DIGOXIN IMMUNE FAB: CLINICAL LAB PERSPECTIVE

Introduction

Digoxin Immune Fab is a specific antidote for digoxin intoxication. It was approved by the FDA in 1986 and is marketed under the trade name "Digibind". Digoxin Immune Fab (Fab) is prepared by immunizing sheep with a digoxin-albumin conjugate and cleaving the resulting antibody with papain to obtain two digoxin-specific Fab fragments. Fab works by binding free digoxin. Bound digoxin is no longer pharmacologically active and the Fab-digoxin complexes are gradually cleared from the plasma by the kidneys and reticuloendothelial system.

The main indication for Fab is to treat life-threatening digoxin intoxication manifested by ventricular arrhythmias, bradycardia, or hyperkalemia unresponsive to standard treatment. Fab may also be indicated in cases of known massive overdoses (i.e., suicide attempts) or if the digoxin concentration is >10 ng/ml in the post-distribution phase (1).

Fab is supplied in vials containing 40 mg of Fab that will bind roughly 0.6 mg of digoxin. The recommended protocol is to give an amount of Fab equimolar to the total body digoxin in an infusion over 30 minutes. Improvement in clinical symptoms of toxicity generally begins within 30 minutes with complete reversal of toxicity in two to six hours. Levels of free digoxin (where measured) are rapidly reduced to undetectable levels after Fab infusion. In patients with normal renal function, the Fab-digoxin complexes have an average initial elimination half-life of 14 hours. Treatment with Fab also reverses the therapeutic effects of digoxin and redigitalization is not recommended until Fab has been completely cleared from the body. This may take several days in patients with normal renal function or a week or more in patients with impaired renal function.

Monitoring Digoxin Levels After Fab Administration

After Fab is given, physicians naturally want to monitor digoxin levels along with clinical response. However, post-Fab monitoring of digoxin levels is misleading both because of the effect of Fab on the total digoxin concentration and because of interference by Fab on the laboratory's assays for digoxin. After administration of Fab, digoxin levels measured by the clinical lab actually rise to peak levels 10 to 20 times the pretreatment level (2,3). This rise in the apparent digoxin level is due to the small volume of distribution of the dig-Fab complex relative to free digoxin. As digoxin diffuses out of the tissues, it is trapped in the vascular space by the Fab molecules. Since the standard assay for digoxin measures total digoxin (bound plus free), the apparent digoxin level rises after Fab is given. (Figure 1)

The standard digoxin assay uses an immunoassay method. Because Fab is also a digoxin-specific antibody, Fab in equimolar amounts with digoxin would be expected to interfere with the assay. This interference may depend on the amount of bound vs free digoxin present or the relative affinity for digoxin of Fab vs the assay antibody. The VAMC uses an immunoassay with a digoxin-specific antibody whose binding is measured by fluorescence polarization (Abbott TDx analyzer). This assay also only measures total
Serum Digoxin Concentration (ng/ml)

![Graph showing serum digoxin concentration over time.]

Arhythmias, normalization of heart rate, and correction of hypokalemia can be monitored by patient's response to treatment, i.e., resolution of arrhythmias, normalization of heart rate, and correction of hypokalemia.

Summary

There is no method as the VAMC lab for measuring free digoxin. These techniques are still being developed and currently the laboratory is using the Abbott TDx system to quantitate the free digoxin prior to computer-assisted assay using the Abbott TDx samples by computer-assisted assay using the Abbott TDx samples. However, the current methods of measuring free digoxin will be measured. One experimental method involves measuring free digoxin levels. The process, however, is not useful in clinical practice because of special equipment required and the length of the assay (4-20 hours).

Ideally, free digoxin levels may prove useful in monitoring digoxin-toxicity. Measuring free digoxin levels is no method as the VAMC lab for measuring free digoxin.

Variability between methods for assaying digoxin in the presence of Fab shows considerable. The method used by the college of American Pathologists also show considerable.

Fab levels were measured by equilibrium dialysis with normal serum. The study by Arakawa et al. used Fab on individual assay methods. One small study by Arakawa et al. used Fab on individual assay methods.
References


