's largest cocaine market.

Pharmacology

Cocaine (benzoylmethylecgonine) is an alkaloid of the *Erythroxylum coca* bush native to north-western South America. The cocaine hydrochloride salt is freely soluble in water and is absorbed through any mucous membrane; it can be inhaled, snorted, or injected intravenously or intramuscularly and has a half-life of 30–90 minutes. Cocaine blocks the reuptake of catecholamines at pre-synaptic sympathetic nerve endings with a consequent increase in their concentration within the synaptic cleft and increased cell receptor stimulation. In addition, it modulates receptors of the endogenous opiate system. Most of the drug is metabolized by plasma or hepatic hydrolysis, although up to 5% is excreted unchanged in the urine (Shanti and Lucas, 2003).

Pathophysiology

Cardiovascular system

Cocaine blocks the reuptake of noradrenaline throughout the sympathetic nervous system. Alpha- and beta-adrenergic driven increases in heart rate, blood pressure, systemic vascular resistance and contractility increase myocardial oxygen consumption. In combination with cocaine-induced coronary vasospasm, this can lead to acute myocardial infarction even in people with normal coronary arteries (Boghdadi and Henning, 1997).

Arrhythmias associated with cocaine use include ventricular tachycardia and fibrillation. Blockage of fast sodium channels may also result in heart block and re-entrant tachycardias which may lead to sudden cardiac death (Shanti and Lucas, 2003).

Chronic cocaine use is associated with accelerated coronary atherosclerosis as well as ventricular hypertrophy and dilatation. High circulating levels of catecholamines can lead to left ventricular dysfunction (both systolic and diastolic) as well as a chronic dilated cardiomyopathy. Cardiac echo may be considered at a later stage if suspicions are high (Shanti and Lucas, 2003).

Respiratory system

Upper respiratory tract: Epistaxis, nasal septal perforation, oropharyngeal ulcers, thermal burns of the face or upper airway, or acute inflammation of tongue, epiglot-

tis, vocal cords and/or trachea may occur as a consequence of direct vasoconstriction, ischaemic necrosis or inhalation of hot vapours (Haim et al, 1995).

Lower respiratory tract: Cocaine has a number of direct and indirect effects, including:

- Direct airway irritation leads to bronchospasm and severe exacerbation of asthma
- Via action as an antigen, immunoglobulin E production is induced resulting in mast cell degranulation and direct lung injury
- Hypersensitivity pneumonitis ('crack lung') results from diffuse alveolar and interstitial infiltrates. Cough, fever, wheeze and shortness of breath and ultimately respiratory failure may result
- Non-cardiogenic pulmonary oedema can result from direct endothelial toxicity, leading to increased permeability of the pulmonary vasculature
- Cardiogenic pulmonary oedema.

Echocardiography can be valuable in differentiating between non-cardiogenic and cardiogenic pulmonary oedema.

Pulmonary vasculature: Cocaine can cause pulmonary and bronchial arterial vasoconstriction and ischaemia, interstitial and alveolar haemorrhage or pulmonary infarction. Pulmonary artery hypertension and hypertrophy may be seen and may lead to cor pulmonale.

Other body systems affected by cocaine abuse are outlined in *Table 2*.

Presentation

The diagnosis of acute cocaine toxicity is often complicated by the myriad of signs and symptoms associated with cocaine use (see above). The diagnosis should be considered in a patient presenting with tachycardia, hypertension and hyperthermia associated with mydriasis, seizures and cardiorespiratory depression.

Critical care management

The management of acute cocaine intoxication is predominantly supportive.

Airway and breathing

This is covered in the section on general principles. However, benzodiazepines are the treatment of choice for cocaine-induced seizure control; barbiturates can be considered as second choice.

Circulation

Cardiac monitoring: Cardiovascular system complications are common and patients should be monitored closely for evidence of arrhythmias and ST changes.

Acute coronary syndromes and blood pressure control: Glyceryl trinitrate and benzodiazepines are first-line therapies in the management of cocaine-induced hypertension or chest pain. There is clear consensus against the use of beta-blockers, as these potentiate cocaine-induced chest pain via unopposed alpha-adrenergic stimulation (McCord et al, 2008). Thrombolysis should only be given when there is angiographic evidence of a thrombus (Vroegop et al, 2009).

