

Recent advances

Management of self poisoning

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Introduction

Around 15%-20% of the workload of medical units and 10% of the workload of accident and emergency departments in the United Kingdom are due to self poisoning.^{1 2} Episodes of self poisoning in the United Kingdom continue to rise, particularly in young men, and alcohol is often taken with the overdose.² In general the severity of poisoning has diminished over the past 10 years with the introduction of safer drugs, such as newer serotonin reuptake inhibitors, but the total number of deaths from poisoning in the United Kingdom remains steady at 4000 per year, and the commonest cause of death by poisoning is carbon monoxide.^{2 3} This article highlights several specific advances in the management of poisoning over the past two or three years.

Methods

We searched Medline and Embase with the keywords "poisoning," "intoxication," "toxin," and "overdose." We included topics as a result of discussion with colleagues in clinical toxicology in the United Kingdom, Europe, Australia, and the United States.

New guidelines on gut decontamination

The American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists have recently produced new guidelines on gut decontamination on the basis of consensus and evidence based statements.⁴⁻⁶ It is important to understand the advances in understanding and changes in practice that come from the guidelines, but the evidence base for them is limited.⁴⁻⁷

Activated charcoal

Activated charcoal should be given as a single dose (50 g for an adult, 1 g/kg body weight for a child up to 12 years) up to 1 hour after ingestion of a substantial amount of toxin.⁴ Beyond this time adsorption is reduced.^{4 8} What constitutes a substantial amount of toxin depends on the toxin but in general it is a dose expected to cause moderate to severe toxicity. The guidelines do not apply to agents for which multiple dose charcoal would be beneficial or for substances that are not readily adsorbed to charcoal (box 1).^{4 5} Charcoal should never be given if the airway cannot be protected, as aspiration pneumonitis is a risk.⁹

Recent advances

In most cases of poisoning with a substantial amount of toxin the preferred method of gut decontamination is to give activated charcoal within 1 hour of ingestion

When a potentially lethal amount of a drug is not adsorbed by activated charcoal, such as iron or lithium tablets, whole bowel irrigation with polyethylene glycol solution is recommended

The role of hyperbaric oxygen in the treatment of carbon monoxide poisoning is controversial

4-Methylpyrazole is a new antidote for the treatment of severe poisoning with methanol and ethylene glycol

Awareness of those at increased risk of paracetamol overdose should lead to appropriate administration of N-acetylcysteine

Ketamine ("special K"), gammahydroxybutyrate, and "sextasy" (ecstasy plus sidafenil) are recent drugs of misuse

Developments in databases have allowed doctors and nurses to access more information on management of poisoning with common substances

Multiple doses of activated charcoal (adults: 50 g immediately followed by 25 g every 2 hours or 50 g every 4 hours; children: 1 g/kg body weight followed by 1 g/kg body weight every 4 hours) should be considered for the adsorption and enhanced elimination of certain toxins (box 2).⁵ The role of more than one dose of activated charcoal in salicylate poisoning remains controversial, but the current guideline states that single dose charcoal should be used up to 1 hour after ingestion.^{4 5}

Gastric lavage

Gastric lavage is only used up to 1 hour after ingestion of a substantial amount of toxin; many clinical toxicologists rarely use this method now.⁶ One study

Box 1: Substances not readily adsorbed to charcoal

Ferrous salts	Acids
Lithium preparations	Alkalis
Potassium salts	Fluorides
Ethanol	Organic solvents
Methanol	Mercury and its salts
Ethylene glycol	Lead and its salts

showed that gastric emptying by lavage and emesis failed to remove all the tablets taken by patients, and that a large residue often remained.¹⁰ An Australian study showed that outcome in poisoning was not improved by gastric lavage and activated charcoal versus activated charcoal alone; however, the number of patients that were seriously poisoned was comparatively small.¹¹ Gastric lavage is absolutely contraindicated after ingestion of corrosive substances and comparatively contraindicated after ingestion of hydrocarbon solvents, such as white spirit, because of the risk of lipid pneumonitis.⁶

Emetics

Syrup of ipecacuanha is now rarely used as an emetic as there is no evidence that it decreases morbidity or mortality in poisoning. Additionally, emetics may increase morbidity by causing symptom free patients to become nauseated and to vomit.¹² It is also difficult to give activated charcoal after an emetic.¹²

Whole bowel irrigation

In whole bowel irrigation a solution of polyethylene glycol is given orally or by nasogastric tube (2 litres per hour in adults) until the rectal effluent becomes clear (usually after 2-6 hours). It is contraindicated in patients with bowel obstruction, perforation, ileus, haemodynamic instability, or where the airway cannot be protected.¹³ Polyethylene glycol should be considered when patients have ingested potentially serious substances—for example, sustained release or enteric coated preparations. It is also of theoretical value after such ingestions of lithium, iron, arsenic, lead oxide, and zinc sulphate.¹³ Polyethylene glycol or laxatives are sometimes used in body packers to remove packets that are beyond the pylorus, although one report described the death of a body packer when ingested condoms dissolved after paraffin was given.¹⁴ Packets in the stomach are best removed endoscopically, and packets in the small or large intestine that contain potentially lethal amounts of drugs should be removed

Box 2: Indications for multiple dose activated charcoal

Slow release preparations such as theophylline (but not lithium)
 Carbamazepine
 Dapsone
 Digoxin
 Paraquat
 Phenobarbitone
 Quinine
 The fungus *Amanita phalloides*

surgically.^{15 16} The alternative is to wait for the packet to pass through the body naturally, which it is possible to do with less toxic drugs such as cannabis.

