

Emergency management of poisoning

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INTRODUCTION

Drug overdose and poisoning is a global public health problem. In the UK it accounts for 120 000 hospital admissions each year (around 1% of the total number) and is a significant proportion of the Emergency Department workload.¹ In 2004 the World Health Organisation estimated that 346,000 people died worldwide from unintentional poisoning, whilst 1 million people died as a result of deliberate self harm, and poisoning accounted for a significant number of these deaths.² Drug overdose is the most frequent presentation of deliberate self-harm and this may complicate medical management. However most patients are young, otherwise medically well and, managed appropriately, the vast majority should recover fully.

GENERAL PRINCIPLES

Many drugs in overdose (e.g. opiates, tricyclics, benzodiazepines) can cause significant depression of cerebral and cardiorespiratory function. Emergency management should always start with a rapid **initial assessment** and **resuscitation** of the airway, breathing and circulation. Careful **history** and **examination** will, in most cases, give an indication as to the likely severity of the overdose and guide subsequent management. Treatment principles include strategies to reduce absorption, increase elimination, general supportive measures and, when available and appropriate, the use of specific antidotes. It is strongly recommended that, in cases where doubt exists regarding the degree of risk, or appropriate management, the Poisons Information Service be contacted. In the UK, they can be reached by dialling **0844 892 0111**, 24-hours-a-day, or information may be obtained via their website www.toxbase.org.

HISTORY

A detailed and reliable account of the drug or drugs taken should be sought; this should include the drug name, amount, preparation type, time of ingestion and the co-ingestion of other substances such as alcohol or recreational drugs, which might influence the patient's clinical state or drug clearance. The presence of vomiting of tablets soon after overdose should be noted but does not preclude significant toxicity.

The medical, social, psychiatric and therapeutic drug history will help to identify high risk patients and also guide subsequent management.

The patient may be uncooperative or unable to give these details and so a collateral and confirmatory history should be acquired from available sources such as drug packets, the ambulance crew, witnesses, a suicide note and the patient's case notes. The MIMS (Monthly Index of Medical Specialties) colour index, BNF (British National Formulary) descriptions or the computerised system 'TICTAC' may aid identification of drugs already removed from packets.

EXAMINATION

The **airway, breathing and circulation** should be reassessed and treated accordingly as a priority. Basic airway manoeuvres, simple adjuncts, supported ventilation and/or cuffed **endotracheal intubation** may be required if the airway and/or breathing is compromised. The patient's level of consciousness may give an indication of the toxicity of the overdose, risk to the airway and guides the level of supportive care needed. It can be expressed on the 'AVPU' scale or as a formal GCS (although not designed for this purpose, it does give a reproducible score which is sensitive to subsequent changes). A GCS equal or less than 8 (or responding to Pain only) increases the risk of airway compromise and endotracheal intubation is indicated unless rapid recovery is anticipated.

Careful attention should be paid to **respiratory function**, particularly with sedative drug toxicity. This should include respiratory rate and tidal volume and the measurement of oxygen saturations using pulse oximetry. A low respiratory rate with decreased oxygen saturations may indicate hypoventilation, but note that a normal saturation does not exclude hypercarbia or indeed hypoxia in carbon monoxide poisoning. If in any doubt, arterial blood gases should be measured. Tachypnoea can be seen with metabolic acidosis (e.g. tricyclics, methanol), anxiety, and stimulant drug overdose and as an early feature of salicylate poisoning (respiratory alkalosis). Supplementary oxygen via facemask should be given to all patients initially, taking account of pulse oximetry (noting the limitations described above).

Summary

This article covers the basic aspects of management of patients who have ingested a poisonous agent. Specific common agents are described in more detail. In particular, the recommendations on the management of paracetamol in the UK have recently been altered in order to make treatment algorithm easier to use and administration of acetylcysteine safer.

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Many drugs exhibit **cardiovascular toxicity** in overdose (e.g. tricyclics, β -blockers, digoxin, lithium). This may manifest as hypotension and or cardiac arrhythmias. Pulse, blood pressure and ECG should be recorded, intravenous access established and initial fluid resuscitation given as appropriate.