Fluid therapy: This is a very important area of management and requires close attention. Fluid overload may lead to unnecessary patient morbidity, particularly when associated with the cardiovascular changes described above (pulmonary oedema often develops insidiously even after relatively small volumes of fluid) (Shanti and Lucas, 2003). The clinician should also be vigilant to cocaine-induced rhabdomyolysis (may need alkaline diuresis) and acute renal failure. Invasive cardiovascular monitoring should be considered early (arterial line and central line), to allow judicious fluid resuscitation guided by physiological parameters.

Table 2. The systemic effects of cocaine

System	Effect	Mechanism
CNS	Ischaemic stroke	Vasospasm
	Haemorrhagic stroke	Hypertensive crisis – rupture of pre-existing arteriovenous malformation or berry aneurysm
	Seizures	Direct muscarinic stimulation
		Serotonin accumulation
		Acute hyperthermia
	Movement disorders	Dopamine accumulation
Gastrointestinal	Peptic ulceration or perforation	α-adrenergic arterial vasoconstriction
	Delayed gastric emptying	Anti-cholinergic action
	Splenic infarction or haemorrhage	Intense vasospasm
	Focal intestinal necrosis or perforation	Mesenteric arterial vasoconstriction
Renal	Acute renal infarction	Renal arterial vasospasm or thrombosis
	Focal segmental glomerulosclerosis	Mesangial cell proliferation
	Renal failure	Renal artery arteriosclerosis
		Rhabdomyolysis
Vascular	Acute small and large vessel occlusion	Vasospasm and thrombosis
	Atherosclerosis with associated end-organ damage	Chronic cocaine use
Haematology	Pro-thrombotic tendency	Increased platelet aggregation
		Decreased protein C and antithrombin III levels
		Increased plasminogen activator inhibitor activity
Metabolic	Hyperthermia	Increased core temperature because of effects on hypothalamus
		Increased muscular activity
		Intense vasoconstriction

Specific therapies

Patients with cocaine-induced hyperthermia should be aggressively cooled and monitored for the development of rhabdomyolysis and disseminated intravascular coagulation (increased prothrombin time, activated partial thromboplastin time, thrombin time, fibrinogen degradation products, D-dimer and bleeding time; decreased platelets and fibrinogen). Involve haematology early with regard to replacement therapy (Vroegop et al, 2009).

Antagonist agents should be used with caution where cocaine is associated with other illicit drug overdose. Flumazenil may potentiate seizures and agitation and increased sympathetic activity. Naloxone may lead to malignant arrhythmias in the presence of cocaine and can cause life-threatening sympathicomimetic toxicity when the inhibiting effect of the opioid is reversed.

Ecstasy

Epidemiology

There are an estimated 12–24 million users of ecstasy worldwide with a UK annual prevalence rate of 1% (United Nations Office on Drugs and Crime, 2009). In 2008 ecstasy was implicated in 2.4% of all drug-related deaths in the UK (Office for National Statistics, 2009).

Pharmacology

Ecstasy (3,4-methylenedioxymethamphetamine, MDMA) is a substituted amphetamine commonly taken in tablet form to produce a mixture of stimulant and mild psychotropic effects. MDMA causes release and inhibits uptake of 5-hydroxytryptamine (5-HT, serotonin), dopamine and noradrenaline within the CNS. It has a duration of action of 4–6 hours and a plasma half life of 8–9 hours. The metabolism of ecstasy is non-linear and displays genetic polymorphism; this may lead to disproportionate rises in MDMA concentration after repeated dosing (Hall and Henry, 2006).

Pathophysiology

The clinical features of acute ecstasy toxicity are generally an exaggeration of its underlying pharmacological effects: disturbance of the central and sympathetic nervous systems. Systemic effects are outlined in *Table 3*.

Specific syndromes

Hyperpyrexia

This is perhaps the most well known (if rare) potentially fatal adverse effect of ecstasy; the combination of hyperpyrexia, rhabdomyolysis and multiorgan failure is well described (Kunitz et al, 2003).

The underlying cause appears to be a failure of central thermoregulation (mediated by dopamine and 5-HT) in association with a warm overcrowded environment, inadequate fluid replacement and excessive exertion (Hall and Henry, 2006). Hyperpyrexia is accompanied by muscle rigidity and hyper-reflexia and is rapidly followed by rhabdomyolysis, disseminated intravascular coagulation, impaired consciousness and multiorgan failure (as a result of a combination of direct cellular damage secondary to hyperpyrexia and high myoglobin levels).

Serotonin syndrome

Ecstasy is a known trigger for this syndrome, which presents with profoundly increased muscle tone and rigidity associated with hyper-reflexia and myoclonus (thought to be the result of a functional blockade of controlling motor neurons). Additional features include confusion, diarrhoea, excessive sweating and cardiovascular instability (Hall and Henry, 2006). The sudden increase in muscle activity can lead to hyperthermia and rhabdomyolysis, so this syndrome may be difficult to differentiate from neuroleptic malignant syndrome and the ecstasy-induced hyperpyrexia described above.

