ABC of Poisoning

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CARDIAC DRUGS

Acute poisoning with cardiac drugs is uncommon, but these drugs all have a narrow toxic to therapeutic ratio and are among the most hazardous drugs in common use. All cases of suspected poisoning with cardiac drugs must be treated seriously: full intensive care facilities may be needed. Poisoning may originate from deliberate, accidental, or even iatrogenic causes and the presence or absence of underlying heart disease may greatly influence the clinical problems. Elderly patients are also at particular risk of cardiac drug toxicity.

Symptoms

- Hypotension
- Arrhythmias
- Gastrointestinal symptoms, such as nausea and vomiting
- Irritability, convulsions, and loss of consciousness

In general poisoning with cardioactive drugs will produce hypotension and all types of arrhythmias. Extracardiac effects include gastrointestinal symptoms, especially nausea and vomiting, and central nervous system effects with irritability, convulsions, and loss of consciousness.

Management

Supportive

- (1) Treat all suspected cases seriously
- (2) Support cardiac and pulmonary function
- (3) Empty stomach and give oral activated charcoal
- (4) Avoid antiarrhythmic drugs
- (5) Consider temporary pacemaker for bradycardia
- (6) Use fluids before vasopressors for hypotension— isoprenaline appears drug of choice
- (7) Persist with cardiac massage if output fails

Once poisoning is suspected even asymptomatic patients must be admitted for observation. In the symptomatic patient support for cardiac and pulmonary function is essential. The minimum duration of observation should be determined with reference to the drug's half life and the formulation taken (some antiarrhythmics and hypotensive agents are formulated for sustained release) and when practicable should be guided by plasma drug concentrations. If immediate admission to an intensive care unit is not possible or not indicated the ward staff should be fully aware of the risks and the intensive care unit warned that its services may be needed. A twelve lead electrocardiogram should be obtained as soon as possible, both to assess underlying myocardial disease and as a baseline to measure progress. A chest radiograph, full blood count, and samples for laboratory analysis should also be taken early.

If the drugs were ingested as a single dose the stomach should be emptied either by emesis or gastric lavage. Activated charcoal is an effective adsorbent for all cardiac drugs and should be given orally in a dose at least 10 times the weight of the suspected overdose.

Whilst supportive treatment is in progress

- (7) Measure electrolytes, urea, creatinine and plasma drug concentrations
- (8) Urgently correct hyperkalaemia
- (9) Correct hypokalaemia—maintaining K^+ in upper normal range
- (10) Consider other treatments:
 - Antibodies for digoxin
 - Haemoperfusion for disopyramide
 - Glucagon/isoprenaline for β blocker
 - Calcium for verapamil

It is also essential to diagnose and correct any metabolic abnormalities. Hypoxia, acidosis, hypocalcaemia, and hyperkalaemia all increase the irritability of the heart and cause arrhythmias. Further doses of antiarrhythmic drugs are likely to increase the cardiac toxicity, and the temptation to treat an arrhythmia by that means should be resisted.

If there is extreme hypotension or cardiac arrest, cardiac output should be maintained by external cardiac massage. Delay may result in hypoxic cerebral damage. A central venous pressure line is usually advisable to help monitor fluid balance. Hypotension may respond to fluids, preferably colloids, which should be given a proper trial before pressor agents are considered. This is particularly important in overdose with vasodilator drugs, where the patient has severe hypotension and warm dry skin. Isoprenaline appears to be the most effective choice when a negatively inotropic agent is responsible for toxicity and often does not add to the problems with heart rhythm. Dobutamine and dopamine are acceptable alternatives. A temporary pacemaker may be useful if there is a bradycardia, but often the heart muscle is unresponsive.

Laboratory analyses

Cardiac drug assays available at the poisons unit laboratory

Cardiac drugs	"Therapeutic" plasma concentrations	Approximate half life
Amiodarone	1.0–2.0 mg/l	– 50 days
Desethylamiodarone	1.0–2.0 mg/l	
Digoxin	1.0–2.0 μ g/l	24–36 hours
Disopyramide	2.0–5.0 mg/l	5– 7 hours
Lignocaine	2.0–5.0 mg/l	1– 2 hours
Mexiletine	0.8–2.0 mg/l	8–14 hours
Oxprenolol	< 500 mg/l	2– 3 hours
Procainamide	4.0–8.0 mg/l	3– 5 hours
Procainamide + NAPA	5–30 mg/l	
Propranolol	50–100 μ g/l	2– 3 hours
Quinidine	3.0–6.0 mg/l	6– 8 hours
Quinine	up to 8 mg/l	
Tocainide	35–9.0 mg/l	15–20 hours
Verapamil	100–200 μ g/l	2– 7 hours

