THE POISONED PATIENT

Approach to ED toxicology

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Acute poisoning is common and varied

- 150-400 per 100,000 ED presentations (0.4%)
- Dynamic, potentially life-threatening illness
- Heterogeneous patient population:
  - deliberate OD
  - recreational drug abuse
  - occupational
  - envenoming
- Frequently represents exacerbation of a chronic psychosocial disorder

→ Need a robust and simple clinical approach

‘Risk assessment’ approach

A distinct cognitive process through which the clinician attempts to predict the likely clinical course and potential complications for the individual at that particular presentation.

Risk assessment should wherever possible be quantitative and take into account the agent, dose and time of ingestion, clinical features and progress, and individual patient factors (e.g. weight and co-morbidities).

Toxicology management guidelines frequently focus on the agent involved. This makes adaptation of treatment recommendations to an individual patient in a particular location difficult.

A risk-assessment-based approach ensures the clinician addresses potentially time-critical management priorities in an appropriate order, but avoids unnecessary investigations or interventions.

Risk assessment is secondary only to resuscitation in the management of acute poisoning. It allows subsequent management decisions regarding supportive care and monitoring, investigations, decontamination, use of enhanced elimination techniques, antidotes and disposition to be made in a sensible structured manner.

Image: risk assessment table 1.1

Resuscitation

Cardiac arrest in poisoning:

- A leading cause of death for patients <40y
- Poisoning is a major differential diagnosis in any cardiac arrest <40y
- Unlike cardiac arrest in the older population, resuscitation following acute poisoning may be associated with good neurological outcomes even after prolonged periods (hours) of CPR

Resuscitation

As always, ABCs come first:

- These priorities are usually managed along conventional lines.
- Basic resuscitative and supportive care measures ensure the survival of the vast majority of patients.
- There are several specific resuscitation scenarios in toxicology where conventional algorithms or approaches may not apply.

Resuscitation

Opiates – naloxone given early can obviate need for intubation and ventilation.

Cholinergic crisis (e.g. organophosphates) – may need massive doses of Atropine to dry secretions in order to ventilate properly.

Digoxin – cardiac arrest / haemodynamic instability in Digoxin toxicity requires immediate DigiFab antidote. Pacing/resusc meds/defibrillation unlikely to work.

Paraquat – avoid O2 unless sats <90%.

VT due to sodium channel blockade (TCAs, local anaesthetics, propranolol) – defibrillation unlikely to work. Need to intubate, hyperventilate, give bicarb.

Resuscitation

Detect and correct SEIZURES:

- Toxic seizures are always generalised.
- Usual causes in Australia: venlafaxine, bupropion, tramadol and amphetamines.
- 1st line: IV Benzodiazepine Diazepam 5-10mg IV
- 2nd line: Barbiturates Phenobarbital 15 mg/kg IV

Phenytoin is contraindicated in toxicological seizures

Resuscitation

Detect and correct HYPOGLYCAEMIA:

- ABC DEFG – 'Don't Ever Forget Glucose'
- Bedside BSL as soon as possible
- Associated with: insulin, sulfonylureas, beta-blockers, quinine, chloroquine, salicylates and valproate.
- Treat BSL <4.0 mmol/L 50 mL of 50% dextrose

  (5 mL/kg 10% dextrose in children)

Resuscitation

Detect and correct HYPER-/HYPOTHERMIA:

- Hyperthermia is associated with a number of life-threatening acute poisonings and is associated with poor outcome.

  T_{core} > 38.5 → start continuous core temp monitoring

  T_{core} > 39.5 → emergency! Paralyse, intubate and ventilate.

- Profound hypothermia (T_{core} < 29) may mimic or cause cardiac arrest.

  Clinical manifestations include coma, fixed and dilated pupils, bradycardia (usually AF) and hypotension.

  Aggressive rewarming is indicated while CPR continues

Risk Assessment

Table 1.3.1 Steps for construction of a risk assessement

Risk Assessment

Sources of history:

1. Patient – usually reliable if conscious.
2. Ambulance officers
3. Family (can be asked to search)
4. Counting missing tablets
5. Medical records / past prescriptions

Under circumstances 2-5, the risk assessment is less accurate and is often based on a ‘worst-case scenario’. This is commonly the case with small children.

As the clinical course progresses, the risk assessment and management plan may be refined.

