The poisoned patient

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Abstract

Poisoning is a common reason for admission to the intensive care unit. The majority of patients are due to deliberate self-harm with common poisons; however, there are occasional unusual poisons which require more detailed assessment. Patients are often obtunded or unwilling to co-operate so a knowledge of toxidromes to recognize symptoms that are related to groups of drugs that act on receptors is essential. Management of poisoned patients is generally supportive, including measures to reduce absorption and increase elimination, as well as the use of specific antidotes and techniques to remove poisons.

Keywords Antidote; high-dose insulin; intralipid; overdose; poisoning; toxicology; toxidrome; toxin

Royal College of Anaesthetics CPD Matrix: 1A02, 1B04, 2C01, 2C03, 2C04, 3C00

Learning objectives

After reading this article, you should be able to:

- perform an initial assessment on any patient presenting with poisoning
- recognize common toxidromes, the receptors they act on and their clinical features
- consider the need for decontamination and enhanced elimination
- be aware of the specific antidotes for poisoning agents
- formulate a plan to deal with patients presenting with toxic alcohol poisoning
- recognize common ECG changes in poisoned patients

Hospital presentations due to deliberate or unintentional poisoning are becoming ever more common. National Poisoning Information Service reports, on average, 160,000 poisoning-related presentations to acute services per year. The UK national toxicology service, TOXBASE, received more than 690,000 visits in the period of 2017–2018, of which almost 2000 required telephone assistance from a toxicology consultant.[1]

In general, many of these patients require only a period of observation with supportive management, and specific antidotes which can be delivered in the emergency department or ward setting. There are patients who, as a result of significant and particular poisoning, require hospital admission and active treatment. Between 3–6% of poisoned patients require admission to an intensive care setting with this accounting for up to 15% of ICU admissions per year.

Assessment

In the case of a poison presentation, there are a number of variables that require consideration:

- the poison ingested
- the timing
- the quantity
- the potential mixing with other pharmaceuticals or chemicals (e.g. alcohol, other hepatotoxins or nephrotoxins).
- patient characteristics/demographics/pre-morbid state.

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Rapid assessment of these patients is paramount, as well as the gathering of information, via direct or collateral history. In the significantly poisoned patient, it is unlikely that there will be much of a direct history; therefore a collateral history becomes crucial.

Often, the desired information is not always available in the initial management of the patient, and at this point the focus is on rapid resuscitation. Treatment should not be delayed until all information is to hand. In cases where there are unknown doses of drugs, e.g. empty pill packets, then a worst-case scenario should be adopted. With ingestions of unknown substances local patterns and access to poisons are important. For example, the ability to access herbicides, such as paraquat, in the developing world.

Toxidrome

In cases where an exact poisoning history is not known, because the patient is obtunded or because they are unwilling to divulge the information, recognition of toxidrome is greatly beneficial (Table 1).

A toxidrome, or a toxic syndrome, is a group of signs and symptoms exhibited by the body, as a direct result of the receptors being activated or inhibited, due to the poison ingested (Figure 1). Recognition of a toxidrome allows for rapid management of the poisoned patient, when there is a lack of information available. Different chemicals will interact with different receptors in the body, exhibiting classical signs. These signs may be masked if more than one type of agent has been ingested.

Management

With regard to acute management, the principles remain the same, irrespective of the poison in question. Resuscitation should focus on the A-E approach with a few caveats.

- **Airway:** the airway should be assessed with particular scrutiny for corrosive injury to the oropharynx.
- **Breathing:** respiration is often depressed with sedatives. Cholinergic agents can cause florid airway and bronchial secretions. Direct cellular injury can occur with certain agents (paraquat)

A list of toxidromes, the receptors involved, the poisons that are responsible and the clinical features