Hyponatraemia

Acute hyponatraemia associated with ecstasy use typically presents with confusion, delirium and persistent seizures which can progress swiftly to coma and death as a result of coning. The underlying aetiology is twofold: excessive water consumption in an attempt to reduce the risk of hyperpyrexia and an MDMA-induced increase in antidiuretic hormone secretion (Ricaurte and McCann, 2005). Treatment is supportive, as below (Greene et al, 2008).

Table 3. The systemic effects of ecstasy

System	Effect
Cardiovascular	Tachycardia
	Hypertension
	Arrhythmias*
	Myocardial ischaemia or infarction*
Respiratory	Tachypnoea
	Non-cardiogenic pulmonary oedema or acute respiratory distress syndrome*
	Pneumothorax or pneumomediastinum*
CNS	Altered mental state (e.g. hyperarousal, agitation, paranoia, confusion)
	Seizures
	Strokes (haemorrhagic or ischaemic)*
	Coma*
	Cerebral venous sinus thrombosis*
Others	Dry mouth
	Diaphoresis
	Tremor
	Bruxism
	Mydriasis

*rare effects

Hepatotoxicity

Hepatic failure associated with ecstasy toxicity may occur as part of the multiorgan failure associated with hyperpyrexia or as a consequence of direct MDMA hepatotoxicity. Patients present with abdominal pain, jaundice and deranged liver enzymes. In severe cases, liver transplantation may be required (Ricaurte and McCann, 2005).

Critical care management

Airway and breathing

Intubation and ventilation are particularly important in cases of hyperthermia, persistent seizures and the serotonin syndrome to facilitate effective treatment. Correcting hypoxia reduces the risk of malignant arrhythmias (Greene et al, 2008).

Seizures are generally short lived and respond well to benzodiazepines.

Circulation

Fluid therapy: Urgent fluid replacement is essential in patients presenting with hypotension and tachycardia suggestive of intravascular depletion and in patients with hyperthermia. Urine output should be maintained at >2 ml/kg/hr in patients with rhabdomyolysis (consider alkaline diuresis) (Hall and Henry, 2006). Conversely, patients with hyponatraemia often respond to fluid restriction (Ricaurte and McCann, 2005). Invasive cardiovascular monitoring should be considered early so as to guide judicious fluid replacement.

Blood pressure control: Benzodiazepines are first-line agents for ecstasy-induced hypertension and tachycardia. Additional treatment options include intravenous glyceryl trinitrate and α-blockers (e.g. phentolamine). Labetalol and esmolol can be used but pure β-blockers should be avoided because of the risk of worsening hypertension secondary to unopposed α-stimulation (Greene et al, 2008).

Arrhythmias: Most sympathetically driven sinus tachycardias will respond to benzodiazepine therapy. Supraventricular and ventricular tachycardias should be managed in the conventional way.

Specific therapies

Agitation: This should be managed aggressively with benzodiazepines to reduce the risk from ongoing sympathetic stimulation (Greene et al, 2008).

Hyperthermia: If temperature >39°C after simple cooling measures the patient should be aggressively cooled and given dantrolene (prevents excitation-contraction coupling in muscle cells, probably by action on the ryanodine receptor) (Devlin and Henry, 2008).

Hyponatraemia: Mild (125–134 mmol/litre) to moderate (120–124 mmol/litre) hyponatraemia should resolve with fluid restriction. Hypertonic saline should only be considered in severe hyponatraemia and correction should be cautious to avoid central pontine demyelination (Ricaurte and McCann, 2005).

Benzylpiperazine

Epidemiology

N-benzylpiperazine (BZP) is a synthetic piperazine which is the major active compound in 'party pills' (Johnstone et al, 2007). In 2009, BZP and related compounds were classified as Class C drugs under the Misuse of Drugs Act, having previously been legal within the UK (Home Office Crime and Policy Group – Drug Strategy Unit, 2009). The prevalence of BZP use within the UK is unknown but the National Poisons Information Service (2009) annual report suggests an increase in use.

