Acutely admitted patients who have taken an overdose: a practical update

Introduction

Drug overdoses account for a significant proportion of emergency medical admissions (Cook et al, 2008) often with an unknown combination of agents. Initial assessment of these patients can often be a challenge as they may present with a decreased level of consciousness, or may be uncooperative. This article first takes an ABCDE approach (airway, breathing, circulation, disability and exposure) and then discusses the principles of managing commonly encountered overdoses. Finally, an approach to overdose with an unknown agent is discussed.

Airway

The assessment of each critically ill patient begins with assessment of airway patency. Partial obstruction may be suggested by gurgling sounds or stridor, and requires immediate intervention and airway support.

Certain drugs such as alcohol, opioids, benzodiazepines and tricyclic antidepressants have a sedative effect, which may render the patient unable to protect the airway as a result of decreased consciousness. Such patients should be nursed in the left lateral position. Unresponsive patients require adjuncts, e.g. nasopharyngeal or a Guedel airway, for airway support. Intubation with an endotracheal tube may be necessary if adjuncts are ineffective.

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Breathing

Certain agents have an effect on the respiratory centre of the brain, resulting in an increase or decrease in respiratory rate.

Salicylate toxicity, most often secondary to aspirin overdose, can initially present with an increased respiratory rate. Hyperventilation results in a respiratory alkalosis in response to salicylate stimulation of the respiratory centre. Other agents, such as opioids, benzodiazepines, and tricyclic antidepressants, cause a depression of the respiratory centre, leading a rise in serum carbon dioxide levels.

Pulmonary oedema can develop secondary to cocaine inhalation, tricyclic antidepressant overdose or, less frequently, heroin (Sporer and Dorn, 2001) and in overdose these patients are at risk of desaturating. In such cases, assisted ventilation must be considered to improve oxygenation (Pierson, 2002).

Circulation

Circulation and haemodynamic stability should be assessed by regular monitoring of blood pressure, heart rate and capillary refill, while the electrocardiogram will also provide essential information.

Cocaine acts on adrenergic receptors, inhibiting the uptake of noradrenaline resulting in tachycardia, hypertension and supraventricular tachycardia or ventricular arrhythmias. Arrhythmias result from inhibition of sodium-potassium channels and potentiation of current through calcium channels (Phillips et al, 2009). Electrocardiogram changes of ischaemia or infarction reflect the tendency of cocaine to induce a procoagulant state and coronary artery vasospasm, alongside increasing myocardial oxygen demand. Benzodiazepines, specifically diazepam, are recommended in coronary artery vasospasm and myocardial ischaemia secondary to cocaine use. Beta-blockers should be avoided as they can contribute to coronary artery vasoconstriction (Ghuran and Nolan, 2000). Standard therapy involves high-flow oxygen and aspirin and/or anticoagulants and/or nitrates plus urgent specialist cardiological intervention if ischaemia continues despite these measures.

Similarly, tricyclic antidepressants induce sinus tachycardia and/or arrhythmias and cause hypotension as a result of a reduction in cardiac contractility and systemic vascular resistance (Kerr et al, 2001). In overdose with arrhythmia and metabolic acidosis, alkalinization with sodium bicarbonate (target pH 7.45–7.55) is recommended before pharmacological management of arrhythmia (Hoffman et al, 1993).

Conversely, opioids may cause bradycardia and hypotension through parasympathetic stimulation. Furthermore, an overdose of antihypertensive medications can produce a life-threatening hypotension. Fluid administration is frequently insufficient to correct these cases, and inotropic therapy should be considered (Ghuran and Nolan, 2000).

An arterial blood gas sample is a key measure of the impact of overdose on ventilatory and cardiovascular function and will detail acid–base balance and electrolyte abnormalities that may be amenable to correction (*Table 1*).

Disability

Assessment of level of consciousness is essential and can serve as a strong predictor of prognosis.

Table 1. Acid–base disturbances in common drug overdoses

	Alkalosis	Acidosis
Metabolic	Gaviscon, loop/thiazide diuretics, fludrocortisone, glucocorticoids, carbon monoxide	Alcohol, metformin, tricyclic antidepressants, antipsychotics, salicylate, ibuprofen
Respiratory	Salicylate	Tricyclic antidepressants, benzodiazepines, opioids

Patients may present in a sedated state following ingestion of opioids, tricyclics or salicylate. Stimulants such as cocaine may present with agitation, which can be treated with either benzodiazepines or butyrophenones (for example haloperidol) (Zimmerman, 2003).

