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Acute poisoning on the medical admissions unit

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Alcohol intoxication, deliberate medicinal overdoses and ingestion of (illegal) substances are common reasons for admission to emergency departments in the UK, particularly in inner city hospitals. The annual health and social costs of misuse of alcohol and illegal drugs in England and Wales are each estimated to be nearly £20 billion. One million people use ecstasy, cocaine or other class A drugs each year and more than 100,000 people are injecting drug users. Both alcohol and other problem drug use are associated with a range of harms and cause substantial morbidity and mortality.¹ This review discusses problems related to the ingestion of selected toxins.

Alcohol intoxication

Ethanol (alcohol) is commonly used in the community. The short- and long-term consequences of overconsumption are well described in the medical literature. This article will concentrate on three other alcohols – ethylene glycol, methanol and isopropyl alcohol – which can produce fatal intoxication through the ingestion of relatively small doses. All three are associated with a high osmolar gap, while ethylene glycol and methanol are also associated with a high anion gap metabolic acidosis.

Ethylene glycol

Ethylene glycol (EG) is a common constituent of antifreeze and screen wash products. Antifreeze overdoses used to be a frequent method of (self) poisoning.

There has been a decline in cases presenting over the last decade, but recently a rise in the number of cases admitted to emergency departments and renal units has been observed – where delayed treatment has rendered patients dialysis-dependent. Acute EG intoxication is a medical emergency that can lead to serious neurological, cardiopulmonary and renal dysfunction; it may result in death, particularly if treatment is delayed.²

EG toxicity is characterised by severe metabolic acidosis, high anion gap, high osmolar gap and calcium oxalate crystals in the urine. Following ingestion, the peak serum concentration is reached in 1–4 hours (half-life 3 hours). EG causes intoxication but the accumulation of toxic metabolites is responsible for the potentially fatal acidosis and renal failure which characterises EG poisoning.

The sequence of clinical events occurs on the following timescale:

- *Stage 1* (30 min–12 hours): depressive central nervous system (CNS) disturbances often similar to alcohol intoxication.
- *Stage 2* (12–24 hours): metabolic acidosis and cardiopulmonary effects.
- *Stage 3* (24–72 hours): acute renal failure.

Further delayed neurological disturbances including cranial nerve palsies and polyradiculopathy are rare but well reported. Neurological complications usually occur 10–14 days postingestion.

Methanol

Intoxication by methanol (wood alcohol) often presents non-specifically. Symptoms include weakness, nausea, headache and a feeling of intoxication. Of significant concern are the eye changes which are (relatively) specific to methanol intoxication. Initial observations may include decreased vision, mydriasis, decreased light reflex and

hyperaemia of the optic disk. Optic atrophy secondary to anoxia in watershed areas of the cerebral and distal optic nerve circulations can lead to blindness.³

Severe intoxication has a significant morbidity. In patients presenting with seizures, coma or an arterial pH below 7.0 mmol/l, mortality rates above 80% have been described.⁴

Treatment for ethylene glycol and methanol intoxication. Treatment options for EG and methanol intoxication include fomepizole (the first line option), ethanol and haemodialysis. They are effective in

Key Points

Ethylene glycol (EG) and methanol intoxication frequently cause a high anion gap metabolic acidosis

The breakdown products of EG and methanol are responsible for the toxic effects, whilst isopropanol is directly toxic

Early diagnosis of the toxin is imperative to prevent (or limit) the catastrophic consequences of these toxins which often appear late

Treatment options for EG and methanol overdose include fomepizole, ethanol and haemodialysis

Poisoning with 'club drugs' has become increasingly common in emergency departments; there is likely to be continued rise in the use of these drugs and toxic presentations to hospitals

In addition to the toxicity from the 'club drug' itself there are typically concerns related to 'polypharmacy' and concurrent ethanol ingestion

The effects from the 'club drug' itself are usually short-acting

Few antidotes are available for 'club drugs' and the mainstays of treatment options are supportive; these may require intubation, mechanical ventilation and other artificial organ support

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preventing the development of toxic metabolites if administered soon after ingestion.⁵

Isopropyl alcohol

Commercially, isopropyl alcohol (isopropanol) is a common constituent of cleaning solvents and is used as a rubbing alcohol.⁶ Unlike EG and methanol, it is the parent compound that is toxic not the metabolites. Even small doses can produce CNS pathology, ataxia, lethargy, coma and myocardial depression (hypotension and cardiac shock). The condition should be suspected in the presence of clinical symptoms, with a high osmolar gap and the absence of metabolic acidosis (or hyperglycaemia). Treatment is predominantly supportive although haemodialysis may be useful in selected cases.⁶

Medicinal overdoses/poisoning

Paracetamol and salicylate overdoses remain by far the commonest medicinal overdoses. Treatment protocols for these overdoses are well described. (Further information is provided in the Cochrane database review for paracetamol overdosing⁷ and in Teece's review of therapies for salicylate poisoning.⁸)

Recreational drug ingestion

Recreational drugs such as marijuana, lysergic acid diethylamide, methamphetamine and opiates have been largely replaced by newer psychoactive agents which are believed to enhance social interaction. These drugs are often illegal, which can retard accurate history taking. In addition, they are often ingested as part of polysubstance abuse and consumed with large quantities of alcohol, making identification of the precise toxin difficult.⁹ Routine urine drug screens are (usually) unable to detect these toxins. Gas chromatography and mass spectroscopy can be used but they are seldom practical in establishing a diagnosis. Awareness to the possibility of recreational drug overdose is required from the attending physician to ensure prompt diagnosis and appropriate treatment.

