Therapeutic Drug Monitoring

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Therapeutic Drug Monitoring involves measuring serum drug levels in patients receiving drugs with a narrow therapeutic window to maximize the effectiveness and minimize the toxic effects. Some of the most common drugs that must be closely monitored with serum blood levels include theophylline, phenytoin, digoxin, and aminoglycoside antibiotics. These all have low therapeutic index.

The therapeutic index (TI) estimates the margin of safety of a drug through the use of a ratio that measures the effective (therapeutic) dose (ED) and the lethal (toxic) dose (LD). The closer the ratio is to 1, the greater the danger of toxicity. \[ \text{TI} = \frac{\text{LD}}{\text{ED}} \]

Drugs with a low therapeutic index have a narrow margin of safety. Drug dosage needs to be adjusted according to plasma drug levels because of the small safety range between the effective dose and the lethal dose. Drugs with a high therapeutic index have a wide margin of safety and less danger of producing toxic effects. Plasma drug levels do not need to be monitored routinely for drugs with a high therapeutic index.

The therapeutic range or window of a drug concentration in plasma should be between the minimum effective concentration in the plasma for obtaining the desired drug action and the minimum toxic concentration. When the therapeutic range is narrow, such as with digoxin (0.5 – 2 ng/ml), phenytoin (10-20 mcg/ml), and theophylline (5-15 mcg/ml), the plasma drug level should be monitored periodically to avoid drug toxicity. Monitoring the therapeutic range is no necessary if the drug is not considered highly toxic.

With the aminoglycoside antibiotics we measure peak and trough levels. Peak drug level is the highest plasma concentration of drug at a specific time and it indicates the rate of absorption. The trough level is the lowest plasma concentration of the drug and it measures the rate at which the drug is eliminated. Peak levels are drawn at a specific time following administration of the medication, for IV gentamicin, this is 30 minutes following completion of the infusion. Trough levels are drawn immediately before the next dose of drug is given. If either the peak or trough level is too high, toxicity can occur. It the peak is too low, no therapeutic effect is achieved. The peak for gentamicin should be between 5-10 mcg/ml. The trough should be <2 mcg/ml.

Another issue that can affect therapeutic drug monitoring is what we refer to as a loading dose. A loading dose is a large initial dose of a medication given to achieve a rapid effective concentration in the blood stream. After a large initial dose, a prescribed dosage per day is ordered. Digoxin requires a loading dose. With digoxin the administration of the loading dose is referred to as digitalization.