Management of poisoning

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Abstract

Management of poisoning involves the assessment and treatment of airway compromise, ventilation impairment and haemodynamic instability. Thereafter, temperature disturbances should be treated, convulsions controlled, fluid, acid–base and electrolyte abnormalities corrected, and complications such as methaemoglobinaemia, rhabdomyolysis and serotonin syndrome diagnosed and managed optimally. There is no evidence that methods to reduce absorption improve clinical outcome. Multiple-dose activated charcoal to enhance drug elimination should be considered if a patient has ingested a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine or theophylline. Urine alkalinization should be employed in patients with moderately severe salicylate poisoning. Haemodialysis/haemodialfiltration should be considered in cases of severe intoxication with ethanol, ethylene glycol, isopropanol, lithium, methanol or salicylate. Newer treatments including intravenous lipid, and insulin and glucose, may have a role in acute poisoning. A psychiatric and/or social assessment should be undertaken.

Keywords acid–base and electrolyte abnormalities; convulsions; hyperthermia; hypothermia; management; methaemoglobinaemia; poisoning; rhabdomyolysis; serotonin syndrome

Initial assessment

Vital functions

The level of consciousness, ventilation, circulation and temperature should be assessed and treatment instituted, if necessary.

Level of consciousness

The Glasgow Coma Scale (GCS) is the method most commonly used to assess the degree of impairment of consciousness. A GCS score of less than 8 (not obeying commands, not speaking, not opening eyes) should prompt careful assessment of ventilation, particularly if the laryngeal (gag) reflex is lost, and consideration for intubation and ventilation.

Ventilation

Food, vomit, secretions and dentures should be removed from the patient's mouth and pharynx, and the tongue prevented from falling back. Patients should be nursed with the head down in the left lateral position to minimize the risk of aspiration of the gastric contents into the lungs.

If, despite these measures, the patient has a peripheral arterial oxygen saturation of less than 95% (by pulse oximetry), is comatose (GCS <8) and/or the laryngeal (gag) reflex is absent, arterial blood gases should be measured. The presence of respiratory insufficiency (as determined by arterial partial pressure of oxygen ≤9 kPa on air and/or arterial partial pressure of carbon dioxide ≥6 kPa) should lead to intubation and mechanical ventilation if central respiratory depression cannot be reversed by administration of a specific antidote, such as naloxone. Even when ventilation is satisfactory on presentation, it must be reassessed periodically as rapid deterioration may occur.

Circulation

Pulse and blood pressure should be measured to assess cardiovascular function, and an electrocardiogram (ECG) performed particularly when a cardiotoxic drug has been ingested.

Hypotension (systolic blood pressure <80 mmHg) may be exacerbated by co-existing hypoxia, acidosis and dysrhythmias and these should be corrected. Volume expansion with IV crystalloid (sodium chloride 0.9%, or equivalent) should be given and invasive haemodynamic monitoring may be required in severely poisoned patients to confirm adequate volume replacement.

Inotropic support is rarely needed; where hypotension is believed to be due primarily to cardiac depression, an inotropic sympathomimetic, such as dobutamine 2.5–10 micrograms/kg/minute or dopamine 2–5 µg/kg/minute, should be given by IV infusion. If hypotension is deemed primarily due to vasodilatation and is resistant to volume expansion, a vasoconstrictor sympathomimetic drug, such as noradrenaline (norepinephrine) 40 µg (base)/ml at 0.16–0.33 ml/minute (via a central line) or metaraminol 0.5–5 mg by IV bolus, followed by an infusion of 15–100 mg according to response, should be given. Metaraminol has a longer duration of action (20 min) than noradrenaline and can be given peripherally (though tissue necrosis may complicate extravasation). It is important to remember that whereas vasoconstrictors raise blood pressure they also reduce perfusion of vital organs such as the kidneys.

Hypertension, if mild and associated with agitation, may be treated with a benzodiazepine. In more severe cases there may be a risk of arterial bleeding, particularly intracranially, and in these circumstances IV isosorbide dinitrate 2–10 mg/hour up to 20 mg/hour can be given.

Abnormalities of temperature

Core and peripheral temperatures should be measured. Hypothermia (a core temperature <35°C) should be treated by placing the patient in a room with moistened air at a temperature of 27–29°C, covering them with a foil space blanket to minimize heat loss.