Toxidrome	Receptor	Example	Clinical features
Cholinergic	Nicotinic Muscarinic	Organophosphates Chemical Neve Agents (e.g. Sarin, VX)	Lacrimation Meiosis Emesis Urination Defaecation Bradycardia Tachycardia
Anticholinergic	Nicotinic Muscarinic	TCAs Antihistamines Antipsychotics	Dry mouth Dry skin Mydriasis Tachycardia Hyperthermia Urinary retention
Serotonergic	$5HT_2$	SSRI MAOI Tricyclics Venlafaxine MDMA Cocaine Amphetamines Triptans	Agitation Confusion Tremor Hyper-reflexia Hypertonia Fever Flushing Restlessness
Sympathomimetic	Adrenergic	Cocaine Amphetamine	Tachycardia Tremor Hyper-reflexia Seizure Hypo/hypertension
Sedative/hypnotic	GABA	Gabapentin Pregabalin Benzodiazepines	Drowsiness Vomiting Tachycardia Respiratory depression Slurred speech Dizziness Ataxia
Opioid	Opioid	Opiates	Hypoventilation Pinpoint pupils Decreased GCS Hypotension

Table 1

- **Circulation:** multiple drugs affect cardiac inotropy or chronotropy. This can either result in severe myocardial depression and/or hypotension. Severe hypertension and tachycardia may be due to a sympathomimetic response.
- **Disability:** Seizures are a common presenting feature of drug ingestion or withdrawal. Benzodiazepines should be used as a first line treatment. Phenytoin should be avoided as this may worsen Na^+ channel blockade. Hypoglycaemia must be ruled out or treated empirically.
- **Exposure:** hyperthermia can complicate a number of poisonings. Temperatures greater than 39.5°C need aggressive treatment, which may include sedation, neuromuscular paralysis and active cooling. Hypothermia can often be a complicating factor in patients who have a delayed presentation. If profound (<29°C), this can mimic cardiac arrest. Extracorporeal life support has been used in patient with profound hypothermia and poisoning with reports of success.

Investigations

All severely poisoned patients should be screened for paracetamol (acetaminophen) as well as electrolytes, liver function tests, full blood count, glucose and coagulation studies. If the time course of ingestion is unclear, then a repeat paracetamol level (at 4 hours from presentation) may be helpful. Although salicylate levels are often requested, the effects are often recognized from blood gas analysis. An ECG is essential in all poisoning patients. Specific drug levels can be requested for certain poisons and may be useful in determining treatment. An unexplained anion or osmolar gap may suggest toxic alcohol poisoning and may be helpful in assessment, as drug levels may not be available for a few days.

The ECG in poisoning

ECG in the poisoned patient is an important screening test.[2] (Figure 2 and Table 2).

Decontamination

Gastric decontamination with activated charcoal is a recognized immediate management option, which has been in use for a number of years.[3] While it is a very effective form of reducing gastric absorption of poisons, activated charcoal is limited in its use due to timing of ingestion and risks in those with reduced consciousness. Its peak effect is within 1 hour of ingestion, at which time it is uncommon for people to present. Certain poisons (toxic alcohols and metals) are relatively unaffected. Multiple-dose activated charcoal has been suggested as a method to enhance elimination for a small number of poisons that have an enterohepatic circulation.

Enhanced elimination

Toxin elimination can be enhanced by a number of methods. Multiple-dose activated charcoal is occasionally useful, and urinary alkalinization can be helpful to promote excretion of acidic drugs in urine (salicylate and phenobarbitone).

If poisoning is significant and refractory to immediate management, extracorporeal treatment is a viable and important option. Over the recent past, there have been many studies looking into the use of extracorporeal removal of toxins in order to treat significant poisoning.[4] These have looked at the differences in efficacy of haemodialysis (HD) versus haemofiltration (CVVHF), and the use of albumin dialysis in cases of poisoning by certain chemicals. HD is most frequently indicated for poisoning of higher molecular weight chemicals but should be used with caution in the haemodynamically unstable patient. In these cases, CVVHF may be better tolerated but is much less effective in removal of the toxic substance. Albumin dialysis with Molecular Adsorbent Recirculating System (MARS) has been used by poisoning by highly protein-bound substances.[5]