Carbon monoxide poisoning**Hyperbaric oxygen**

Carbon monoxide causes severe hypoxia by forming carboxyhaemoglobin, which impairs oxygen delivery from blood to tissues and prevents the use of available oxygen by combining with cytochrome oxidase.¹⁷ Death may result from cardiac and neurological sequelae acutely but subacute and chronic exposure are also important. The scientific rationale for hyperbaric oxygen improving outcome in carbon monoxide poisoning is that the half life of carboxyhaemoglobin is reduced, and that the reduced amounts of carbon monoxide bind to the enzyme.^{17 18} To date, however, five randomised trials have disagreed on whether treatment with hyperbaric oxygen works in clinical practice.¹⁹⁻²³ Limitations to the trials were too few patients, inclusion of patients exposed to other toxins in fires, and different protocols for hyperbaric oxygen therapy. The latest study suggested that hyperbaric oxygen therapy might be harmful, but only 46% of patients attended follow up.²³ The current recommendation is that hyperbaric oxygen therapy should be considered if a patient has been unconscious at any stage since exposure, if carboxyhaemoglobin concentrations have exceeded 40% at any time, or if there are neurological or psychiatric features. The logistical difficulties in transporting patients to hyperbaric oxygen chambers should not be underestimated.

Paracetamol poisoning

Paracetamol continues to generate the greatest number of emergency inquiries to the National Poisons Information Service of any single agent, and it constitutes 48% of hospital admissions for poisoning in the United Kingdom.²⁴ A practical wall chart for management of paracetamol poisoning has been approved by physicians of the National Poisons Information Service, paediatricians, and accident and emergency clinicians.²⁵

Patients at increased risk from paracetamol poisoning are those with enzyme induction such as patients taking anticonvulsants or those with glutathione depletion such as anorexic patients. Such patients should receive N-acetylcysteine at lower plasma paracetamol concentrations than patients at normal risk.²⁵⁻²⁷ Defining those at risk is not new, but there is greater awareness both of who they are and of failure to provide appropriate antidotal treatment. The main message in paracetamol poisoning is "if in doubt, treat with N-acetylcysteine." Anaphylactoid reactions occur in about 5% of patients given N-acetylcysteine, often within an hour of starting the infusion.²⁸

Management difficulties in paracetamol poisoning include patients presenting 15 hours or more after ingestion of the drug or patients taking staggered overdoses—in excess of 150 mg/kg/day body weight or 12 g for an adult, whichever is the lesser. A poisons centre or a liver transplant unit should be contacted if there is evidence of hepatotoxicity or doubt about its management. This ensures that referral takes place

Box 3: Poisons databases**TOXBASE**

Primary toxicology database of the United Kingdom, produced by the National Poisons Information Service Centres; free access to healthcare professionals (in viewdata format but internet version available soon). Contact Scottish Poisons Information Bureau (tel 0131 536 2303)

CD Roms

Poisonous plants in Britain and Ireland and Poisonous fungi in Britain and Ireland. Contact National Poisons Information Service (London) (tel 0171 771 5383)

toxnet.nlm.nih.gov/servlets/simple-search

Toxicology database of the National Library of Medicine—access to Pubmed, Toxline, and hazardous substance databank

www.pharmacy.arizona.edu/centers/poison-center/
Arizona Poisons Centre

www.intox.org

World Health Organisation and international programme on chemical safety

www.nihs.go.jp/GINC/index.html

Global information network on chemicals

www.nihs.go.jp/GINC/webguide/csinfo.html

Comprehensive global information network on chemicals

www.rmpcdc.org/poisoncenter/index.cfm

Rocky Mountain Poisons Center

www.atsdr.cdc.gov/atsdrhome.html

Agency for Toxic Substance and Disease Registry; slow access from NHS Net

before the criteria for liver transplantation are met (a prothrombin time greater than 100 seconds, serum creatinine concentration greater than 300 $\mu\text{mol/l}$, and grade III or IV encephalopathy or a pH of less than 7.3 at 24 hours or more after ingestion, after correction of hypovolaemia) and that intensive care support is appropriate.²⁹ N-acetylcysteine is also used in patients with fulminant hepatic failure (encephalopathy and renal failure) due to paracetamol and it is not acting by glutathione repletion at this stage. N-acetylcysteine may scavenge free radicals or exert some haemodynamic effect, although its role is debatable.^{30–32}

