ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Cardiac glycoside poisoning

Digoxin was originally derived from *Digitalis lanata*, a foxglove species. There are two mechanisms of action. One, cardiac glycosides block the Na^+/K^+/ ATPase pump, which leads to intracellular Ca^{++} increase. Higher concentrations of intracellular Ca^{++} increase cardiac contractility (squeeze). (*Am J Cardiovasc Drugs. 2006;6(2):77-86*). Second, it increases the parasympathomimetic innervation to the heart. This results in slower SA firing, a decrease in heart rate (HR) (chronotropy), and reduced conduction velocity through the AV node (negative dromotropy).

In poisoning, these effects are enhanced. Acute toxicity may include nausea, vomiting, abdominal pain, lethargy, bradycardia, dysrhythmias, and hyperkalemia. Chronic toxicity may include bradycardia with or without heart block, other dysrhythmias, nausea, delirium, and vision changes.

For early acute ingestion, we recommend GI decontamination. After initial stabilization, the antidote for life-threatening arrhythmias or hyperkalemia due to digoxin toxicity is digoxin immune Fab (DigiFab®, abbreviated as Fab). Each vial of Fab binds 0.5 mg of digoxin. For acute ingestions of an unknown amount, empiric administration of 10 vials is reasonable, and can be redosed with an additional 10 vials.

Acute ingestions of a known dose, use the following calculation:

*(ingested dose (mg) * bioavailability (tablets = 0.8, capsules = 1))/0.5 mg = number of vials*

Once a steady state concentration is obtained, the following calculation is used:

(serum digoxin concentration (ng/mL) x weight (kg))/100 = number of vials (round up)

Most digoxin consults received by our poison center are chronic exposures, above the therapeutic range of 0.5-1 ng/mL. For chronic toxicity, an empiric dose of 3-6 vials for adults or 1-2 vials for children can be used. If the serum concentration is known, use the steady state calculation above. Non-digoxin cardiac glycosides (e.g., oleander, lily of the valley) require higher doses of Fab. The recommended initial dose is 10 vials.

Reversing digoxin poisoning with Fab may exacerbate underlying heart failure (*Circulation. 1990 Jun;81(6):1744-52*). A small prospective observational study found that one or two vials of Fab were sufficient to bind free digoxin for most chronic digoxin poisonings. Although clinical response (HR and serum K^+) was only moderately improved, GI side effects did improve (*Clin Toxicol (Phila). 2016 Jul;54(6):488-94*). An extension of this study with a "initial observation control arm" suggested that Fab did not benefit mortality, length of stay, HR, and serum K^+ (*Clin Toxicol (Phila). 2019 Jul;57(7):638-643*).

Once Fab is administered, avoid digoxin monitoring in the immediate days, as the total digoxin level can be falsely elevated due to binding with the Fab-bound digoxin. Free digoxin lab test is more accurate but it is not routinely available. The Fab-digoxin complex is eliminated renally. In patients with renal insufficiency, the Fab-bound digoxin complex may break down, and digoxin toxicity may recur (*Drug Saf. 2004;27(14):1115-33*). Also, do not give Fab if known allergy to papaya or pineapple.

Contact your local poison center at 1-800-222-1222 for treatment recommendations.

***Digitalis lanata* Paris**
Wikimedia Commons

Did you know?

There are several toxins that cause bradycardia after overdose. The following are key examples to consider.

- Alpha-2 adrenergic agonists
- Benzodiazepines
- Beta-blockers
- Calcium channel blockers
- Cardiac glycosides
- Cholinergic toxins (e.g., organophosphates, carbamates, nicotine)
- *Crataegus mexicana* (Tejocote)
- Grayanotoxin
- Opioids
- Sedatives (e.g., baclofen)

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