Risk Assessment

Other helpful hints:

- Correlate agent with what is locally available

  e.g. young adult male with CNS/Respiratory depression + miosis:

  - In urban Australia = opiate
  - In rural Sri Lanka = organophosphate

- Correlate agent, dose and time since ingestion with the patient's current clinical status

  The risk assessment may need to be reviewed and revised.

Risk Assessment

Acute poisoning is a dynamic process:

- Important decisions can often be made at particular time points according to expected pharmacokinetics of the toxin(s).
- Beware delayed absorption!
    - Slow release preparations
    - Side effect of toxin
    - Effect of other co-ingestant

Risk Assessment

Low risk (vast majority):

- Medically trivial poisonings.
- Reassures attending staff, family and patient
- Avoidance of unnecessary investigations, interventions and observation.
- Early psychosocial assessment and discharge planning may begin. This usually shortens hospital length of stay.

Risk Assessment

High Risk:

- Early identification of potentially serious poisonings.
- Early implementation of a tailored proactive management plan.
- Balanced decisions about decontamination can be made and appropriate investigations selected.
- If a specialised procedure or antidote might be required in the next few hours, early communication and disposition planning may begin.

Risk Assessment

Role of the Poisons Information Centre:

- The Australian Poisons Information Centre network comprises centres located in Sydney, Perth, Brisbane and Melbourne.

- In a time-critical poisoning, phoning the PIC is the most rapid way to obtain accurate information and individualised risk assessment.

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Supportive Care and Monitoring

- Poisoning morbidity and mortality usually result from the acute effects of the toxin on the cardiovascular, central nervous or respiratory systems.

- Support of these and other systems for the duration of the intoxication will ensure a good outcome for the vast majority of acute poisonings.

- Monitoring is essential:
  - To detect the progress of the intoxication
  - To indicate the institution, escalation or withdrawal of supportive care and other measures.

Supportive Care and Monitoring

- An initial period of close observation in the ED is usually appropriate.
  - During this time the patient's clinical status is monitored closely to ensure that it correlates with the previous risk assessment.

- If early complications are expected
  - (e.g. decreased LOC requiring intubation in the following 2 hours)
  - preparations can be made to secure the airway as soon as the intoxication declares itself, and before the patient is moved elsewhere.

- If unexpected deterioration occurs at any time, priorities revert to resuscitation prior to revising the risk assessment.

- The duration of observation depends on the agent(s) ingested, the formulations involved (e.g. sustained-release preparations) and potential complications.
- Disposition from the emergency department depends on the current and expected clinical status of the patient. If specific complications are anticipated, the chosen inpatient clinical area must be resourced to detect and manage them

The accuracy and skill of the initial management and risk assessment is wasted if the subsequent plan of management is not documented and communicated to the treating team. Good practice includes the documentation of a comprehensive management plan that informs the team looking after the patient of:

1. Expected clinical course
2. Potential complications according to the individual risk assessment
3. Type of observation and monitoring required
4. Endpoints that must trigger notification of the treating doctor or further consultation
5. Management plans for agitation or delirium
6. Criteria for changing management
7. Provisional psychosocial risk assessment with contingency plan should the patient attempt to abscond prior to formal psychosocial assessment.

Criteria for admission to an emergency observation unit following acute poisoning include:

1. Ongoing cardiac monitoring not required
2. Adequate sedation achieved
3. Clinical deterioration not anticipated.

Criteria for admission to an intensive care unit following acute poisoning include requirements for:

1. Airway control
2. Ventilation
3. Prolonged or invasive haemodynamic monitoring or support
4. Haemodialysis

Supportive care methods table 1.4.1

Investigations

Screening tests:

Insert table 1.5.1

Salicylate poisoning is now relatively uncommon in Australasia. Significant acute intoxication is associated with an easily recognised pattern of symptoms and acid–base disturbances and is rarely occult. Therefore, routine screening for salicylate in patients without symptoms or signs of salicylism does not comply with the rationale for screening

Investigations

Other investigations are ordered selectively where it is anticipated that the results will assist risk assessment or management.

Insert table 1.5.2

Investigations

Other investigations are ordered selectively where it is anticipated that the results will assist risk assessment or management.

Insert table 1.5.3

Investigations

Qualitative urine screens for drugs of abuse (e.g. opioids, benzodiazepines, amphetamines, cocaine, barbiturates and cannabinoids) rarely alter the management of the acutely poisoned patient. Patients with acute intoxication with one or more of these agents may be managed according to their clinical presentation. False positives and negatives occur. A positive result from a patient without corresponding symptoms of intoxication rarely alters acute medical management.