Pharmacology

Benzylpiperazine inhibits re-uptake of dopamine and serotonin within the CNS and stimulates peripheral α_2-receptors in a manner similar to amphetamine but with lower potency (Gee et al, 2005). It is sometimes mixed with TFMPP (trifluormethylphenylpiperazine) in an attempt to mimic the effects of ecstasy. Onset of effect may be delayed by several hours leading to repeated dosing to achieve the desired effect. A 100 mg dose of BZP has a duration of action of 6–8 hours (Wilkins et al, 2008). The metabolism of BZP in humans is not fully elucidated but is thought to involve the cytochrome P450 enzyme system CYP2D6 which is also involved in the metabolism of paroxetine, imipramine and ecstasy (among others) and may lead to potentially fatal drug interactions (Murphy et al, 2009). A large proportion of the drug is excreted unchanged in the urine.

Pathophysiology

The clinical effects of BZP are similar to those experienced with amphetamine use including euphoria, increased energy and psychoactive effects (particularly when taken with TFMPP). Information regarding BZP toxicity is mainly gathered from case series.

Patients with minor toxicity present with palpitations, agitation, nausea, vomiting and confusion (Gee et al, 2005).

Serious adverse effects include seizures, status epilepticus, severe metabolic acidosis, hyponatraemia, prolonged QT interval, acute kidney injury (Alansari and Hamilton, 2006) and toxic psychosis (Gee et al, 2010).

Co-ingestion of BZP and MDMA can lead to potentially fatal sympathetic and/or serotonergic toxicity with hyperthermia, rhabdomyolysis and multiorgan failure (Gee et al, 2010).

Critical care management

Patients presenting with mild BZP toxicity can be managed conservatively with reassurance and a period of observation. Those with moderate toxicity may require treatment with intravenous fluids, antiemetics and benzodiazepines and should be monitored for seizure activity (Gee et al, 2005). For those patients with severe toxicity management is described below.

Airway and breathing

This does not differ from advice given in the section on general principles. Seizures may persist, but usually respond readily to benzodiazepines.

Circulation

Dehydration is often an associated feature of BZP toxicity as with ecstasy toxicity. Fluid resuscitation should be aggressive in the face of potential rhabdomyolysis but care should be taken to check for evidence of hyponatraemia.

Management of patients with hyperthermia or suspected serotonin syndrome is as described above.

γ-hydroxybutyrate and γ-butyrolactone

Epidemiology

Gamma-hydroxybutyrate (GHB) is a naturally occurring precursor of the neurotransmitter γ-aminobutyric acid (GABA) (Abanades et al, 2006). Illegal within the UK it is licensed in several European countries for the treatment of narcolepsy, alcohol withdrawal and as a licensed anaesthetic induction agent (Dupont and Thornton, 2001). Since the early 1990s, GHB has been increasingly recognized as a drug of abuse causing euphoria, relaxation and reduction of social inhibitions. Additional effects include short-term antegrade amnesia, increased libido and suggestibility which, along with its ease of administration, have led to its use in drug-facilitated sexual abuse or 'date rape' (Abanades et al, 2006).

Gamma-butyrolactone (GBL) is a precursor of GHB and is rapidly metabolized in vivo to the active drug. GBL is used widely as an industrial chemical in the manufacture of rubber and plastics and as a component of nail varnish remover and paint solvent (Dupont and Thornton, 2001). Both GHB and GBL have been added to 'dietary supplements' marketed for their performance-enhancing and anabolic effects (Wood et al, 2008). GHB and all its precursors are classified as Class C controlled substances under the Home Office Misuse of Drugs Act (Home Office Crime and Policy Group – Drug Strategy Unit, 2009).

Pharmacology

GHB and GBL are analogues of GABA, one of the major inhibitory neurotransmitters within the CNS. They are thought to exert their effects via the $GABA_B$ receptor although high-affinity GHB-specific receptors have been identified within the CNS. In addition, GHB affects endogenous opioid, serotonin and dopamine pathways (Mason and Kerns, 2002). The drugs are readily absorbed via the gastrointestinal tract with a duration of action of 6–10 hours and an elimination half life of 27 minutes. GHB is metabolized to carbon dioxide and eliminated via the lungs with ~1–5% excreted unchanged in the urine (Shannon and Quang, 2000).

Pathophysiology

The clinical effects of GHB intoxication are dose-related and worsened by co-ingestion with other CNS suppressant drugs such as alcohol and benzodiazepines. Co-ingestion is extremely common and signs and symptoms should be interpreted in light of the high probability of polypharmacy (Shannon and Quang, 2000). Systemic effects of GHB or GBL use are outlined in *Table 4*.