Drugs of misuse

Ecstasy

Drugs of misuse continue to present problems, particularly in inner city areas. Ecstasy (methylenedioxymethamphetamine or MDMA) causes dehydration with hyperthermia, agitation, and fits. Deaths still result from ecstasy poisoning. Treatments that may decrease mortality, particularly if the rectal temperature exceeds 40°C, include active cooling measures such as cool intravenous fluids, and use of the muscle relaxant dantrolene.³³ The extent to which dantrolene is of value is, however, in doubt and it has dose dependent adverse effects such as hepatitis.³³ Hepatotoxicity has occurred with ecstasy poisoning, and this has been treated with liver transplantation.^{34 35} Other features of ecstasy poisoning include hyponatraemia, cerebral infarction, or haemorrhage due to uncontrolled hypertension, or vasculitis.³⁵ Many substances are now added to ecstasy tablets such as caffeine and ketamine.³⁶ Ketamine is a veterinary anaesthetic, which in man causes a dissociative state and has led to it being used for “date rapes.”³⁶ Ketamine has also resulted in accidents as the drug causes pain free floating sensations with vivid dreams.

A current vogue is the use of sildenafil (Viagra) with ecstasy for enhanced effects, so called sextasy.

Liquid Ecstasy

Another recent drug of misuse is gammahydroxybutyric acid (GHB or “liquid ecstasy”).³⁷ The drug is dissolved in water to produce a clear liquid and is consumed until a “high” is reached.³⁷ Liquid ecstasy increases intracerebral dopamine and if taken in excess causes drowsiness followed by seizures, hypoventilation, and loss of consciousness.^{37 38} The response is unpredictable, and coma and seizures have been produced by as little as 5 ml in an adult. Liquid ecstasy acts synergistically with ethanol to produce central nervous system and respiratory depression.^{37 38} Naloxone has been shown to reverse some of the effects of liquid ecstasy in animals, but its efficacy in man is unknown.³⁸

Ethylene glycol and methanol poisoning

Poisoning with ethylene glycol and methanol have traditionally been treated by a combination of haemodialysis to remove toxic metabolites and ethanol to competitively inhibit enzymes responsible for production of the toxic metabolites. Like ethanol, 4-methylpyrazole is a competitive inhibitor of alcohol dehydrogenase, blocking the metabolism of ethylene glycol into its toxic metabolites glycolate and oxalate.³⁹ 4-Methylpyrazole is licensed for use in several countries, including the United States and United Kingdom, and is used to treat severe methanol or ethylene glycol poisoning. Compared with treatment with ethanol it has the advantage of reduced central nervous system depression, although haemodialysis may still be needed to remove accumulated metabolites and for the management of renal failure.^{39 40}

Poisons databases

In the United Kingdom several databases have been developed to meet the increasing needs of doctors and nurses for information on poisons (box 3). In addition, easy internet access to a wide variety of sources of poisons information, including lethal “recipes,” enables people both to be better informed and to be at greater risk from serious poisoning.

Self poisoning is an important clinical problem, and several advances in recent years have been initiated by cases reports, which are then developed into multicentre—often multinational—collaborations. Information on the management of particularly unusual or serious cases can be obtained from the National Poisons Information Service.

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Lesson of the week

Insulin as a substance of misuse in a patient with insulin dependent diabetes mellitus

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The relation between substance misuse and poor compliance with treatment is well established in both general medicine and psychiatry.^{1,2} Although young patients with insulin dependent diabetes mellitus may have lower rates of comorbid substance misuse,³ there is direct evidence that their compliance with treatment is poor.⁴ Patients with insulin dependent diabetes mellitus have an increased risk of developing a psychiatric disorder, particularly in the early course of their illness,³ and treating the psychiatric disorder improves glycaemic control.⁵

Hypoglycaemic events are common in people with insulin dependent diabetes mellitus⁶ and may be associated with cognitive, affective, and sometimes life threatening sequelae.⁷ Specific mood changes caused by changes in blood glucose concentrations are idiosyncratic, and although negative affective states are the most common, positive changes such as giddiness and

euphoria are also seen.⁸ Although there is a strong relation between severe hypoglycaemia and tight glycaemic control,⁹ cases of deliberate misuse of insulin have been reported. Typically, these patients either attempt suicide or feign illness.¹⁰ We report the rare case of a patient with insulin dependent diabetes mellitus and no history of a psychiatric disorder who misused insulin regularly over a two year period for its euphoric effects. The consequences were ultimately serious.

Case report

A 30 year old man with insulin dependent diabetes mellitus was admitted to hospital. He had lost consciousness for two hours as a result of severe hypoglycaemia, and had then experienced prolonged confusion. The man, a college lecturer, was unmarried. Since his diagnosis three years previously, his diabetic control had been erratic (HbA_{1c} values ranged from 8%

Doctors should be alert to the possibility of insulin misuse, and should consider psychological evaluation, in an insulin dependent diabetic patient with poor control

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