General examination may give corroborating evidence of significant ingestions or clues in unknown overdoses. Many drugs (SSRIs, tricyclics, phenothiazines) have serotonergic or anticholinergic effects with pupil dilatation, and extrapyramidal movements, whilst opioid type drugs will cause sedation and pin point pupils.

Temperature, blood glucose (low in β -blocker, ethanol poisoning) and weight should also be recorded. Weight is important in calculating whether the patient is likely to have received a toxic dose and may guide treatment, for example in paracetamol overdose.

Examination should reveal any associated injury (accidental or deliberate self harm) which may require treatment, or the presence of other substances such as alcohol. If their clinical condition allows, an assessment of the patient's mental state should be made.

FURTHER MANAGEMENT

Additional investigations

Samples should be sent for laboratory investigation – urea, electrolytes and blood glucose as a minimum. Blood gases are helpful in providing a rapid assessment of acid-base disturbance as well as assessing adequacy of ventilation in patients with reduced conscious level. Creatinine kinase (CK) should be measured if there is a possibility of rhabdomyolysis or serotonin syndrome is suspected.

Appropriately timed drug levels (e.g. paracetamol, salicylate, lithium) should be taken when indicated. Paracetamol levels should be sent if there is any possibility of paracetamol poisoning – this includes all unconscious patients. Many Emergency Departments measure paracetamol levels in all patients presenting where poisoning is suspected, as paracetamol poisoning is associated with a lack of early clinical signs. There is no need to routinely measure salicylate concentrations in conscious overdose patients who deny taking salicylate-containing preparations and who have no features suggesting salicylate toxicity. Salicylate levels should be measured in all unconscious patients or where poisoning is suspected.

Treatment

Supportive treatment of the cardiorespiratory and neurological systems should be given by standard intensive care methods.

Induced emesis is no longer recommended and is contraindicated in volatile or corrosive substances.³ Drug absorption can be reduced by the use of activated charcoal, given either orally or nasogastrically. A single dose (50g in adults, 1g.kg⁻¹ in children) should be given up to one hour after the ingestion of a substantial amount of toxin (i.e. a dose expected to cause moderate to severe toxicity). After this time adsorption is reduced. Multiple doses of activated charcoal should be considered for the adsorption and enhanced elimination of certain toxins (see Box 1). Certain other substances (including alcohols, ferrous salts and lithium) however, are not readily adsorbed to charcoal and this treatment is not indicated for poisoning with these substances.

An unprotected airway is an absolute contraindication to charcoal administration, as aspiration pneumonitis is a risk.

Box 1. *Toxins for which multiple doses of activated charcoal are indicated⁴*

- Carbamazepine
- Dapsone
- Digoxin
- Paraquat
- Phenobarbitone
- Quinine
- Slow release preparations such as theophylline
- Amanita phalloides fungus
- Multiple doses may also be considered in life threatening overdose of other drugs (e.g. tricyclic antidepressants).

There is little evidence to support the use of gastric lavage and current literature suggests that this should only be considered in patients who present within 1 hour, who have ingested a substantial amount of a toxin with high lethality.⁵ It is contraindicated if the airway cannot be protected and in the ingestion of hydrocarbons (risk of aspiration and chemical pneumonitis) and corrosives.

If metabolic acidosis due to poisoning persists, despite the correction of hypoxia and adequate fluid resuscitation, then correction with intravenous sodium bicarbonate should be considered. Rapid correction is particularly important if there is prolongation of the QRS or QT intervals on the ECG. In adults an initial dose of 50mmol of sodium bicarbonate may be given and repeated if necessary (as guided by arterial blood gas monitoring).

In cases of severe poisoning, haemodialysis should be considered as a means of extracorporeal toxin removal as well as for management of acute kidney injury.⁶ Seizures should be controlled initially with intravenous diazepam (10–20mg in adults; 0.25mg.kg⁻¹ body weight in children) or lorazepam (4mg in adults; 0.1mg.kg⁻¹ body weight in children).

SPECIFIC POISONS

Alcohol

Blood ethanol concentrations may be used to demonstrate exposure, but are levels not reliable due to individual tolerance and do not exclude co-ingestions or head injury as a cause for symptoms or signs. They should therefore be interpreted with caution.

