

## Updates to Digoxin Toxicity Management

Digoxin is a sodium-potassium pump inhibitor with a narrow therapeutic range. Toxicity can be seen even from therapeutic use if there is a change in kidney function or a drug-drug interaction.

The clinical and laboratory manifestations of acute digoxin toxicity include elevated digoxin levels, bradycardia, hyperkalemia, gastrointestinal upset, dysrhythmias, and/or shock. Chronic toxicity is less likely to cause gastrointestinal upset, but more often causes visual disturbances in addition to elevated digoxin levels, bradycardia, dysrhythmias and/or shock. While hyperkalemia in acutely poisoned patients is a well-known predictor of fatalities, its use as a prognostic marker in chronic toxicity has not been well studied.

Management of either acute or chronic digoxin poisoning includes the use of digoxin-binding antibodies (digoxin immune Fab). This antidote is indicated for patients with life-threatening ventricular arrhythmias, symptomatic bradycardia, third-degree heart block unresponsive to atropine, or in patients with hyperkalemia ( $K^+ > 5.5$  mEq/L). The antidote is additionally indicated in acute ingestions with a level higher than 10 ng/mL (obtained at a minimum of 6 hours post-ingestion), or a known ingestion of at least 10 mg in adults and 4 mg in children. Even though this antidote has been in use for many years, the dosing of digoxin immune Fab continues to be controversial with the possibility that lower doses may be as effective and less costly.

The DORA study prospectively studied 36 patients with chronic digoxin toxicity who had supratherapeutic digoxin levels, hyperkalemia, or renal failure. In these patients, free digoxin concentrations were measured and were significantly reduced even with the use of only one or two vials. Nine patients had rebound free digoxin concentrations that were supratherapeutic. However, none of these patients required further immune fragments and had no clinical sequelae that were attributed to digoxin (*Clin Toxicol (Phila)*. 2016;54(6):488-494).

The DORA study later published a prospective observation study of 23 patients with acute or acute on chronic digoxin overdoses who were symptomatic and had supratherapeutic digoxin levels. The patients who were given large doses of the immune fragment (doses per package insert) received a median of 10 vials, compared to the patients in the titration group (as needed doses based on clinical effects) who received a median of 4 vials. Regardless of the dosing strategy used, free digoxin concentrations decreased to almost zero and patients responded well to titrating doses (*Clin Toxicol (Phila)*. 2022;60(4):433-439).

The Maryland Poison Center recommends 4 vials of IV digoxin immune Fab in acute digoxin toxicity for a known OR unknown amount, with an additional 4 vials, if necessary, based on the patient's clinical response. In chronic digoxin toxicity, an initial 1-2 vials are recommended which may be repeated if symptomatic bradycardia or bradyarrhythmias persist. For additional information about digoxin immune Fab, please see the Maryland Poison Center's [Digoxin Immune Fab Antidote Facts](#).

For treatment recommendations for digoxin toxicity or any other poisoning, call your local poison center at 1-800-222-1222.



Foxglove (*Digitalis purpurea*)

### Did you know?

Sir William Withering published that *Digitalis Purpurea*, or foxglove, could be used to treat dropsy in 1785 which is known today as heart failure.

Cardiac glycosides can be found from other natural sources including yellow oleander, red squill, or in bufotoxin from *Bufo* spp. Toads (pictured below).



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