In hyperthermia cooling measures, including ice baths, should be instituted, sedation with diazepam given and dantrolene 1 mg/kg body weight IV (to a cumulative maximum dose of 10 mg/kg) considered if the temperature is greater than 39°C due, for example, to cocaine and amphetamines (particularly MDMA; ecstasy).

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Complications of poisoning and their management

Fluid, acid–base and electrolyte imbalance

Patients who are vomiting, sweating excessively or passing large quantities of urine should be given IV fluids to replace gastrointestinal, dermal and renal losses. Acid–base abnormalities, particularly respiratory acidosis (due to central nervous system depression) and metabolic acidosis (due to lactic acidaemia or derangements of intermediary metabolism), are common presentations in acute poisoning.[1] Respiratory alkalosis is a feature of early salicylate poisoning.[2] After correction of hypoxia and hypotension, metabolic acidosis may rarely need to be treated with sodium bicarbonate, 50–100 mmol as a bolus with further doses as necessary.

Other poison-induced biochemical abnormalities, such as hypokalaemia and hyperkalaemia, hypoglycaemia and hyperglycaemia, and hepatic and renal failure should be diagnosed and treated appropriately. Carboxyhaemoglobinaemia, methaemoglobinaemia and depressed erythrocyte cholinesterase activity are of assistance in the diagnosis and management, respectively, of cases of poisoning due to carbon monoxide, methaemoglobin-inducing agents and organophosphorus insecticides.

Skin blisters

Skin blisters may occur in poisoned patients. Bullous lesions should be left intact until they burst, to reduce the risk of infection. When the blister bursts, de-roofing should be performed and a non-adhesive dressing applied.

Convulsions

These may occur in poisoning, for example, due to tricyclic antidepressants, mefenamic acid or opioids. Usually seizures are short-lived, but if prolonged, diazepam 5–20 mg IV or lorazepam 4 mg IV should be administered. Persistent fits should be treated with a loading dose of phenytoin 20 mg/kg IV, via a central line at a rate not more than 1 mg/kg/minute (maximum 50 mg/minute), with ECG monitoring. Alternatively, fosphenytoin (a pro-drug of phenytoin) can be given more rapidly and causes fewer injection site reactions. Theoretically, phenytoin is contraindicated in poisoning due, for example, to tricyclic antidepressants as it may exacerbate sodium channel blockade and increase the risk of cardiac arrhythmias. Rarely, muscle relaxation and mechanical ventilation are required in addition to phenytoin.

Rhabdomyolysis

Rhabdomyolysis is a condition in which there is dissolution of striated muscle fibres, with leakage of muscle cell contents (enzymes, myoglobin, potassium and phosphate).[3] Two clinically important complications are observed: acute renal failure (which may be non-oliguric) and peripheral nerve damage (secondary to compartment syndrome), resulting predominantly in wrist or foot drop. Experimentally, urine alkalinization (see below) has been shown to reduce the likelihood of renal failure developing; however, limited experimental and clinical data suggest that early volume replacement is more important than urine alkalinization.

Methaemoglobinaemia

Poisoning with a number of oxidizing drugs and chemicals may be complicated by methaemoglobinaemia.[4] Methylthioninium chloride (methylene blue), which acts as an electron donor to reduce methaemoglobin, should be given in a dose of 1–2 mg/kg IV over 5–10 minutes as a 1% solution.

Serotonin syndrome[5]

Serotonin toxicity results from an excess of serotonin in the CNS, which can be due to inhibition of the metabolism of serotonin (monoamine oxidase inhibitors), prevention of the reuptake of serotonin into nerve terminals (serotonin reuptake inhibitors), increased serotonin precursors (tryptophan) or increased serotonin release (serotonin-releasing agents such as amfetamines and fenfluramine).[6] Seven features[7] assist in making the diagnosis:

- clonus (spontaneous, inducible and ocular)
- agitation
- diaphoresis
- tremor
- hyperreflexia
- hypertonicity
- hyperthermia.