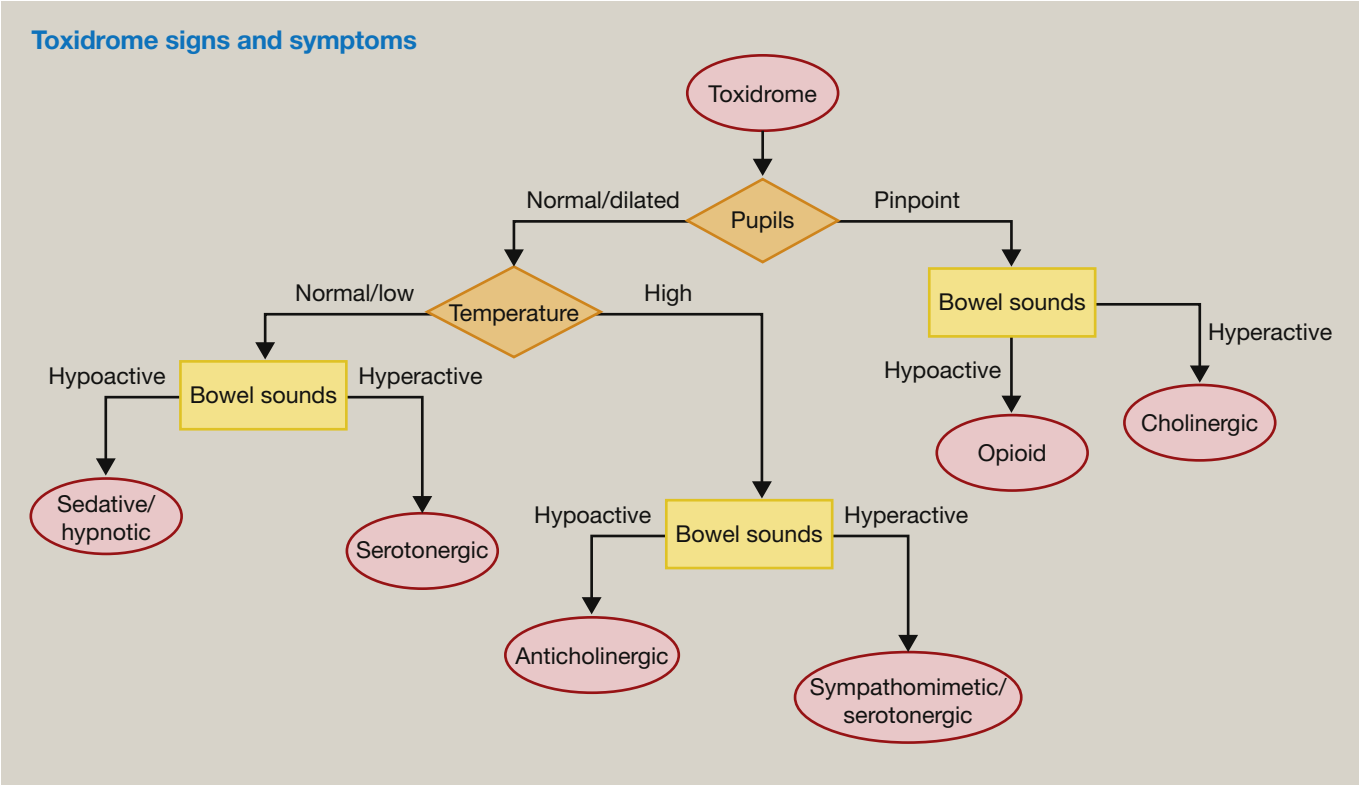

Figure 1

Antidotes

There are a number of poisons that have specific antidotes (Table 3). Once the poison has been identified, and this is known to have a specific antidote, the clinician can opt to use this to reverse effects of the poison or prevent further damage.

In cases where the poison is common and the antidote well known, the use of it is far more common, as there is often great experience in its effects; for example, naloxone for opiate poisoning.

However, new antidotes or rare poisoning agents have far less evidence behind their use, and, as such, the use of these is far more clinician dependent; for example, high-dose insulin for calcium channel blocker (CCB) overdoses.