Clinical features

With increasing blood concentrations, features are progressive from ataxia, dysarthria, and nystagmus, to hypothermia, hypotension, stupor and coma. In severe cases, especially children, convulsions, respiratory depression, cardiac arrhythmias and acidosis may occur.

Specific hazards

These include aspiration of vomit, hypoglycaemia (especially in children), and rhabdomyolysis (especially following a period of unconsciousness).

Treatment

Alcohol is rapidly absorbed from the gut, and therefore gut decontamination is unlikely to be of benefit.

Intravenous thiamine (e.g. Pabrinex®) should be given to chronic alcohol abusers to protect against the onset of Wernicke's encephalopathy. This should be achieved before administration of glucose to treat hypoglycaemia.

Hypoglycaemia should be treated as quickly as possible with oral glucose if the patient is awake, or otherwise intravenous 5% or 10% glucose.

If facilities allow, haemodialysis should be considered if the blood concentration is greater than 5g.L^{-1} , if arterial pH is <7.0 , or if the patient's condition deteriorates in spite of maximal supportive measures.

Paracetamol

In therapeutic doses paracetamol conjugation to inactive metabolites is the major route of metabolism. Oxidation by cytochrome P450 enzymes is a minor route of metabolism and produces N-acetyl-p-benzoquinoneimine (NAPQI). NAPQI binds covalently to sulphhydryl (-SH) groups in glutathione to form a non-toxic conjugate. When larger doses of paracetamol are taken more NAPQI is formed, hepatic glutathione stores are exhausted and NAPQI binds to hepatic cellular proteins, resulting in cellular injury.

Ingestion of as little as 150mg.kg^{-1} (75mg.kg^{-1} in high risk patients, see Box 2) is potentially fatal. Note that for obese patients (weighing $>110\text{kg}$) the toxic dose in mg.kg^{-1} should be calculated using 110kg , rather than their actual weight.

Box 2.

There is increased risk of paracetamol toxicity if the patient:

- is malnourished, has a nutritional deficiency and/or chronic illness and therefore likely to be glutathione deplete e.g. acute or chronic starvation, eating disorders, children with 'failure to thrive', cystic fibrosis, AIDS, alcoholism, hepatitis C.
- has hepatic enzyme induction or evidence of ongoing liver injury e.g. is on long term treatment with enzyme inducing drugs (including phenytoin, phenobarbital, carbamazepine, primidone, rifampicin, rifabutin, efavirenz, nevirapine, St John's Wort), regularly consumes ethanol in excess of recommended amounts. Note enzyme induction with drugs or alcohol may occur within a few days.

Clinical features

There are often none. Mild nausea and vomiting and anorexia may occur, but patients are generally asymptomatic up to 4 hours post ingestion. Right subchondral pain and tenderness, jaundice, vomiting

and acute liver failure may be seen at 24-36 hours. Confusion and encephalopathy develop over 36-72 hours.

Specific hazards

Hepatocellular necrosis is maximal 3-4 days after ingestion, and may be associated with hypoglycaemia, haemorrhage, encephalopathy and death.

Treatment guidelines

Intravenous acetylcysteine is the antidote of choice. It must be started within 8 hours if maximal benefit is to be gained,⁷ however there is evidence that acetylcysteine can improve outcome, even in patients with encephalopathy, so those that present more than 8 hours after ingestion should also be considered for treatment.⁶ Knowledge of the timing of ingestion, and whether there has been a single ingestion or repeated or 'staggered' ingestions (taken over 1 hour or more) is vital. Treatment is dependent on the weight of the patient (this should be measured as estimates are often inaccurate) and an accurately timed paracetamol plasma level for non-staggered overdoses. Acetylcysteine is highly effective especially within 8 hours of a toxic dose and generally should be used if any doubt that a toxic amount of paracetamol has been ingested. Specific management advice for paracetamol poisoning is otherwise based on the duration since ingestion:

Presentation less than 8 hours after ingestion

Consider activated charcoal if more than 150mg.kg^{-1} (75mg.kg^{-1} if high risk) has been taken within the previous hour.

4 hours after ingestion, take a venous blood sample for plasma paracetamol level, as well as baseline biochemistry and haematology (including INR). Plasma concentrations should not be measured less than 4 hours after ingestion, as levels are unreliable before this time.