Pupil size may aid diagnosis. Pinpoint pupils are highly suggestive of opioid toxicity, and have also been reported in benzodiazepine overdose (Palenzona et al, 2004). In contrast, the antimuscarinic effects of tricyclic antidepressants and cocaine may result in pupillary dilatation.

Blood glucose level measure is essential for assessing mental status. Hypoglycaemia may be the result of insulin, metformin or gliclazide overdose, or drugs that cause hepatic failure, such as salicylates or the later stages of paracetamol toxicity. Dextrose infusion should be preceded by intravenous Pabrinex in patients exposed to alcohol to reduce the risk of Wernicke's encephalopathy.

Exposure

The patient should be exposed completely and a full external examination undertaken.

Abdominal pain or tenderness is a non-specific feature with impending hepatic necrosis and failure secondary to paracetamol overdose one of the most serious differentials to consider.

Paracetamol-containing medicines have also been implicated in the development of acute pancreatitis (Trivedi and Pichumoni, 2005). Poisoning may also present with epigastric pain or tenderness as a result of gastric irritation.

Another cause of abdominal tenderness in patients suspected of drug misuse is the presence of foreign bodies in the gastrointestinal system such as wrapped drug packages carried by 'body-packers'. Symptoms may result from package rupture and/or resultant drug absorption. This can often be managed conservatively by inducing gut motility, unless there is suggestion of serious toxicity or bowel obstruction, in which case surgery is indicated (Beckley et al, 2009).

Cocaine, in addition to being a common content of such packages, also causes rhabdomyolysis and subsequent renal failure; suspicion of this should be raised in patients with overdose who complain of muscle pain or tenderness.

Further examination of the patient may reveal evidence of self-harm, needle-tracks, smoking or alcohol excess. *Figure 1* summarizes additional relevant features on examination.

Common agents of overdose

Paracetamol

Paracetamol accounts for approximately 39% of all poisoning admissions (Banham-Hall et al, 2009). The clinical features of a paracetamol overdose can be split into several stages. In the first stage (<24 hours post ingestion) patients can be asymptomatic or may present with nausea and vomiting. Serum paracetamol levels must be measured from 4 hours post ingestion (Wallace et al, 2002). Deranged pH and international normalized ratio on admission are poor prognostic factors, and ingestion of >150 mg/kg is considered hepatotoxic.

In the second stage (24–72 hours post ingestion) patients present with signs of hepatic injury such as right subchondral pain, jaundice and acute confusion. Blood tests will reflect hepatic damage through a rise in transaminase levels (aspartate aminotransferase and alanine aminotransferase) and prolongation of coagulation markers (e.g. international normalized ratio, prothrombin time) (Heard, 2008).

In significant paracetamol overdoses, the third stage (72–96 hours post ingestion) is characterized by signs of acute hepatic failure (coagulopathy, encephalopathy and sepsis), alongside acute renal failure in a proportion of patients. The development of multi-organ failure is potentially life-threatening.

If treatment is deemed necessary, the dosing regimen for N-acetyl cysteine (Parvolex) should be followed as in *Table 2*.

Salicylates

Following salicylate overdose patients typically present with abdominal pain, sweating, nausea, vomiting, tinnitus, oliguria and tachypnoea. An initial respiratory alkalosis provokes compensatory mechanisms causing a metabolic acidosis to develop. The severity of salicylate overdose can be classified by serum salicylate levels (peak levels can be ascertained through serial blood levels) mild: 300–600 mg/litre, moderate: 600–800 mg/litre and severe: >800 mg/litre. In severe overdose patients present with respiratory depression, agitation, tremors, convulsions or comatose (Dargan et al, 2002).

Typically a spectrum of electrolyte derangement is seen in these patients including hypokalaemia, hyper- or hyponatraemia, or hyper- or hypoglycaemia. Furthermore, in large overdose or in

Figure 1. Possible presentations and basic investigations in the overdosed patient.