The precipitating drug(s) should be discontinued and seizures and agitation controlled with a benzodiazepine. Hyperthermia should be treated with cooled IV fluids and tepid sponging, and paralysis and assisted ventilation employed if these measures do not reduce muscle activity. Myoclonic jerks may be helped by clonazepam 1 mg IV over 2 minutes. The 5-HT2A antagonists cyproheptadine 4–12 mg orally and chlorpromazine 50 mg parenterally have been used to treat serotonin syndrome.[7]

Antidotes

There are a small number of poisons for which there is a specific antidote (Table 1) and few antidotes are employed regularly in clinical practice.[8] Those that are include acetylcysteine,[9] naloxone[10] and flumazenil.[11]

Reduction of poison absorption

While it appears logical to assume that removal of unabsorbed drug from the gastrointestinal tract ('gut decontamination') will be beneficial, the efficacy of current methods (activated charcoal, gastric lavage, syrup of ipecacuanha, cathartics and whole bowel irrigation) remains unproven and efforts to remove small amounts of 'safe' drugs are not worthwhile or appropriate.[12]

Methods to increase poison elimination

Multiple-dose activated charcoal interrupts the entero-enteric and, in some cases, the enterohepatic circulation of drugs.[12] Multiple-dose activated charcoal should be considered if a patient has ingested a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine or theophylline.[13] In an adult, after an initial dose of 50–100 g, charcoal should be administered at a dose equivalent to 12.5 g/hour[13]; a total dose of 200 g is usually sufficient.

Urine alkalinization is a treatment regimen that increases poison elimination by producing urine with a pH $\geq$7.5.[12,14] The administration of sodium bicarbonate 225 ml (225 mmol) over 1 hour should produce initial urine alkalinization; further boluses will be required to maintain the urine pH over 7.5. Urine alkalinization is employed mainly in moderately severe salicylate poisoning. Close monitoring of systemic pH and serum

Antidotes of value in poisoning

Poison	Antidotes
Aluminium (aluminum)	Desferrioxamine (deferoxamine)
Arsenic	Succimer (DMSA)
Benzodiazepines	Flumazenil
β-Adrenoceptor blocking drugs	Atropine, glucagon
Calcium channel blockers	Atropine, glucagon
Carbamate insecticides	Atropine
Carbon monoxide	Oxygen
Copper	D-Penicillamine, unithiol (DMPS)
Cyanide	Dicobalt edetate, hydroxocobalamin, oxygen, sodium nitrite, sodium thiosulphate
Diethylene glycol	Fomepizole, ethanol
Digoxin and digitoxin	Atropine, digoxin-specific antibody fragments
Ethylene glycol	Fomepizole, ethanol
Hydrogen sulfide	Oxygen
Iron salts	Desferrioxamine (deferoxamine)
Lead (inorganic)	Sodium calcium edetate, succimer (DMSA)
Methaemoglobinaemia	Methylthioninium chloride (methylene blue)
Methanol	Fomepizole, ethanol
Mercury (inorganic)	Unithiol (DMPS)
Nerve agents	Atropine, obidoxime, pralidoxime
Oleander	Digoxin-specific antibody fragments
Opioids	Naloxone
Organophosphorus insecticides	Atropine, obidoxime, pralidoxime
Paracetamol	Acetylcysteine
Thallium	Prussian (Berlin) blue
Warfarin and other anticoagulants	Phytomenadione (vitamin K_1)

DMSA, dimercaptosuccinic acid; DMPS, dimercaptopropanesulphonate.

Table 1

potassium along with maintenance of a good urine output (typically 80–100 ml/hour in an adult) are crucial during urine alkalinization.

Haemodialysis (haemodialfiltration is more widely available but is less efficient) is the treatment of choice in all cases of severe poisoning with ethanol, ethylene glycol, isopropanol, lithium, methanol and salicylate.[15]

New therapeutic interventions in poisoning

Lipid emulsion therapy (Intralipid® 20% 1.5 ml/kg of as an IV bolus followed by 0.25–0.5 ml/kg/minute for 30–60 minutes[16] to an initial maximum of 500 ml) has been used successfully in the treatment of life-threatening poisoning due to lipid-soluble drugs, particularly calcium channel blockers and tricyclic antidepressants. The mechanism of benefit is likely to be via a 'lipid-sink' effect.

High-dose insulin/glucose therapy is a novel inotropic therapy used in the treatment of severe β-adrenoceptor blocker or calcium channel blocker poisoning. Three mechanisms are proposed: increased inotropy, increased intracellular glucose transport and microvascular dilatation.[17] The typical insulin dose is 0.5–2.0 unit/kg/hour by infusion, titrated to clinical response; the infusion rate may be increased by 2 unit/kg/hour every 10 minutes to a suggested maximum of 10 unit/kg/hour if no increase in cardiac output or clinical improvement is seen.

Psychiatric and social assessment

While most cases of self-poisoning do not require intensive medical treatment, all patients require a sympathetic and caring approach, psychiatric and social assessment[18] and sometimes psychiatric treatment. ◆

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