Bon Secours Richmond Health System
Pharmacy & Therapeutic Committee
Digibind Protocol
1/2002

Recommendations:

- Pharmacists will monitor all patients receiving Digibind and notify the lab when Digibind is dispensed.
- The lab will place an addendum on reported digoxin levels for patients who have received Digibind.
- Pharmacists will verify the dose when dispensing Digibind to ensure proper dosage. Digoxin distributes into lean tissue and dosage of Digibind is best based on lean body weight.
- Post Digibind digoxin serum levels are not recommended as the assay measures total digoxin levels (free and Digibind bound). Total levels increase 10-30 times those before treatment within minutes of administration. Levels of the Digibind-digoxin complex remain elevated for day's post Digibind therapy with 95-100% of the measured level being Digibind-digoxin complex. The elimination half-life of the complex is 16-24 hours in normal renal function and 65-330 hours in severe renal dysfunction (creatinine clearance less than 20 ml/min) and is comparable to digoxin half-life.
- Patients who require redigitalization must wait 4-5 half-lives (4-7 days in normal renal function) for the complex to be eliminated.
- Pharmacy will offer a digoxin dosing service to physicians and will leave dosage recommendations for all patients receiving Digibind.
- Indications for Digibind
  - Patients with life-threatening digoxin toxicity
    - Severe ventricular arrhythmias: ventricular tachycardia or ventricular fibrillation.
    - Progressive bradyarrhythmias: sinus bradycardia leading to 2nd and 3rd degree heart block unresponsive to atropine.
    - Serum Potassium levels > 5mEq/L in the presence of digoxin toxicity. (55% mortality rate was reported in patients with K+>5.0 mEq/L who were treated by conventional means. Gaultier M. Bismuth C:L intoxication ditalique aigue. La Rev dPracticien 1978;28:4565-4579) Note: Do not use any therapeutic maneuvers to reduce hyperkalemia prior to FAB treatment. This may lead to severe rapid hypokalemia after Fab infusion has occurred.
  - Acute ingestion of > 10 mg in adults, > 4 mg in a child or a steady state serum level of > 10 ng/ml 6-8 hours post ingestion often results in cardiac arrest.
- Recommended serum levels of digoxin in CHF are 0.5-1 ng/ml, which allows for non-toxic drug accumulation if the patient decompensates. Studies have shown that higher concentrations are not associated with more positive effects on neurohormones or cardiac function, but are associated with increased incidence of toxicity.

Suggested patient monitoring:

- Obtain a STAT digoxin level (at least 6 hours after last dose as digoxin has a very prolonged distribution phase and levels drawn too early do not reflect tissue concentrations), current height, and weight, as well as chemistries to include: serum creatinine, BUN, potassium, and magnesium levels.
- Serum potassium should be monitored hourly post Digibind until stabilized and potassium replenished as needed.
- EKG monitoring

Findings:

- Under dosing of Digibind has been related to return of signs and symptoms of toxicity after an initial response to therapy usually after 3 days, but as late as 11 days after therapy.
- Each vial of Digibind contains 38 mg of digoxin-specific immune FAB that binds approximately 0.5 mg of digoxin.
- If patient's life is thought to be in eminent danger the physician may want to initiate Digibind prior to receiving digoxin levels. Most digoxin toxicity in adults from chronic administration can be treated with 6 vials of Digibind. If the patient is a child and weighs less than 20 kg then 1 vial usually suffices. Once the digoxin levels are obtained further amounts of Digibind can be administered as needed.
- Digibind has high affinity for digoxin and quickly removes it from its pharmacologically active binding site within tissue and sequesters it in the extracellular fluid.
- The elimination half-life of digoxin-Fab complex in patients with renal dysfunction is similar to that of digoxin.
- Digoxin does not dissociate for the digoxin-Fab complex in patients with or without renal dysfunction.
- The major route of elimination of Digibind is by glomeruli filtration.
- In patients with severe renal dysfunction (serum creatinine > 3 mg/dl) free digoxin levels peak on average 55 $\pm$ 28 hours post therapy and ESRD 127 $\pm$ 40 hours post therapy at 1.7$\pm$ 1.3 mmol/l.
- Digoxin is 20-25% protein bound.

- Patients with normal renal function eliminate digoxin-Fab complex very quickly and free digoxin levels are rarely needed. Patients with ESRD eliminate digoxin-Fab complex very slowly and recurrences of digoxin toxicity has been shown to correlate with a rebound in free serum digoxin concentration. Free levels may be useful in these patients.
- Plasmapheresis clears digoxin-Fab complexes in patient with renal failure. One 70 minute treatment has been shown to decreases complex levels by 50%.
- CHF may be precipitated in patients who require digoxin to maintain cardiac output. Increase in ventricular rate might be noted in patients being treated with digoxin for atrial fibrillation.
- Patients with CHF are highly susceptible to toxicity, as they are generally older, may have decreased lean muscle mass, are commonly treated with interaction drugs, and often have baseline renal insufficiency. Renal dysfunction occurs with CHF decompensation and renal insufficiency is likely to worsen as CHF progresses. Maintaining low digoxin concentrations provides a larger margin of safety should renal function decline.
- The full effect of maintenance digoxin, without a loading dose, is achieved in 4-5 half-lives.
- Digoxin is distributed to lean tissue and loading and maintenance doses are based on lean (ideal) body weight
- Pharmacist to evaluate for:
  - drug interactions
  - renal function
  - dosing weight
  - indication

Selected Studies

Wenger TL, Treatment of 63 Severely Digitalis-Toxic Patients with Digoxin-Specific Antibody Fragments. JACC 1985;5:118A-123A

Antman EM. Treatment of 150 cases of Life-Threatening Digitalis Intoxication with Digoxin-Specific FAB Antibody Fragments. Circulation 1990;81:1744-52

- Total serum digoxin concentrations increase rapidly after Digibind to values typically 10-20 fold higher than pretreatment levels.
- In all patients who had elevated serum potassium concentrations, treatment with Digibind reversed hyperkalemia with the mean nadir occurring 3-4 hours post infusion. Hypokalemia developed rapidly in 4% of patients.
- No relationship between pretreatment hyperkalemia and mortality was found.
- Symptoms of intoxication
  - Third degree AV block 53%
  - Ventricular tachycardia 46%
  - Ventricular fibrillation 33%
  - Ventricular asystole 11%
  - Hyperkalemia 37%
- Time to Response from end of infusion
  - Initial response 19 minutes
  - Complete response 88 minutes (30-360 minutes) with most patients responding by 1 hour.

1.5 mg/dl = 132 umol/l scr , divide umol/l by 88.4 to get mg/dl
0.8 ng/l = 1.02 nmol/l digoxin

Bon Secours Richmond Health System
Pharmacy & Therapeutics Committee

To: All Pharmacists
From: Marshall Pierce
Subject: Digibind Patients
Date: 1/29/2002

Please review the attached protocol on Digibind. A digoxin dosing program will be distributed and inservices will be scheduled with the staff.

Thanks

Marshall