If the patient is at risk according to the 'plasma paracetamol - time from ingestion graph' (see Figure 1), start acetylcysteine according an appropriate dosing schedule available.

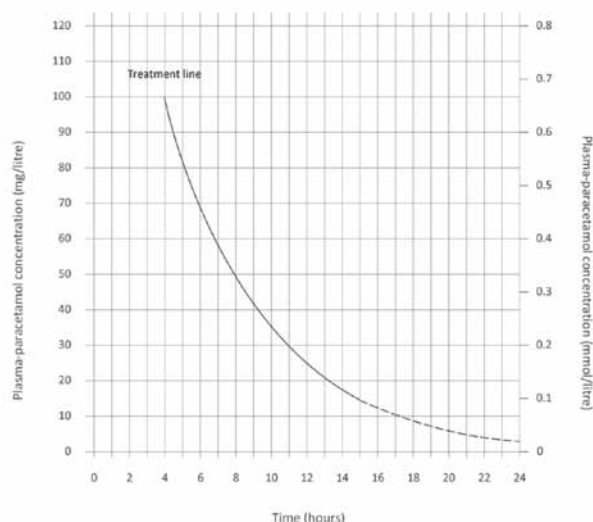


Figure 1. Revised paracetamol overdose treatment nomogram (reproduced courtesy of the College of Emergency Medicine, UK and available at <http://www.collemergencymed.ac.uk/Shop-Floor/Clinical%20Guidelines/Clinical%20Guidelines/Paracetamol%20Overdose/>)

If the patient is not at risk according to the appropriate treatment line, no treatment is necessary.

Adult and paediatric dosing tables for acetylcysteine are available at: <http://www.collemergencymed.ac.uk/Shop-Floor/Clinical%20Guidelines/Clinical%20Guidelines/Paracetamol%20Overdose/>. Note that the College of Emergency Medicine (UK) now recommends that the first infusion is completed over 1 hour (not 15 minutes).

In children under 6 years old where there is absolute certainty that a single dose of less than 150mg.kg⁻¹ body weight (or 75mg.kg⁻¹ in those in high risk group) has been ingested the need for measuring plasma paracetamol concentrations can (according to NPIS advice) “reasonably be considered unnecessary and the child discharged”.

Presentation at 8-24 hours after ingestion

DO NOT wait for the result of the plasma paracetamol level. Give acetylcysteine immediately unless certain that the ingestion has been less than 150mg.kg⁻¹ (75mg.kg⁻¹ in the high risk group). The efficacy of acetylcysteine in protecting against hepatotoxicity declines rapidly during this period.

Take blood urgently for paracetamol level, ALT, creatinine, and INR.

If the patient is determined not to be at risk, when the paracetamol level is reported, INR plasma creatinine and transaminases are normal, and the patient is asymptomatic, acetylcysteine may be discontinued.

If the risk of liver damage is confirmed, continue administration of acetylcysteine, and keep the patient under observation.

Presentation 24-36 hours

Give acetylcysteine immediately unless certain that the ingestion has been less than 150mg.kg⁻¹ (75mg.kg⁻¹ in the high risk group).

Measure plasma creatinine, ALT and INR, paracetamol levels and venous blood gases. The plasma paracetamol concentration is unlikely to be detectable after 24 hours, even after significant overdose. If elevated it suggests either a very large overdose, that the timing of ingestion is not accurate or that the overdose was staggered.

If the patient has evidence of liver injury or raised paracetamol levels continue administration of acetylcysteine, and keep the patient under observation.

Presentation after 36 hours

Unless the patient has hepatic tenderness or is jaundiced wait for lab results before commencing treatment (there is no evidence that delaying treatment with acetylcysteine for a short time affects patient outcome in those presenting more than 36 hours after overdose).

Measure plasma creatinine, ALT and INR, paracetamol levels and venous blood gases.

If the patient has evidence of liver injury or raised paracetamol levels commence treatment with acetylcysteine, keep the patient under observation and discuss with the regional poisons or liver unit according to local guidelines.

Additional notes

- For staggered overdoses, the risk of serious damage is minimal if

<150mg.kg⁻¹ has been ingested in 24 hours (75mg.kg⁻¹ per 24 hours in the high risk group). For all patients who have consumed more than this, consider treatment with acetylcysteine. Plasma levels cannot be interpreted and should not be used to guide treatment in these cases.