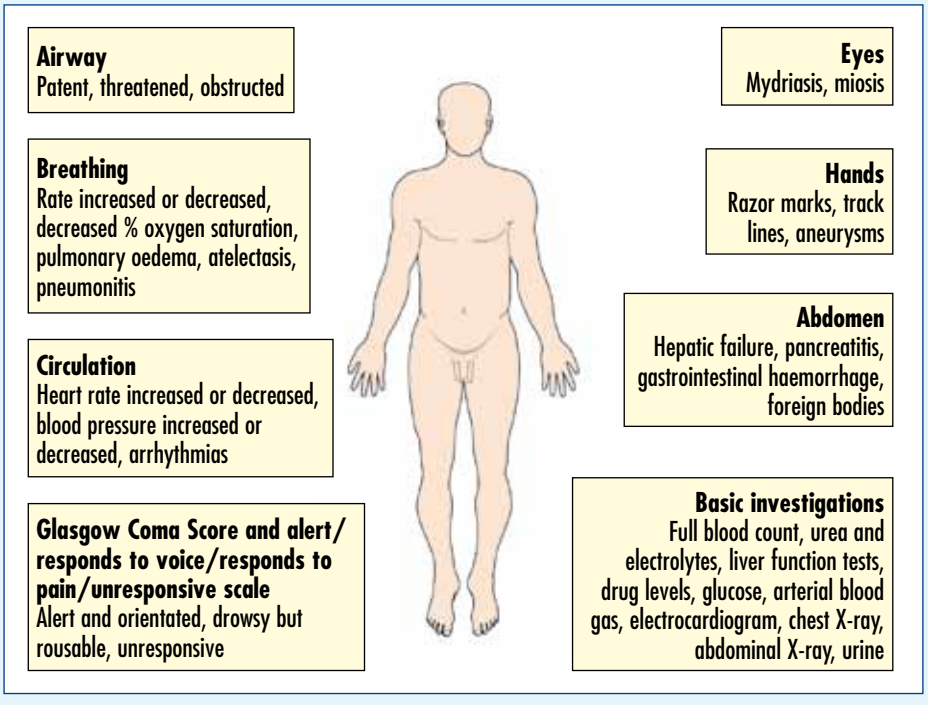

Table 2. Standard dosing regimens of common antidotes

Antidote	Initial dose	Infusion
Parvolex	150 mg/kg (max 16.5 g) in 200 ml 5% glucose over 15 minutes	50 mg/kg (max 5.5 g) in 500 ml 5% glucose over 4 hours Then 100 mg/kg (max 11 g) in 1 litre 5% glucose over 16 hours
Flumazenil	200 μg intravenously over 15 seconds	100 μg (max 1 mg) at 60-second intervals. If no response to repeated doses, consider alternative diagnoses
Glucagon	5–10 mg intravenously	4 mg/hr (reducing gradually)
Digibind (digoxin antibodies)	Please refer to Toxbase (specialized drug)	Please refer to Toxbase (specialized drug)
Naloxone	0.4–2 mg intravenous boluses Repeat at 2–3-minute intervals (max 10 mg) If no response to repeated boluses, consider alternative diagnoses	Calculate as 60% of total initial intravenous dose, to be infused over first hour, then titrate rate as per clinical response

patients with co-existing renal impairment, acute renal failure may occur.

If the patient presents up to 1 hour post-ingestion gastric lavage should be considered. Blood should be taken on admission and then every 3 hours to obtain a peak concentration as some salicylate preparations are slow release, and ingested matter can sometimes form a mass. In patients found to have severe salicylate poisoning, therapy may include the use of sodium bicarbonate elimination, with the aim of maintaining a urinary pH between 7.5 and 8.5. Dehydration and hypokalaemia require correction with intravenous fluids. Occasionally, haemodialysis may need to be considered. Poor prognostic factors include pulmonary oedema, progressive or worsening acidosis, fever and coma (Dargan et al, 2002; Eldridge et al, 2005).

Metabolic acidosis results from an increase in H+ either from increased production of endogenous acids or ingestion of exogenous acids such as salicylates. In addition, endogenous acids such as lactate can be produced in response to failure of end-organ perfusion and can contribute to acidosis and increase in the anion gap. Calculation of the anion gap in shown in *Figure 2*.

In salicylate overdose there is an initial respiratory alkalosis as a result of direct stimulation of the respiratory centre causing hyperventilation and increased removal of carbon dioxide. This is usually only an initial response to mild overdose; in significant overdose, the acid–base disturbance is commonly metabolic acidosis secondary to the exogenous H+. Clinically, tachypnoea may represent either initial respiratory centre stimulation secondary to salicylates or respiratory compensatory mechanisms caused by metabolic acidosis (Gabow et al, 1978). Concurrently, one would expect the blood gas to show a lower than normal carbon dioxide secondary to hyperventilation. In severe salicylate toxicity, the CNS and respiratory centres are depressed and the patient may be bradypnoeic on presentation (Dargan et al, 2002).