Gastrointestinal Decontamination

Insert table 1.6.1

Unfortunately, the tendency has been to overestimate the potential benefits while underestimating the potential hazards of gastrointestinal decontamination procedures. These procedures do not provide significant benefit when applied to unselected deliberate self-poisoned patients and are no longer considered routine.

Gastrointestinal Decontamination

Insert table 1.6.2

Gastrointestinal Decontamination

Insert fig 1.6.1

Gastrointestinal Decontamination

Induced emesis (Ipecac):

Insert video from family guy.

Gastrointestinal Decontamination

Induced emesis (Ipecac):

The mean time from administration to vomiting is 18 minutes.

For many years it was routinely recommended for home use following accidental paediatric ingestions with the intention of reducing the time to decontamination and the need for hospital referral.

It is now clear that the amount of toxin removed is unreliable and decreases rapidly with time to the point that it is negligible by 1 hour.

Syrup of ipecac-induced vomiting also renders subsequent administration of activated charcoal more difficult.

emergency departments no longer stock syrup of ipecac and poisons information centres no longer advise it to be kept in homes with small children.

Gastrointestinal Decontamination

Gastric Lavage:

This previously widely favoured method of gastrointestinal decontamination has now been all but abandoned and few emergency departments remain experienced in its use.

The amount of toxin removed by gastric lavage is unreliable and negligible if performed after the first hour.

It does not confer any clinical benefit when performed routinely on unselected patients presenting to the emergency department following deliberate self-poisoning.

There are few situations where the expected benefits of this procedure might be judged to exceed the risks involved and where administration of charcoal would not be expected to provide equal or greater efficacy of decontamination.

Needs a resus bay and a protected airway.

Gastrointestinal Decontamination

Single dose Activated Charcoal:

- Activated charcoal (AC) is produced by the super-heating of distilled wood pulp. The resulting fine porous particles are suspended in water or sorbitol prior to oral or nasogastric administration.
- The enormous surface area provided by these particles reversibly adsorbs most ingested toxins preventing further absorption from the gastrointestinal tract.

Gastrointestinal Decontamination

Oral AC is generally the preferred method of decontamination. However, it does not improve clinical outcome when applied to unselected patients with self-poisoning and should not be regarded as routine.

indicated where it is likely that toxin remains in the gastrointestinal tract (within the first hour for most agents) and where the potential benefits outweigh the potential risks.

Gastrointestinal Decontamination

Complications of AC

Vomiting (30% of patients given AC vomit within 1 hour)

Mess

Pulmonary aspiration

Direct administration into lung via misplaced nasogastric tube (potentially fatal)

Impaired absorption of subsequently administered oral antidotes or other therapeutic agents

Corneal abrasions

Distraction of attending staff from resuscitation and supportive care priorities.

Gastrointestinal Decontamination

Insert table 1.6.3

Gastrointestinal Decontamination

Technique

Give 50 g (adults) or 1 g/kg (children) as a single oral dose placed in a cup for self-administration

Mixing with ice cream improves palatability for children

In the intubated patient, AC may be given via oro- or nasogastric tube after tube placement is confirmed on chest x-ray.

Enhanced Elimination

Insert table 1.7.1

In practice, these techniques are useful in the treatment of poisoning by only a few agents that are characterised by:

- Severe toxicity
- Poor outcome despite good supportive care/antidote administration
- Slow endogenous rates of elimination
- Suitable pharmacokinetic properties.

Antidotes

Only a few antidotes exist for a limited number of poisonings and many are used only extremely rarely.

Like all pharmaceuticals, antidotes have specific indications, contraindications, optimal administration methods, monitoring requirements, appropriate therapeutic end points and adverse effect profiles.

The decision to administer an antidote to an individual patient is based upon a risk–benefit analysis. An antidote is administered when the potential therapeutic benefit is judged to exceed the potential adverse effects, cost and resource requirements. An accurate risk assessment combined with pharmaceutical knowledge of the antidote is essential to clinical decision making.

It is frequently cheaper and safer to transport an antidote to a patient rather than vice versa.

Disposition

Insert table 1.9.1

Disposition

Psychosocial assessment:

Most episodes of acute poisoning represent an exacerbation of an underlying psychosocial disorder and the final disposition of the patient is made in this context.

