Cardiac Glycoside Poisoning

Toxicology

1 Introduction

Cardiac glycosides, like digoxin, are prescribed in the management of chronic atrial fibrillation, particularly in the setting of cardiac failure. They inhibit the Na⁺/K⁺ ATPase pump, leading to intracellular accumulation of Ca²⁺ and improved cardiac automaticity and contractility. Digoxin has a very narrow therapeutic window and can cause significant cardiotoxicity above the therapeutic range. Ingestion of natural occurring cardiac glycosides like oleander and toad venom can also lead to poisoning.

A digoxin-Fab fragment is available to bind circulating digoxin and counteract toxicity. It is indicated in the setting of significant arrhythmia and can reduce morbidity, mortality and length of stay.

Toxicokinetics

Digoxin is water soluble with a bioavailability between 60 and 80%. It’s average plasma half-life is 40h, but can be prolonged to more than 100h in renal failure. It has a large volume of distribution of 5–10 L/kg with extensive tissue distribution and low protein binding (20%). It is predominantly excreted by the kidneys.

Oleander and toad venom undergo extensive enterohepatic circulation making them amenable to MDAC decontamination.

2 Risk Assessment

Digoxin poisoning results nausea, vomiting and diarrhoea. More importantly it causes cardiac conduction abnormalities. Bradyarrhythmias (AV nodal block, slow AF), accelerated escape rhythms and ventricular tachycardias can all occur.

Hypokalemia, hypomagnesemia, hypercalcemia, hypoxia, ischemic heart disease, hypothyroidism and advanced age all increase the likelihood of digoxin toxicity.

All patients require an urgent ECG, digoxin level and
electrolytes (including magnesium). These will need to be performed serially to track progress. Once Digoxin-Fab has been given the digoxin level cannot differentiate between free and bound digoxin so is not useful clinically. Free digoxin assays are available at some centres.

3 Management

Resuscitation
Life threatening arrhythmia is an indication for Digoxin-Fab fragment therapy. See below
Hypokalaemia and hypomagnesaemia should be corrected. Atropine can be given for significant bradycardia initially while sourcing Digoxin-Fab fragment.
In chronic toxicity there should be less reliance on the antidote and more consideration of treating haemodynamic instability and hyperkalaemia along standard lines.

Decontamination
SDAC should be administered in the co-operative patient following an acute digoxin overdose of >0.1mg/kg who presents within 2 hours. 3
MDAC should be administered in oleander or toad venom poisonings. 4

Antidote
Digoxin-Fab fragment should be administered if there is an arrhythmia associated with haemodynamic instability or evidence of automaticity.
While equations exist to calculate the body load of digoxin and subsequent dose of Fab fragment required this overestimates the total amount required due to the toxicokinetics (specifically the distribution) of digoxin.

A far more practical approach is 1

- **Acute toxicity:** give 2 vials & repeat hourly as required
- **Chronic toxicity:** give 1 vial & repeat hourly as required

Recent research 5 has questioned the role of digoxin-Fab in patients with chronic toxicity as it produced a median increase in heart rate of 8 beats per minute and a median decrease of 0.3 mmol/L potassium in a group of 36 patients with chronic digoxin toxicity. This group typically has multiple co-morbidities and take multiple cardiovascular medications such as beta blockers, calcium channel blockers and ACE inhibitors. Digoxin-Fab should not be relied upon in isolation to improve heart rate nor correct hyperkalaemia.

Supportive Measures
Patients should be observed on telemetry in the Short Stay Unit. Antiemetics should be prescribed to limit vomiting and possible associated vagal surge. Maintain normal ranges for potassium and magnesium.

4 Disposition
Given the potential for cardiotoxicity, all patients with acute digoxin poisoning should be discussed with the toxicology team. A prolonged period of observation is required following Fab fragment administration to ensure that there is no rebound toxicity once tissue redistribution has occurred.
5 Further reading


6 References


3. Wikitox Digoxin 2.1.6.1.2
   [http://curriculum.toxicology.wikispaces.net/2.1.6.1.2+Cardiac+glycosides](http://curriculum.toxicology.wikispaces.net/2.1.6.1.2+Cardiac+glycosides)