Figure 2. Anion gap calculation.

$$\text{Anion gap} = (Na^+ + K^+) - (Cl^- + HCO3^-)$$

The anion gap represents the substances contributing to metabolic acidosis that are not measurable by the arterial blood gas. Na^+, K^+, Cl^- and HCO_3^- are easily measured by arterial blood gas sampling. Common agents causing a raised anion gap include salicylates, ethylene glycol (antifreeze), metformin and other acids. The normal range for anion gap is 8–16 mmol/litre.

Osmolar gap

The osmolar gap has some clinical relevance in assessment of patients with high anion gap acidosis but is rarely used in practice. A high osmolar gap suggests ethylene glycol or methanol poisoning.

Antidepressants

Tricyclic antidepressant overdose is a considerable problem in the acute setting, accounting for 95% of deaths attributable to antidepressants (Shah et al, 2001).

In tricyclic antidepressant overdose, mild symptoms develop within several hours and result from anticholinergic effects, notably a dry mouth, blurred vision, jerking movements, agitation and hallucinations. The relevant signs are dilated pupils, tachycardia and urinary retention. Other effects include cardiac arrhythmias, hypotension (reported in around half of patients post tricyclic antidepressant overdose), seizures and coma (Woolf et al, 2007; Banham-Hall et al, 2009).

An electrocardiogram should be performed to identify cardiac dysrhythmias and QT interval prolongation. An arterial blood gas often shows a metabolic acidosis. Once the QRS prolongation exceeds 160 ms the patient has a much higher risk of developing ventricular arrhythmias (Thanacoody and Thomas, 2005).

Gastric lavage is beneficial within the first hour post overdose (Kerr et al, 2001). In severe overdose, the literature supports the use of alkalinization with sodium bicarbonate boluses (aiming for a pH of 7.45–7.55), before pharmacological management of any dysrhythmia (Hoffman et al, 1993). Cardiac monitoring must continue until the patient's electrocardiogram normalizes. If CNS depression or post-overdose hypotension is severe, patients may require high dependency unit or intensive therapy unit admission.

Benzodiazepines

Benzodiazepines enhance the effect of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) leading to CNS depression. Patients will typically present with the following within several hours of ingestion: drowsiness, slurred speech, ataxia and hypotension. In

patients who have taken a larger quantity or a particularly potent benzodiazepine, symptoms of coma, respiratory depression or even cardiorespiratory arrest may result.

Although benzodiazepines can be detected through blood testing, diagnosis in the acute setting relies largely on the clinical presentation and patient history.

Flumazenil can be used as an antidote, with doses as per *Table 2*. It is only recommended in severe overdose causing significant cardiorespiratory depression. In these instances, it should be used with caution especially in patients with reduced seizure threshold (chronic alcoholics, epileptics, simultaneous tricyclic antidepressant ingestion) (Hoffman and Goldfrank, 1995; National Collaborating Centre for Mental Health, 2004; Joint Formulary Committee, 2010). In cases of respiratory depression, airway and ventilator support is indicated.

Opioids

Patients presenting following an opioid overdose (either intravenous or oral) classically present with a decreased level of consciousness, respiratory depression and pinpoint pupils, and may appear cyanotic and comatose. As intravenous opioids can cause non-cardiogenic pulmonary oedema, these patients must have a chest X-ray (Sporer et al, 2001). As opioids are often used in conjunction with paracetamol-containing preparations, investigations as per a paracetamol overdose must also be instigated. Opioid overdoses can be safely reversed using naloxone through regimens such as that outlined in *Table 2*.

Antipsychotics

All antipsychotics have dopamine antagonist actions, with most also acting as α-adrenergic antagonists; some also have anticholinergic and antihistamine actions (Burns, 2001). With those antipsychotics that cause potassium channel blockade there is the risk of cardiac arrhythmias. A patent who has taken an overdose of antipsychotics typically presents with some of the following features: decreased consciousness, hypothermia, arrhythmias (caused by QT interval prolongation), seizures, decreased respiratory rate and hypotension (Tan et al, 2009). Additionally, a patient may present with signs of neuroleptic malignant syndrome with a fluctuating Glasgow Coma Score, fever, muscle rigidity and autonomic instability (Trollor et al, 2009). There are subtle differences in the overdose manifestations of typical *vs* atypical antipsychotics, which need to be considered when assessing individual patients. Severe acidosis may be corrected with sodium bicarbonate. Elimination of the overdose agent is not recommended, as it is unlikely to be of any benefit (Bateman, 2007).