All patients with deliberate self-poisoning should undergo psychosocial assessment prior to discharge. Ideally, this process begins before the medical treatment of the poisoning is complete so that final disposition is facilitated.

Night time discharges discouraged, esp. CNS agents

Amphetamines

Methamphetamine – ‘Ice’

MDMA – ‘ecstasy’

Dexamphatamine

Methyphenidate – Ritalin

Amphetamine-related presentations represent a significant burden on emergency departments, accounting for over 1% of emergency department presentations. Most of these presentations relate to medical, social and psychiatric sequelae of acute amphetamine intoxication.

Insert table 2.13.1

Amphetamines, particularly methamphetamine, are highly addictive and patients may also present in withdrawal or develop withdrawal during admission for other reasons.

No pharmacological agent has been demonstrated to be effective in the treatment of amphetamine withdrawal, dependence or abuse. Management relies on counselling and social support.

Withdrawal:

Prolonged or heavy use of amphetamines results in tachyphylaxis (reduced response to repeated doses). This phenomenon is thought to be due to depleted concentrations of neurotransmitters. The symptoms are largely psychiatric and mood related, and include depression, fatigue, insomnia, increased appetite and cognitive impairment. Symptoms usually peak 2–4 days following cessation of use but may continue for 7–14 days. Amphetamine withdrawal in itself is rarely severe enough to warrant medical admission. Management consists of referral for appropriate psychosocial support.

Amphetamines

Toxic mechanism

Amphetamine is structurally related to ephedrine. Substitutions on the basic amphetamine structure yield numerous derivatives with varying receptor affinities. Amphetamines enhance catecholamine release and block their reuptake. Inhibition of monoamine oxidase also occurs. CNS and peripheral noradrenergic, dopaminergic and serotonergic stimulation occurs. Long-term CNS effects occur due to neurotransmitter and receptor adaptation, as well as permanent destruction of dopaminergic neuro-pathways. MDMA at standard recreational doses sometimes induces the syndrome of inappropriate antidiuretic hormone secretion (SIADH), leading to profound hyponatraemia, coma and convulsions.

Amphetamines

Toxicokinetics

The amphetamines are well absorbed following ingestion and insufflation. They are lipid-soluble weak bases and have large volumes of distribution (methamphetamine 3.5 L/kg). Most amphetamines undergo hepatic metabolism to form metabolites that are excreted in the urine. Elimination half-life varies from 8–30 hours.

Amphetamines

Clinical Features

Patients may present with symptoms of acute intoxication, medical complications of abuse or psychiatric sequelae. The most frequent presentation is agitation with sweating, tachycardia and hypertension. Acute clinical features may persist for 24 hours and include:

Central nervous system

- Euphoria
- Anxiety, dysphoria, agitation and aggression
- Paranoid psychosis with visual and tactile hallucinations
- Hyperthermia, rigidity and myoclonic movements
- Seizures

Cardiovascular

- Tachycardia and hypertension
- Dysrhythmias
- Acute coronary syndrome
- Acute cardiomyopathy
- Acute pulmonary oedema
- Haemoptysis

Peripheral sympathomimetic

- Mydriasis, sweating and tremor

Clinical features associated with medical complications

- Rhabdomyolysis, dehydration and renal failure
- Hyponatraemia and cerebral oedema following MDMA ingestion, due to temporary SIADH and increased water ingestion
- Aortic and carotid artery dissection
- Subarachnoid and intracerebral haemorrhage
- Ischaemic colitis

Note: Psychotic symptoms such as paranoid ideation may accompany acute intoxication and persist as part of a post-amphetamine psychosis when other features of acute intoxication have resolved.

Amphetamines

Investigations

Screening tests in deliberate self-poisoning

- 12-lead ECG, BSL and paracetamol level

Specific investigations as indicated

- EUC
  - Detect hyponatraemia and renal failure
- ECG, CK and troponin
  - Detect myocardial ischaemia, acute coronary syndrome and rhabdomyolysis
- Chest x-ray
  - Detect aortic dissection and aspiration
- Decreased mental status or focal neurological signs prompts exclusion of hyponatraemia, hypoglycaemia, aortic dissection or intracranial haemorrhage
- Note: Serum or urine amphetamine levels are not readily available and do not assist acute management.