- UK guidelines (extrapolated from a 1979 study⁸) suggest that if the INR exceeds 1.3 or transaminase activity has increased to more than twice baseline values then acetylcysteine infusion should be continued at a dose of 100mg.kg⁻¹ over 16 hours until results are acceptable.
- Severe liver injury due to paracetamol poisoning can be associated with renal failure.⁹ Isolated renal failure occurs rarely – mostly in patients who are already glutathione depleted, those who have taken nephrotoxic compounds in addition to paracetamol, those who have become dehydrated, or those who have pre-existing renal insufficiency.¹⁰
- Methionine is an alternative antidote to paracetamol poisoning but it is not recommended for use unless acetylcysteine is not available and there will be a delay in transfer to hospital (animal studies suggest it is less effective¹¹).
- Acetylcysteine commonly causes nausea and vomiting, and can provoke an anaphylactoid reaction.¹² Almost all reactions can be treated effectively by interrupting the infusion and providing symptomatic relief with antihistamine and nebulised β_2 -adrenergic receptor agonists. Once the reaction has subsided the entire dose of acetylcysteine should still be given (at a slower rate of infusion).

Tricyclic antidepressants (TCAs)

Clinical features

Toxicity is due to anticholinergic effects at autonomic nerve endings and in the brain, sodium channel blockade and alpha-1 adrenergic receptor blockade. Peripheral signs include tachycardia, dry skin, dry mouth and dilated pupils. Central signs include ataxia, nystagmus, seizures, drowsiness and coma. There may also be increased tone and hyperreflexia. ECG features include lengthening of the PR, QRS and/or QT intervals and, together with a metabolic acidosis, these increase the risk of ventricular arrhythmias. Rarely, skin blisters are seen, which should be treated as burns. A serotonin syndrome may occur (see Box 3).

Box 3. Serotonin syndrome

An adverse drug reaction that may result from intentional self-poisoning (but more commonly therapeutic drug use or inadvertent drug interactions).

Results from an excess of intrasynaptic 5-hydroxytryptamine (5HT).

Characterized by the triad of:

- altered mental status (confusion, agitation, anxiety, delirium, hallucinations, drowsiness, coma)
- neuromuscular hyperactivity (myoclonus, hyperreflexia, muscle rigidity, tremor)

- autonomic instability (hyperthermia, diaphoresis, tachycardia, hyper/hypotension, diarrhoea, vomiting).

Life threatening complications include coma, seizures, rhabdomyolysis, DIC.

Features occur over a period of minutes to hours.

Treatment is supportive - IV fluids, benzodiazepines to control delirium, cooling measures, haemodialysis/filtration as required.

Dantrolene (1mg.kg⁻¹) may be considered in difficult to control hyperthermia.

5HT₂ antagonists cyproheptadine and chlorpromazine have both been used to treat serotonin syndrome but there are no controlled trials to support the use of either.

Differential diagnosis is neuroleptic malignant syndrome (in NMS onset and resolution of symptoms usually takes days to weeks, rigidity is "lead pipe" and rhabdomyolysis and metabolic acidosis are more common).

Treatment guidelines

- Activated charcoal (50g) by mouth or nasogastric tube is indicated if the patient presents within 1 hour of potentially toxic ingestion. A second dose of charcoal should be considered 1-2 hours later. In patients with features of toxicity provided the airway can be protected.
- Patients who are asymptomatic with normal ECGs at 6 hours are unlikely to develop late problems.
- Arrhythmias should be treated in the first instance by correction of hypoxia and acid/base disturbance.
- Sodium bicarbonate alters the binding of TCAs to the myocardium, and therefore 50mmol should be given intravenously to an adult with ECG changes or arrhythmias, even in the absence of acidosis.
- If cardiotoxicity is unresponsive to sodium bicarbonate consider the use of lipid emulsion (Intralipid).¹³ In both adults and children give an initial IV bolus of 1.5ml.kg⁻¹ of 20% Intralipid followed by 0.25-0.5ml.kg⁻¹.min⁻¹ for 30-60 minutes to an initial maximum of 500ml. This can be repeated in cases of persistent cardiovascular collapse or asystole.
- Convulsions should be treated with diazepam or lorazepam, NOT phenytoin, as the latter, in common with TCAs, block sodium channels and hence potentiates cardiotoxicity.
- Consider glucagon 1mg IV every 3 minutes to treat refractory hypotension and myocardial depression.