In cases where the poisoning agent is rare, or the use of an antidote is not fully understood, contacting the local poisons information service (e.g. National Poisons Information Service) is strongly encouraged. Antidotes can have significant side effects, and their use should be reserved for severe cases and by clinicians who fully understand these. For example, the use of high-dose insulin in calcium channel blocker overdoses has the risk of causing severe hypoglycaemia, which can be catastrophic if not recognized early.

High-dose Insulin Euglycaemic Therapy (HIET)

High-dose insulin has been recommended for overdoses due to beta-blockers or calcium channel-blocker poisoning.[6] Historically glucagon therapy was the treatment of choice, but there are many difficulties in clinical practice both with regards to sourcing the volume of glucagon required, as well as relatively complex dosing schedules. There are no published clinical human trials of HIET, but animal evidence suggests superiority to catecholamines, calcium and glucagon and multiple case series support safety. HIET aims to improve cardiac function by increasing myocardial glucose uptake. There is also evidence of positive effects on vascular dilation. Concurrent vasoconstrictor use is often required however, and this should be guided by invasive cardiovascular monitoring and echocardiography. Therapy is commenced with a bolus of short-acting insulin at a dose of 1 unit/kg and an infusion is commenced at 0.5–2 units/kg/h. This is titrated up to a maximum of 10 units/kg/h depending on patient response. During this, potassium and glucose must be checked and replaced meticulously.

Extracorporeal support

If, despite conventional and novel inotropic and vasopressor support, there continues to be evidence of circulatory failure or cardiogenic shock, then consideration should be given to the use of extracorporeal support. There are numerous case-reports of successful outcome with extracorporeal circulatory support for severe cardiovascular failure secondary to poisoning.

Lipid emulsion

Lipid emulsions (Intralipid™) given intravenously was first postulated for local anaesthetic toxicity. It may act via a number of mechanisms including functioning as a 'lipid sink' to encapsulate free local anaesthetic, increasing free fatty acid uptake by mitochondria, or by interference with Na^+ or Ca^{2+} channels.[7] A number

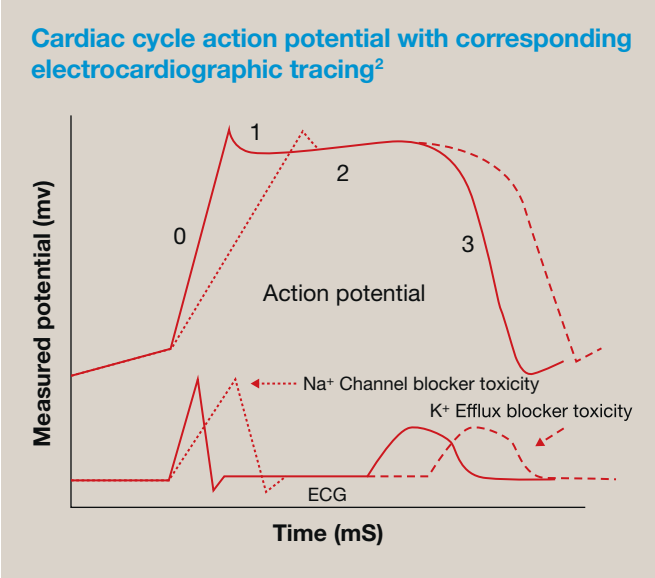

Figure 2 Dotted line indicates the changes associated with Na^+ channel blocker toxicity. Dashed line indicates the changes associated with K^+ efflux blocker toxicity.

of animal studies and case series in humans support its use in local anaesthetic toxicity and various other case reports have suggested its use in refractory poisoning to a number of lipophilic agents. The use of lipid emulsion therapy can have effects on subsequent laboratory tests which can lead to erroneous results.

Toxic alcohols

This term refers specifically to methanol, ethylene glycol and diethylene glycol. These compounds are relatively non-toxic, but when ingested and subsequently metabolized by alcohol dehydrogenase, they become toxic, with fairly non-specific symptoms that, if untreated, can result in irreversible organ damage and death.[8] In many cases of poisoning by ingestion of toxic alcohol, there is co-ingestion of ethanol. This is a competitive substrate for alcohol dehydrogenase, delays production of the toxic metabolites, delaying the effects toxic alcohols in turn. Toxic alcohol ingestion can occur by a variety of means, and these, along with times of onset and common clinical features are outlined in Table 4.

