

Safety and Monitoring of Cardiac Glycosides: Digoxin

Mechanism:

Therapeutic effects = increase force of contraction (+inotropy) by increasing cytosolic Ca

With myocyte depolarization, L-type Ca channels allow Ca entry which triggers more Ca release from SR and contraction

After contraction Ca is pumped out of cell via Na/Ca transporter – pump is run by Na concentration gradient (Na in + Ca out) (the amt of intracellular Na determines amt Ca extruded)

Digitalis blocks Na/K ATPase – increases intracellular Na – subsequently prevents Ca extrusion

Atrial & ventricular myocytes = increase automaticity & excitability

Conduction & nodal tissue = decreases velocity (blocks)

Vagus nerve = increases outflow – SA/AV block

Pharmacokinetic and dosing: Digoxin clearance primarily renal (70%), Calculated loading dose (0.75-1 mg);

Administer in three divided doses of 50%, 25% and 25% of total calculated dose with 6 hours between each dose.

Assumes no drug on board. **Loading dose is a loading dose.** Needed for AF, but optional for HF. **Usual Goal for**

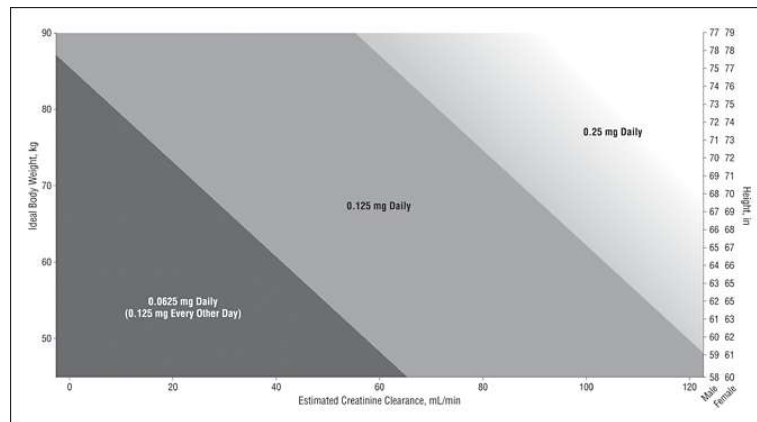
Atrial Fibrillation: Digoxin 1.0-2 ng/ml (mcg/liter), **Heart Failure:** Digoxin 0.5-0.9 ng/ml (mcg/liter).

If used in low doses, digoxin is unlikely to cause digoxin toxicity for older adults with HF. Start at 0.125 mcg/day. In patient with normal renal function, there is no need for routine laboratory testing of serum digoxin concentrations in most patients.

Heart Failure? Clearance reduced 60%, Concurrent Quinidine? Clearance reduced 50%, Vd reduced 30%,

Concurrent Amiodarone? Clearance reduced 50%, Concurrent Verapamil? Clearance reduced 25%, Clinically

Hypothyroid? Clearance and Vd reduced 30%. (Bauman, J. L. et al. Arch Intern Med 2006;166:2539-2545)



Toxicity: N/V, abdominal pain, lethargy, confusion, weakness, blurred vision

Hyperkalemia is common finding with acute (better predictor of lethality than initial ECG or serum dig

level). Hypokalemia may precipitate digoxin toxicity (inhibits Na/K ATPase) esp if <2.5

Digoxin toxicity can cause almost any rhythm except rapid a-fib and SVT without block

Measurement of levels before 6 hours may be misleadingly high – post distribution levels correlate better clinically

Endogenous digitalis-like substances reported with **pregnancy, renal failure**, neonates, liver disease, CHF,

acromegaly, hypothermia – may cross-react with dig assay

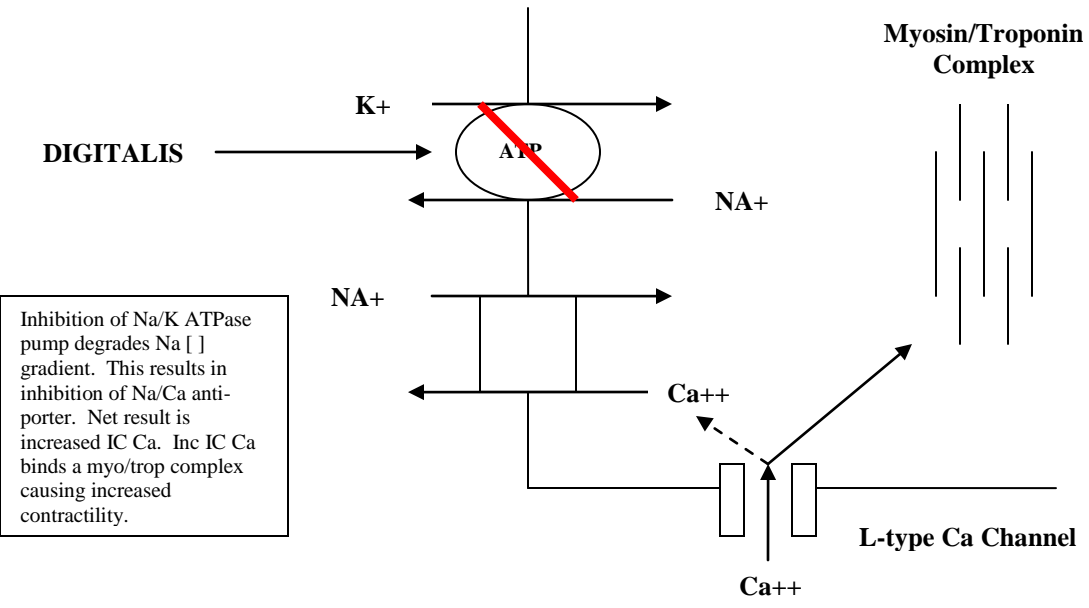
Treatment of Digoxin Toxicity: Digitalis Fab is standard of care for **life-threatening digoxin poisoning** =

dysrhythmias **#Vials = Dig[] x Wt (kg) / 100** or ingested mg / 0.5 (mg/vial), ADR related to Digibind

- » Exacerbation of CHF
- » Increase in vent response to afib/flutter
- » Hypokalemia
- » Allergic reactions
- » Plasma Dig level measurement unreliable after given digibind

Important to address hyperkalemia = bicarb, insulin/glucose, kayexalate, lasix. Fab will also lower K

Hypomagnesemia increases myocardial digoxin uptake. Mag decreases inward Ca current, suppresses vent ectopy, and antagonizes dig. Mag supplementation may be helpful – **contraindicated with bradycardia or AV block.**



Inhibition of Na/K ATPase pump degrades Na^+ gradient. This results in inhibition of Na/Ca antiporter. Net result is increased IC Ca^{++} . Inc IC Ca^{++} binds a myo/trop complex causing increased contractility.