Salicylates

An ingested dose of 500mg.kg⁻¹ is potentially fatal. The toxic effects of salicylates are complex and include the direct stimulation of respiratory centres, inhibition of the citric acid cycle and uncoupling of oxidative phosphorylation, and increased metabolism of fatty acids.

Clinical features

Nausea, vomiting, tinnitus, lethargy and dizziness may occur in mild poisoning (usually <125mg.kg⁻¹ body weight ingestion). Dehydration, restlessness, sweating, vasodilation and hyperventilation occur in moderate poisoning (>250mg.kg⁻¹ body weight ingestion). Less commonly haematemesis, renal failure, hyperpyrexia can occur. Presence of CNS signs, e.g. confusion, coma, convulsions are commoner in children, but are an indicator of severe poisoning in all.

Specific hazards

In adults, a mixed respiratory alkalosis and metabolic acidosis is usual. In children less than 4 years, a metabolic acidosis is seen, which increases salicylate transfer across the blood-brain barrier.

Assessment of severity of poisoning

Plasma concentrations of >350mg.L⁻¹ indicate salicylate intoxication. Most deaths in adults are associated with a level of >700mg.L⁻¹. Risk factors for death include age (<10 years and >70 years), acidosis, CNS features, late presentation, and the presence/development of pulmonary oedema.

Treatment guidelines

- Give activated charcoal if >125mg.kg⁻¹ has been ingested within the past hour.
- If >125mg.kg⁻¹ has been ingested, do a plasma salicylate level at least 2 hours (in symptomatic patients) or 4 hours (in asymptomatic patients) after ingestion. A repeat sample (2 hours later) may be needed in patients with suspected severe poisoning, as there may be continued absorption.
- Arterial blood gas analysis is helpful. If a metabolic acidosis is present, and the serum potassium is normal, give intravenous sodium bicarbonate, as below, to correct acidosis and alkalize the urine which increases salicylate excretion. If the potassium is low, correct this **before** giving the bicarbonate.
- Salicylate concentration in adults >500mg.L⁻¹ (3.6mmol.L⁻¹) - give 1.5L of 1.26% sodium bicarbonate (or 225ml 8.4%) over 2 hours
- Salicylate concentration in children (<5years) >350mg.L⁻¹ (2.5mmol.L⁻¹) - give 1ml.kg⁻¹ 8.4% bicarbonate diluted in 0.5L 5% glucose at 2-3ml.kg⁻¹.hr⁻¹.
- Aim to achieve a urinary pH of 7.5-8.5, repeating treatment if necessary to achieve a falling plasma salicylate level.
- The previously used forced alkaline diuresis should not be used as it carries a significant risk of pulmonary oedema.
- In severe poisoning with evidence of cardiac or renal failure, haemodialysis is the treatment of choice.

Ethylene glycol (antifreeze, coolant, brake fluid)

Ethylene glycol is a clear, viscous fluid with a sweetish taste. It is rapidly absorbed from the gut and peak plasma concentrations occur 1 to 4 hours after ingestion. The fatal dose is 100g for a 70kg adult. Inhalation and skin absorption are not serious hazards to health. Toxicity is due to glycolic, glyoxylic and oxalic acids which are products of ethylene glycol metabolism. Glycolic acid is largely responsible for

the metabolic acidosis seen in severe cases. Early administration of the antidote prevents the production of toxic metabolites and minimises the development of complications.

Clinical features

Onset of symptoms is rapid. In the first 12 hours post-ingestion the patient appears inebriated but does not smell of alcohol. Nausea and vomiting, ataxia and dysarthria occur followed by convulsions, coma and severe metabolic acidosis. Between 12 and 24 hours after ingestion, cardiac failure, hypertension, respiratory distress and oliguric renal failure occur. If untreated death from multiorgan failure occurs between 24 and 36 hours after ingestion.