Critical care management

Despite the often profound respiratory and CNS depressant effects of GHB and its precursors mortality associated with overdose is low and the majority of patients recover respiratory function and consciousness within 2–6 hours. The vast majority of reported deaths associated with GHB occur pre-hospital (Mason and Kerns, 2002).

Airway and breathing

Intubation and ventilation is indicated in patients with severe respiratory depression and obtunded airway reflexes. Post intubation sedation with a short-acting sedative or hypnotic is recommended to prevent the agitation associated with rapid emergence from GHB-induced coma (Mason and Kerns, 2002).

Prolonged seizures associated with GHB toxicity are uncommon and respond well to benzodiazepines.

Circulation

Bradycardia responds well to atropine. Additional arrhythmias or electrocardiogram changes are unusual with isolated GHB overdose and should prompt a search for an additional agent (Mason and Kerns, 2002).

Table 4. The systemic effects of gamma-hydroxybutyrate and gamma-butyrolactone

System	Effect
CNS	Ataxia
	Confusion or amnesia
	Agitation or rapid emergence
	Seizures
	Unconsciousness
	Coma
Respiratory	Respiratory depression (including loss of airway reflexes)
	Cheyne–Stokes respiration
	Respiratory arrest
Cardiovascular	Bradyarrhythmias
	Hypotension
Others	Nausea and vomiting
	Excessive salivation
	Metabolic acidosis
	Hypothermia

Hypotension is uncommon and responds well to fluid therapy.

Specific therapies

Physostigmine: This has been proposed as an antidote for GHB intoxication based on its use in the reversal of anaesthesia induced by GHB. Given the high incidence of co-ingestion in cases of GHB overdose and the consequent risk of precipitating seizures or arrhythmias, physostigmine is not recommended as a reversal agent in GHB toxicity and does not alter outcome or shorten hospital stay (Mason and Kerns, 2002).

Withdrawal: Chronic users of GHB and its precursors are at risk of an acute withdrawal syndrome on abrupt cessation of use similar to that seen in alcohol withdrawal. Characteristic features include anxiety, agitation, hallucinations and autonomic dysfunction which may be severe. Management is mainly supportive but large doses of benzodiazepines are often required; symptoms can last between 3 to 12 days (Dyer et al, 2001).

Mephedrone

Mephedrone (4-methylmethcathinone) is a synthetic derivative of a naturally occurring plant alkaloid (cathinone) extracted from the leaves of the evergreen khat shrub (*Catha edulis*) found predominantly in Africa and the Middle East (Wood et al, 2010). Structurally, cathinone is very similar to amphetamine, representing its β-keto analogue, and is thought to exert its stimulatory effects via the release of presynaptic catecholamines (Meyer et al, 2010). Until recently, mephedrone was readily available over the internet, predominantly marketed as a plant food. A number of high profile deaths and concerns over the rapid increase in use led to all the cathinone compounds being reclassified as Class B drugs under the Misuse of Drugs Act 1971 from April 2010.

Mephedrone can be inhaled, swallowed or injected; its perceived effects are dose related and include euphoria, increased energy, feelings of empathy and increased libido (Winstock et al, 2010). Information on the possible harmful effects of mephedrone is limited and comes predominantly from case studies and self-reporting. Reported undesirable effects include tachycardia, hallucinations, restlessness, anxiety and bruxism (Wood et al, 2010). Reports of acute toxicity include CNS hyperstimulation, serotonin syndrome and features consistent with sympathomimetic toxicity (Morris, 2010; Wood et al, 2010). Cases presenting with acute mephedrone toxicity have thus far been admitted for ongoing observation and managed with benzodiazepines (Advisory Council on the Misuse of Drugs, 2010).

Conclusions

Drug abuse within the UK is common and the risk of serious and life-threatening side effects means that the modern physician must be armed with the knowledge to treat an ever-expanding field of illicit drugs. In the emergency setting the vast majority of illicit drug toxicities can be managed with a logical ABC approach; ongoing management should be guided by the most likely substance involved. Doctors should be cautious about the generic use of naloxone and flumazenil in the light of potential polypharmacy. BJHM

Conflict of interest: none.

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KEY POINTS

- Drug misuse is common with approximately 1 in 3 people aged 16 to 59 years admitting to using an illicit drug in the past.
- Initial management should follow an 'airway, breathing, circulation' approach with simultaneous clinical examination to help identify the substance involved.
- The use of naloxone and/or flumazenil should be carefully considered in light of patient presentation, likely causative substance and the potential for polypharmacy.
- The specific substance involved should guide ongoing patient management.
- Reference to online information services (e.g. Toxbase) can be invaluable in the management of specific drug poisoning.

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