Toxidromes

Clinical toxidromes are outlined in *Table 3*.

Reduction of absorption of overdose agents

Gastric lavage and activated charcoal are methods for reducing absorption of toxins, but these techniques are largely outmoded. In the emergency setting, lavage and activated charcoal use is only indicated if presentation was within 1 hour of overdose and the amount of ingested agent is life-threatening. Its use is not recommended in poisoning with corrosives. In addition, the airway must either be self-maintained or protected by a cuffed endotracheal tube.

There is little evidence to support the use of charcoal; however, it is most effective when used for poisons which are dan-

Table 3. Clinical toxidromes

	Observations	CNS effects	Gastrointestinal effects	Respiratory effects	Cardiovascular effects
Adrenergic (cocaine, amphetamines)	Increased respiratory rate Increased heart rate Increased blood pressure Pyrexia	Agitation Dilated pupils Delirium Psychosis Seizure	Nausea and vomiting Abdominal pain	Tachypnoea	Hypertension Tachycardia
Anticholinergic (tricyclic antidepressants, atropine, phenothiazines)	Normal respiratory rate Increased heart rate Normal or increased blood pressure Pyrexia	Reduced Glasgow coma scale Confusion Psychosis Agitation	Ileus Reduced bowel sounds	Respiratory failure (in severe overdose)	Hypertension Tachycardia
Opioids (morphine, heroin)	Decreased respiratory rate Normal or decreased heart rate Normal or decreased blood pressure Normal or decreased temperature	Reduced Glasgow coma scale or coma Pupillary constriction Euphoria Seizures Ataxia	Constipation Reduced bowel sounds	Respiratory depression or arrest Acute pulmonary oedema	Hypotension Bradycardia
Sedative (benzodiazepines)	Decreased respiratory rate Normal or decreased heart rate Normal or decreased temperature	Reduced Glasgow coma scale CNS depression Pupils equal and reactive to light	Normal bowel sounds	Respiratory depression	Bradycardia
Sympathomimetic (amphetamines, cocaine, adrenaline)	Increased respiratory rate Increased blood pressure Pyrexia	Excitation Psychosis Seizure Pupil dilatation			

gerous in small quantities, such as tricyclic antidepressants. Induced emesis is not recommended as it does not reduce absorption.

Elimination of overdose agents

Haemofiltration or dialysis in the intensive care setting can be used in cases of severe poisoning, but is limited to a small number of specific agents such as salicylates, ethylene glycol, chlorates, methanol and lithium (Zimmerman, 2003).

Unknown overdose agents

Attempts should be made to trace common sources of unknown possible agents, e.g. drugs the patient normally takes, medicines prescribed to members of their household, or medicines found at their address. Consult a national poisons database, (e.g. Toxbase), and take serum and urine toxicology samples. Keeping the patient in hospital for 48–72 hours and observing closely – with frequent assessment of observations, level of consciousness and repeated measurement of renal function, liver function, blood count and coagulation screen – may be recommended. The use of mass spectrometry has been tested in the emergency department setting to help identify the composition of agents present in the patient's urine samples. This has produced mixed results, largely as a result of technological limitations (Krasowski et al, 2009), but remains a potential area of development nonetheless.

Psychological considerations

In addition to taking a detailed history regarding quantities and types of overdose agents taken, it is also vital that patients receive sufficient emotional support. In taking a history, it is important to elicit if the overdose was intentional or accidental, and what the patient's aim was in taking the overdose (e.g. analgesic relief). In all patients, in particular those who are refusing medical treatment of their overdose, psychiatric input should be sought to help decide if treating the patient under the Mental Health Act is appropriate.

Conclusions

Drug overdose is a common yet complex presentation in emergency departments. All patients who have taken an overdose require a psychiatric assessment from mental health services before hospital discharge. This article reviews the salient features of handling the most common overdose agents, alongside a safe and systematic approach to their acute management. BJHM

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KEY POINTS

- Overdose is an extremely common reason for presentation to emergency departments.
- Patients can be critically ill with life-threatening complications at presentation.
- Measurement of circulating drug levels and obtaining toxicological samples may be crucial.
- Patients may present with an unknown source of poisoning.
- Careful use of supportive therapies and reversal agents is often necessary.