Specific hazards

Calcium oxalate monohydrate crystals precipitate resulting in cerebral oedema and renal failure (calcium oxalate monohydrate crystalluria is diagnostic of ethylene glycol poisoning). Hypocalcaemia occurs as calcium is consumed in the circulation.

As glycol is absorbed over the first few hours, patients develop a high osmolal gap. After this, as glycol is metabolised to acids the osmolal

gap falls whilst the anion gap increases and acidosis worsens. A severely poisoned patient presenting shortly after ingestion may have a normal anion gap and normal pH, however their osmolal gap will be high (see Box 4).

Treatment guidelines

Consider gastric lavage if the patient presents within 1 hour of ingestion. Charcoal is not indicated as it does not adsorb significant quantities of ethylene glycol.

Ethylene glycol concentration levels can be measured but this assay is often not available locally and thus is not often determined early enough to be useful in emergency treatment. However these should be taken and sent (at least 2 hours post ingestion) as they will guide later treatment.

Whether to commence treatment is guided by clinical suspicion and the presence of high osmolar gap or high anion gap metabolic acidosis.

Treatment with an antidote should be commenced if:

- There is suspicion that any amount of ethylene glycol has been ingested and objective evidence of toxic alcohol exposure e.g. high anion gap metabolic acidosis, osmolal gap $>10\text{mosmol.kg}^{-1}$ (without another likely cause).
- There is strong suspicion that $>10\text{g}$ (in adults) or 0.1g.kg^{-1} (in a child) of ethylene glycol has been ingested within the last 12 hours whilst awaiting ethylene glycol levels

Once initiated an antidote should be continued until the plasma ethylene glycol concentration is less than 50mg.L^{-1} .

Both antidotes - ethanol and fomepizole - work by competing with ethylene glycol for alcohol dehydrogenase, which is responsible for the conversion of the ethylene glycol to its toxic metabolites (see table 1 for examples of dosing regimes). Both are also antidotes to methanol poisoning.

Box 4. Calculating osmolal gap

The osmolal gap is the difference between the measured and calculated serum osmolality and provides a means of assessing osmotically active constituents in serum. It is calculated as follows:

$$\text{Osmolal gap} = (\text{Measured osmolality}) - (\text{Calculated osmolality})$$

$$\text{Calculated osmolality} = (2 \times \text{sodium}) + (\text{potassium}) + (\text{urea}) + (\text{glucose})$$

(all measured in mmol.L^{-1})

The normal osmolal gap is about 10mOsm.kg^{-1} .

Table 1. Typical antidote dosing regimes in treatment of ethylene glycol poisoning.

	Ethanol	Fomepizole
Loading dose	2.5ml/kg of 40% v/v orally or 10ml/kg of 10% v/v IV Both given over 30 minutes	15mg/kg IV over 30 minutes
Maintenance	0.375ml/kg/hr of 40% v/v orally or 1.5ml/kg/hr of 10% v/v IV	10mg/kg IV over 30 minutes every 12 hours for next 4 doses then 15mg/kg IV every 12 hours thereafter
Notes	Above doses are for an average adult. Doses vary in children, heavy drinkers, those undergoing haemodialysis	Above doses would be suitable in children also. Continuous infusion is required in those undergoing haemodialysis

Fomepizole does not cause any alteration in the patient's mental state, hypoglycaemia, or respiratory depression, and may be preferable to the use of ethanol in pregnant patients¹⁴ or hepatic disease. The main drawback is cost.

Ethanol is cheaper and often more readily available, and can be given orally or IV. However, adverse effects include hypoglycaemia (particularly in children and malnourished patients), respiratory and CNS depression, and clinical features of alcohol intoxication, potentially making the patient difficult to manage.

Correct metabolic acidosis with IV sodium bicarbonate.

Hypocalcaemia should be corrected with 10-20ml (0.2-0.3ml.kg⁻¹) IV 10% calcium gluconate only if there is evidence of prolonged QTc on ECG or persistent seizures. Routine correction of hypocalcaemia may increase the formation of calcium oxalate crystals.

In severe poisoning with evidence of cardiac or renal failure, haemodialysis is the treatment of choice.

