TDM of Digoxin

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Drug profile

Indications of drug

- ✓ CHF i.e. dilated ventricles with poor ejection fraction
- ✓ Atrial fibrillation i.e. Atrial tachyarrhythmia

Half life

In patients with normal renal function: 30-50 hrs

In ESRD patients: 100-200 hrs (50-75% eliminates through renal system)

Time to reach peak serum concentration: 6-8 hrs

Time to reach steady state concentration: 7-12 days

VoD: 7.3 L

Protein binding: 25%

Toxic level: $\geq$ 2.5 ng/mL

Therapeutic range

Varies between 0.7 to 2.0 ng/mL

1. Atrial fibrillation: 1.5- 2.2 ng/mL
2. CHF: 0.9-1.8 ng/mL

Dose

Loading dose is 10-15 mcg/kg/day in 3 divided doses

Maintenance dose is 0.125- 0.5 mg/day

- This doses is in normal renal function
- In renal failure the frequency of administration has to be altered and has to be adjusted every 3-5 days.

Indications for TDM

- ✓ To evaluate digoxin toxicity:

- ✓ To assist in differential diagnosis:

  To distinguish between drug related adverse effects from disease symptoms

- ✓ To evaluate suspected drug-drug interaction:

  Quinidine-digoxin interaction resulting in increased plasma digoxin concentration

- ✓ To assess medication adherence: poor therapeutic response

Assay method

Volume of sample: 1-4mL

Tubing:

- Evacuated tubes are used
- Earlier red stopper tubes were used which contains plasticizer interact with drug and inhibits binding of drugs to alpha-glycoprotein in serum

Sampling time:

Atleast 6-8 hours following an oral dose

Drug Interactions:

Drugs INCREASING Digoxin levels	Drugs DECREASING Digoxin levels
Amiodarone, Anticholinergic drugs, Diltiazem, Propafenone, Quinidine, Spiranolactone, Verapamil	Antacids, Cholestyramine, Domperidone, Metoclopramide, Sulfasalazine

Radio Immuno Assay:

Principle:

Digoxin in serum sample competes with the radio labelled (I-125 digoxin) derivative for binding sites on the antibody to the Digoxin

The unbound digoxin is then separated from bound form

One of these is quantitated by radio active counting and the concentration of unbound digoxin in the serum is calculated by comparison to Digoxin standards

Advantages: Sensitive, precise and easy to perform

Disadvantages: Low specificity

Enzyme immuno assay method:

Principle:

Digoxin-enzyme competes with serum digoxin for digoxin antibody binding site

Either free or antibody bound digoxin enzyme is then reacted with excess substrate for the enzyme along with cofactors

The enzyme-reaction produces a chromophore which is measured spectrophotometrically or fluorometrically

Advantages: the precision and sensitivity are similar to RIA

Fluorescence polarization immuno assay:

Principle:

Ability of flurescent labelled digoxin tracer to compete with unlabelled serum digoxin for the binding site on antibody to digoxin

Upon excitation by single wavelength polarized light, the unbound label and antibody bound florescent label exhibit widely different degree of polarisation of emission florescence

Advantage: excellent reproducibility

Pharmacokinetic evaluation

If the SDC is lower than anticipated,

- Patient compliance
- Error in dosage regimen
- Poor bioavailability
- Rapid elimination of drug
- Increased VOD
- SSC may not be reached
- Timing of blood sampling

If the SDC is higher than anticipated

- Patient compliance
- Error in dosage regimen
- Increased bioavailability
- Smaller VOD
- Slow elimination of drug

If the SDC is proper but patient is not responding to the therapy, then it may be due to

- Altered receptor sensitivity
- Possible drug-drug interaction at receptor site
- Look for co-morbid conditions like thyroid disease and malabsorption syndrome

Steps in the analysis

- Define the problem
- Select the correct sample
- Choose the best analytical method
- Standardize the assay
- Process the sample
- Perform the assay competently
- Interpret the results