Because of the prevalence of these agents at dance parties, raves and nightclubs they are commonly referred to as 'club drugs'. The most prominent are:

- 3,4-methylenedioxymethamphetamine (MDMA or ecstasy)
- gamma-hydroxybutyrate (GHB or liquid ecstasy)
- flunitrazepam (Rohypnol), and
- ketamine (Ketalar).

MDMA (ecstasy)

Ecstasy is the most common stimulant found in dance clubs and at raves. MDMA stimulates both the CNS and the sympathetic nervous system, mainly through the release of serotonin, dopamine and norepinephrine from presynaptic neurons. It blocks their reuptake inactivation through the inhibition of monoamine oxidase.

It is difficult to establish an accurate incidence of the side effect profile for MDMA ingestion, owing to a bias on the reporting of adverse effects. There exists only limited data and reporting on how commonly MDMA is ingested without complication. Common reported side effects of MDMA include tachycardia, hypertension, tremor, arrhythmias, mydriasis, parkinsonism and urinary retention.¹⁰

Far more serious side effects (including death) are reported if the 'serotonin syndrome' develops. This usually manifests with gross hyperpyrexia, severe hyponatraemia, in part related to a direct rise in antidiuretic hormone, myoclonus and rigidity (often with elevated creatinine kinase).¹¹ End-organ damage, including rhabdomyolysis, renal failure, hepatic failure, adult respiratory distress syndrome and disseminated intravascular coagulopathy are described.¹²

Treatment of MDMA intoxication is predominantly supportive. With hyperpyrexia, active cooling is advised. Benzodiazepines are advocated as first line drugs to reduce agitation. Urinary acidification, which can increase urinary amphetamine excretion, is not recommended because of the possibility of renal myoglobin precipitation. Renal replacement therapy, liver support,

including transplantation and intubation for respiratory support, may be required.

Gamma-hydroxybutyrate (liquid ecstasy)

GHB is a derivative of the inhibitory neurotransmitter gamma-aminobutyric acid. It occurs naturally in the CNS and regulates sleep cycles, core temperature, memory and cerebral glucose metabolism.¹³ GHB and its precursor, gamma-butyrolactone (GBL) are emerging substances of abuse, in both the USA¹⁴ and Europe.¹⁵

Use of GHB as an anaesthetic and also as a sleep aid in hospital was common in the 1960s. When used recreationally, GHB is reported to cause euphoria and increase sensuality and disinhibition.¹⁴ GHB intoxication has serious complications and is potentially fatal. Several clinical features appear to be typical of GHB/GBL intoxication: deep coma with sudden wakening, bradycardia, hypoventilation and agitation. In addition, vomiting, transient agitation, myoclonic jerking and seizure are well described.¹⁵

GHB is metabolised very quickly: it can be detected for only eight hours in blood and 12 hours in urine. The median duration of symptoms is usually short (two hours) and coma rarely lasts longer than four hours.¹⁵

Interestingly, in a Swiss epidemiological study of 141 patients with GHB/GBL intoxication, 86 patients (61%) presented comatose.¹⁵ Death is well described with GHB/GBL intoxication, even if taken without alcohol or other 'drugs'. Significantly, there are no reported deaths in hospitalised patients,¹⁶ making GHB a very serious intoxication in the prehospital setting. The deaths are related to cardiorespiratory depression, loss of airway and injuries associated with diminished judgement.

Flunitrazepam (Rohypnol)

Flunitrazepam is a potent benzodiazepine, with very rapid onset. It is abused for its intoxicant and relaxant effects and has been used in 'date rape'.¹⁷ The side effect profile is similar to that of other benzodiazepines and is dose-

related. Somnolence, impaired psychomotor behaviour, confusion, amnesia, visual disturbances, hallucinations and respiratory depression are all described.⁹ Chronic use of flunitrazepam can induce dependence.

Ketamine (Ketalar, K, special K)

Ketamine, a phencyclidine derivative, which acts through the inhibition of neuronal uptake of norepinephrine, dopamine, serotonin and glutamate activation,¹⁸ is used as a dissociative anaesthetic in the hospital setting. It became popular because it causes anaesthesia without respiratory depression, though the adverse effects are known to include vivid dreams and hallucinations post-anaesthetic. These have limited its medical use but made it popular amongst recreational drug users.

The effects of ingestion appear rapidly and last from 30–60 minutes. The short duration of action often leads to sequential dose-taking. Acute pharmacological side effects include tachycardia, hypertension, visual hallucinations and impaired cognitive function.¹⁹ Toxic effects of ketamine include hyperexcitability, severe agitation and paranoid psychoses and, rarely, respiratory depression.

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