Carbon monoxide (CO)

Toxicity is primarily due to impairment of oxygen delivery and subsequent cellular hypoxia. Carbon monoxide combines with haemoglobin to produce carboxyhaemoglobin, reducing the oxygen carrying capacity of the blood and shifting the oxyhaemoglobin dissociation curve to the left. The half-life of carboxyhaemoglobin is 320 minutes when breathing air. This is reduced to 80 minutes when breathing 100% oxygen.

Clinical features

These are related in the main to tissue hypoxia as a result of impaired oxygen carrying capacity of haemoglobin. Therefore headache, nausea, irritability, agitation and tachypnoea, progressing to impaired consciousness and respiratory failure. A metabolic acidosis and cerebral oedema may develop in severe cases, and progression to multi-organ failure may ensue

Chronic carbon monoxide poisoning is less easy to diagnose, and usually occurs in more than one member of a household, associated with the use of gas heaters in under ventilated areas. The main symptoms are headache and flu-like symptoms.

Specific hazards

Late complications, occurring weeks later in survivors of the acute exposure, may include psychiatric and Parkinson-like movement disorders.

Treatment guidelines

- Remove from exposure.
- Give oxygen in as high a concentration as possible to reduce the half-life of carboxyhaemoglobin and hence improve oxygen delivery to the tissues. Pulse oximetry is unreliable in carbon monoxide poisoning, as it overestimates oxygen saturation.
- Metabolic acidosis generally improves with oxygen therapy. However, if acidosis persists or is severe it can be corrected with sodium bicarbonate.

- If a patient has been exposed to carbon monoxide due to a house fire consider the possibility of concurrent cyanide poisoning and treat accordingly.
- Treat raised intracranial pressure conventionally.
- Use of hyperbaric oxygen should be discussed with the national/regional poisons unit. In the UK, the NPIS does not currently recommend hyperbaric oxygen as "the evidence base is insufficient to support the transport of patients over long distances".

Organophosphates

Organophosphate compounds are a diverse group of chemicals used in a variety of settings including as insecticides, nerve gases, and antihelmintics. Organophosphate poisoning remains a significant issue in developing countries – there are an estimated 300 000 fatalities globally each year.

Clinical features

Organophosphates can be absorbed through skin, inhaled via the lungs or ingested. Poisoning causes nicotinic (muscle weakness, fasciculations, and respiratory muscle weakness), muscarinic effects (hypersecretion, bronchospasm, vomiting and diarrhoea, urinary incontinence), and central nervous system (irritability, seizures, coma) effects.

Treatment guidelines

- Avoid self contamination – wear protective clothing.
- Prevent further absorption by removing source, including soiled clothing.
- Wash patient with soap and water.
- Consider gastric lavage if ingestion within 1 hour.
- If intubation is required avoid suxamethonium because of prolonged effect.
- Give atropine (2mg for adults, 0.02mg/kg for children) IV every 10-30 minutes until adequate atropinisation is achieved. Continuous atropine infusions can be used in doses of 0.02-0.8mg/kg/hr, titrated to effect.
- The dose of atropine required is maximal on day 1 and decreases over the next few days. When the patient improves the dose should be slowly reduced over the next 24 hours. Rebound toxicity may occur due to organophosphates being lipid soluble.
- Oximes (pralidoxime, obidoxime) reactivate phosphorylated acetylcholinesterase before deactivation occurs, and are clinically used to reverse neuromuscular blockade (atropine has no useful effect on the neuromuscular junction). The World Health Organisation recommended dosing regime is 30mg.kg⁻¹ pralidoxime chloride bolus followed by 8mg.kg⁻¹.h⁻¹ infusion. Although the evidence base for this is limited,¹⁵ oxime use is still recommended for use in patients with moderate to severe organophosphorus poisoning.¹⁶
- Benzodiazepines should be given to reduce agitation and control convulsions.¹⁷

SUMMARY

Poisoning is a significant global health problem and a common presentation of deliberate self-harm. Treatment should focus on supportive measures using an ABC approach, with the addition of further interventions to reduce absorption and increase elimination, and where appropriate administration of an appropriate antidote. Whenever possible, reference should be made to national poisoning centre guidelines.

References

Reference has been made to the National Poisons Information Service guidelines throughout (www.toxbase.org).

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