Delays in treatment of poisoning by toxic alcohols can be catastrophic, and as such, therapy should be commenced when there is a suspicion of ingestion of toxic alcohol, or when faced

Specific poisons and their antidotes

Poison	Antidote
Cholinergics	Atropine
Benzodiazepines	Flumazenil
Beta blockers	Glucagon
	High-dose Insulin
Calcium channel blockers	High-dose Insulin
	Calcium
	Glucagon
Digoxin	Digibind (digoxin antibodies)
Iron	Desferrioxamine
TCAs	Sodium Bicarbonate
	Glucagon (case reports)
Opiates	Naloxone
Paracetamol	N-Acetylcysteine

Table 3

ECG manifestations due to ingestion of poisons, with the biochemical imbalance or channelopathy responsible

Channel type	ECG changes
Fast sodium channel blockade leads to slowed phase 0 of the cardiac action potential	Widened QRS
	Right axis deviation of the terminal QRS
	Bradycardia (although tachycardia secondary to other factors is more commonly observed)
	Ventricular tachycardia and ventricular fibrillation
Blockade of potassum efflux during cardiac repolarization (phase 3)	Prolongation of the QT interval
	Torsade de pointes
Na^+-K^+-ATPase pump blockade by cardiac glycosides	Increased automaticity
	Decreased AV node conduction (1st to 3rd degree heart block)
Calcium channel blockade	Sinus bradycardia
	Decreased AV node conduction (1st to 3rd degree heart block)
	Intraventricular conduction defects
Beta-adrenergic receptor blockade	Sinus bradycardia
	Decreased AV node conduction (1st to 3rd degree heart block)
Myocardial ischaemia	ST segment depression or elevation
	Conduction abnormalities
Hyperkalaemia	Peaked T waves
	Conduction abnormalities
Hypocalcaemia	QT prolongation

Table 2

List of the most common toxic alcohols, potential sources, important clinical features and onset of symptoms. Please note, for most clinical features, the onset is several hours post ingestion

Alcohol	Source	Clinical Features	Onset of symptoms without ethanol with ethanol hours after exposure
Methanol	Windscreen-washer fluid. carburettor cleaner, octane boosters, racing fuels, camp stove fuel, adulterated ethanol ('moonshine')	Inebriation, abdominal pain, decreased vision with blindness, Parkinson-like features (rare)	6–24 72–96
Ethylene glycol	Antifreeze, engine coolants, de-icing fluids	Inebriation, acute kidney injury	12–24 48–72
Diethylene glycol	Automotive brake fluids, hydraulic fluids, adulterated liquid medications	Abdominal pain, nausea and vomiting, acute pancreatitis, acute kidney injury	24–48 48–72 (limited data available)

Table 4

with a poisoned patient of unknown aetiology, with a high osmolar or anion gap. Unlike with other poisons, gastric absorption of alcohols is rapid, and as such, gastric decontamination is not helpful. Along with basic resuscitative efforts and supportive measures, the mainstay of treatment for poisoning by toxic alcohols is with ethanol or fomepizole. Ethanol acts as a preferred substrate for the toxic alcohol metabolic pathway, whereas fomepizole blocks metabolism by alcohol dehydrogenase, allowing excretion without the toxic effects of metabolites. While both have been shown to significantly reduce mortality, fomepizole has shown to have superior outcomes;[9] however, it is an unlicensed medication in many locations. Haemodialyis is effective in removing toxic alcohols.

Outcomes

Outcomes from the majority of poisoned patients in the ICU are generally good. The majority of patients make a full recovery and can be discharged after appropriate periods of observation and psychiatric assessment. A small number may have significant long-term effects either related to acquired brain injury from a hypoxic episode or renal injury from rhabdomyolysis. ◆

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FURTHER READING

Toxbase, http://www.toxbase.org (Clinical toxicology database of the National Poisons Information Service in UK).