Other cardiac drug assays are either under investigation or could be developed to meet a clinical need. If your local laboratory cannot help, contact the National Poisons Information Service for further information

While these measures are being undertaken, laboratory analysis should be requested for electrolytes, calcium, urea, creatinine, and plasma drug concentrations. High potassium concentrations may cause asystolic cardiac arrest and should be corrected urgently with intravenous glucose and insulin followed by oral or rectal calcium resonium. The treatment of hypokalaemia is less urgent but intravenous potassium should be given and it is preferable to maintain the serum potassium concentration at the upper end of the normal range, particularly if arrhythmias are the main problem. Renal failure may profoundly influence both the severity of the toxicity and its duration. Renal function must therefore be maintained. If possible plasma drug concentrations should be measured to determine whether the clinical condition is related to the toxic effects of the drug, to pre-existing heart disease, or to secondary damage caused by the overdose—for example, aspiration of vomit or coma due to another agent ingested.

Comparison of findings in digoxin toxicity with those in digoxin poisoning

Findings	Patients in heart failure (digoxin toxicity)	Often healthy patients (digoxin poisoning)
Non-cardiac symptoms	Wide range of gastrointestinal, ocular, central nervous system, and non-specific manifestations are present	Nausea and vomiting are common; other classic symptoms are not reported with consistency
Cardiac symptoms	Premature ventricular contractions are the most common arrhythmias; atrial tachycardias, sometimes associated with block, also are seen	Ventricular arrhythmias are uncommon; supraventricular arrhythmias with heart block are the most characteristic findings; bradycardia is often reported
Serum potassium on admission	Generally low serum K^+ secondary to concomitant diuretic therapy	Normal to raised serum potassium depending on the degree of $Na^+ - K^+ ATP$ -ase pump inhibition
Serum digoxin values	Variable but may be within the therapeutic range	High concentrations are always seen in patients with symptoms of toxicity
Serum half life of digoxin	Reasonably constant in adults and children	Reported to be shortened in acute poisoning, although this has not been consistent

Specific treatment

In addition to the general plan of management specific treatment should be considered.

Digoxin—Acute poisoning presents with distinct differences from the digoxin toxicity seen in treatment. Most patients recover with the supportive treatment outlined above plus the use, when necessary, of atropine for bradycardia and phenytoin for ventricular arrhythmias. Fab antibody fragments specific for digoxin have also been developed as an antidote, and appear to be effective in the rare severe cases where other measures fail. The antidote is held at some poisons treatment centres. Amiodarone (600 mg intravenously slowly) is also helpful in treating arrhythmias due to digoxin poisoning.

Disopyramide—In experiments, both in vivo and in vitro, haemoperfusion has been effective in removing clinically important amounts of drug. Its value in clinical use has not yet been proved. A major problem with disopyramide, however, is its severe depressant effect on cardiac output. Death can occur within two hours of ingestion. Isoprenaline infusion rapidly restores the cardiac output.

β -Adrenoceptor blocking drugs—The negative inotropic effects of these drugs, particularly propranolol and oxprenolol, may lead to profound hypotension, coma, and convulsions. Intravenous glucagon (4–10 mg as a bolus) is the drug of choice since it activates myocardial adenyl cyclase by a different mechanism from that of the β adrenoceptor agonists. The symptoms can, however, also be reversed by high doses of β -adrenoceptor agonists such as isoprenaline by infusion (10–100 mg/min) or prenalterol. Profound bradycardia or asystole may require cardiac pacing, and prolonged external cardiac massage may be lifesaving in refractory cases. When emesis or lavage are used, atropine should be given to prevent extreme bradycardia or cardiac arrest from vagal stimulation.

Calcium blocking drugs—Intravenous calcium gluconate (10–20 ml of a 10% solution given slowly) has been claimed to reverse both hypotension and cardiac arrhythmias but more recent reports question its value. Large amounts of intravenous fluids may help to counter the hypotension.

Monitoring cases of cardiac drug overdose

Examples of suspected cardiac drug overdoses reported to NPIS, 1983

Drug	No of cases
Digoxin	65
Disopyramide	10
Propranolol	58
Amiodarone	7
Verapamil	3

Total cases reported were in excess of 33 000

In view of the rarity and severity of cardiac drug overdose, it is important that all cases are accurately documented so that the information may help in the management of future cases. The National Poisons Information Service monitors all reports of such cases and is prepared to help with clinical advice and laboratory analyses when necessary. (Telephone: 01 635 9191 (emergencies); 01 407 7600 ext 4001/4002 (for non-urgent inquiries).)

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