Amphetamines

Management

Resuscitation, supportive care and monitoring

- Amphetamine intoxication is a potentially life-threatening emergency and patients should be managed in an area capable of cardiorespiratory monitoring and resuscitation
- Clinical features that require immediate intervention include:
  - Hypertension
  - Seizures and agitated delirium
  - Hyperthermia
  - Hyponatraemia (MDMA)
- Treat tachycardia and hypertension with titrated parenteral benzodiazepines. If hypertension is refractory to benzodiazepine sedation consider:
  - Phentolamine 1 mg IV repeated every 5 minutes
  - Titrated vasodilator infusion (sodium nitroprusside, glyceryl trinitrate)
  - Note: Beta-adrenergic blockers are contraindicated (see Handy tips)
- Seizures are managed with IV diazepam (see Chapter 2.6: Approach to seizures)
- Agitation is managed with titrated diazepam. Oral diazepam may be considered in mild cases (10–20 mg diazepam PO with further doses of 10 mg every 20 minutes until agitation controlled) but IV diazepam should be instituted early where agitation is moderate or severe. Give diazepam 2.5–5 mg IV. Further doses of 10–20 mg IV every 5–10 minutes to a maximum dose of 60 mg may be required (See Chapter 2.7: Delirium and agitation). Second-line drugs in resistant cases include droperidol 2.5 mg IV or olanzapine 10 mg IM.
- Hyperthermia:
- Temperature >38.5°C is an indication for continuous core-temperature monitoring, benzodiazepine sedation and fluid resuscitation
- Temperature >39.5°C requires rapid external cooling to prevent multiple organ failure and neurological injury. Paralysis, intubation and ventilation may be required
- Hyponatraemia:
- Immediate correction with hypertonic saline is indicated if profound (serum Na^+ <120 mmol/L) and associated with altered mental status or seizures. Give hypertonic saline (3% sodium chloride) 4 mL/kg over 30 minutes and repeat serum sodium. Further doses should be given to achieve a serum Na^+ >120 mmol/L until resolution of SIADH manifests by diuresis and spontaneous correction of hyponatraemia (this usually occurs within 24 hours)

Decontamination

- Amphetamines are rapidly absorbed and associated with an increased risk of seizures and delirium; therefore, activated charcoal is not advised

Enhanced elimination

- Not clinically useful

Antidotes

- None available.

Disposition And Follow-Up

Children with potential ingestions should be observed in hospital for 4 hours. If they do not develop symptoms during that period they may then be safely discharged

Patients whose intoxication is adequately controlled with benzodiazepine sedation and have a normal blood pressure and 12-lead ECG may be managed supportively in a ward environment. They may be discharged when clinically well

Patients with significant alteration of conscious state, hyperthermia or ongoing chest pain are admitted to a high-dependency or intensive care unit.

Handy Tips

Early control of agitation with adequate doses of IV benzodiazepines calms the patient and improves tachycardia, hypertension and hyperthermia

Ongoing chest pain or headache requires further investigation

Acute coronary syndrome is managed according to normal protocols. CT brain should be performed prior to anticoagulation or angiography if headache is a feature

Administration of beta-adrenergic blockers is contraindicated in the acute management of amphetamine intoxication as it leads to unopposed alpha stimulation and vasoconstriction.

Pitfalls

Failure to adequately sedate the agitated patient

Failure to recognise and treat hyperthermia

Failure to detect and treat hyponatraemia in a patient presenting with altered mental status or seizures following MDMA use—permanent neurological injury can result.

Controversies

The role of antipsychotics in acute amphetamine intoxication. They are frequently effective in the treatment of persistent psychosis but have theoretical drawbacks in acute intoxication: anticholinergic side effects and lowered seizure threshold.

ARC guidelines

Cocaine/Amphetamines

Sympathetic overstimulation associated with amphetamine/cocaine toxicity may cause agitation, symptomatic tachycardia, hypertensive crisis, hyperthermia and myocardial ischaemia with angina. Small doses of intravenous benzodiazepines (midazolam, diazepam, lorazepam) are effective first-line drugs. Glyceryl trinitrate and phentolamine can reverse amphetamine/cocaine induced coronary vasoconstriction. Possible myocardial necrosis should be assessed using the ECG and cardiac markers (e.g. troponin) in patients with amphetamine/cocaine-related chest pain. [Deakin 2010]

Recommendations

If cardiac arrest occurs in the setting of toxicity due to cocaine/amphetamines, follow standard resuscitation guidelines. [Class A, Expert Consensus Opinion]