

Editorial



Therapeutic drug monitoring

Therapeutic drug monitoring (TDM) is the experimental measurement of a drug concentration that leads to determination of drug dosage, to keep plasma/blood drug concentrations within a targeted therapeutic window. Back to the 1970s, drug monitoring was initiated to evaluate the incidence of toxicity to drugs such as digoxin, phenytoin, lithium, and theophylline. Drug monitoring is used to evaluate the efficacy, compliance, drug-drug interactions, and also to prevent drug toxicity. When the drug is being used as prophylaxis, it is impossible to monitor a response. Thus, the physician can select a dosage that will produce a certain target plasma concentration. For example, lithium in preventing manic-depressive, phenytoin in preventing seizures after neurosurgery or trauma, and cyclosporine in preventing transplant rejection. In some cases, plasma concentration measurements obtained during treatment enable the physician to avoid toxic plasma concentrations. For example, digoxin toxicity may mimic certain symptoms of heart disease, and measuring the plasma concentration in cases in which toxicity is suspected may be helpful in confirming the diagnosis. Similarly, nephrotoxicity of aminoglycoside antibiotics is difficult to distinguish clinically from that caused by a severe infection. Other important aspects of modern TDM is to individualize dosing, by understanding the molecular mechanisms involved in drug effects. Genotyping is used to determine the appropriate dosage for each person based on polymorphisms in involved proteins. The combination of TDM and the genotyping of drug metabolizing enzymes or transporters provide a more precise method to predict drug target levels. Today, TDM is used along with genotyping to predict the required therapeutic dose of certain drugs. Genetic difference in cytochrome P450 enzymes causes variable metabolism capacities among individuals. Understanding the polymorphisms of the genes encoding metabolizing enzymes or target molecules could guide the physician to suggest the appropriate dosing required for each individual.

TDM is routinely used in four areas of pharmacotherapy: immunosuppression, epilepsy, infectious diseases and psychiatry. Both chromatographic and immunochemistry techniques have been used for TDM services. The recent development in chromatography, which combines liquid chromatography and mass spectrometry (LC-MS) is the preferred technique for assaying chemical compounds in body fluids. The LC-tandem MS (LC-MS/MS) technique provides even more selectivity than single MS detection methods. In the future, LC-MS/MS will likely be replaced with conventional TDM services because it enables us to simultaneously analyze several agents in biological fluids instead of just one specific compound. Moreover, the high-resolution MS can be used in metabolic studies and in studies on biomarkers of genetic polymorphisms.

Another novel application of TDM is the use of new biological matrices such as “dried blood spots” in neonatal screening and “oral fluid” for testing drugs of abuse. The advantage of dried blood spot is its simple blood collection method without the involvement of professional personnel. However, for dried blood spot, it is still necessary to standardize the sampling regarding the exact blood volume. In oral fluid, one possible advantage might be that the oral fluid sample better reflects the un-bound fraction of the drugs in blood.

There is strong link between TDM service and researches. Properly stored drug concentration data and associated clinical information can be used as a database for pharmacological research. The routine TDM data, if available in sufficient case number, could be used for research purposes. The computerized data recording made data extraction easier than the past. Moreover, utilizing pharmacokinetic-based mathematical models for the evaluation of drug concentrations would more precisely predict the effect of suggested dose adjustment.

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