Therapeutic drug monitoring (TDM)

Therapeutic drug monitoring (TDM) is the clinical practice of measuring specific drugs at designated intervals to maintain a constant concentration in a patient's bloodstream, thereby optimizing individual dosage regimens. It is unnecessary to employ TDM for the majority of medications, and it is used mainly for monitoring drugs with narrow therapeutic ranges, drugs with marked pharmacokinetic variability, medications for which target concentrations are difficult to monitor, and drugs known to cause therapeutic and adverse effects.

The process of TDM is predicated on the assumption that there is a definable relationship between dose and plasma or blood drug concentration, and between concentration and therapeutic effects.

Therapeutic drug monitoring (TDM) refers to the measurement and interpretation of principally blood pr plasma drug concentration measurements with the purpose of optimising a patient's drug therapy and clinical outcome while minimising the risk of drug-induced toxicity.

Objectives of TDM

• To attain desired pharmacological effect of the drug.

• To reach the maximal effect in shortest possible time.

• To decrease the risk of toxicity.

TDM is useful in drugs:

• With a narrow therapeutic index.

• Which is highly protein bound.

• Which are liable to interact.

• In which the metabolite might be toxic.

PURPOSE OF THERAPEUTIC DRUG MONITORING

The indications for drug monitoring have widened to include efficacy, compliance, drug-drug interactions, toxicity avoidance, and therapy cessation monitoring

Process for reaching dosage decisions with therapeutic drug monitoring.

The use of TDM requires a combined approach encompassing pharmaceutical, pharmacokinetic, and pharmacodynamic techniques and analyses. The appropriate use of TDM requires more than a simple measurement of patient blood drug concentration and a comparison to a target range. Rather, TDM plays an important role in the development of safe and effective therapeutic medications and individualization of these medications. Additionally, TDM can help to identify problems with medication compliance among noncompliant patient cases. When interpreting drug concentration measurements, factors that need to be considered include the sampling time in relation to the dose, the dosage history, the patient's response, and the desired clinical targets. This information can be used to identify the most appropriate dosage regimen to achieve the optimal response with minimal toxicity

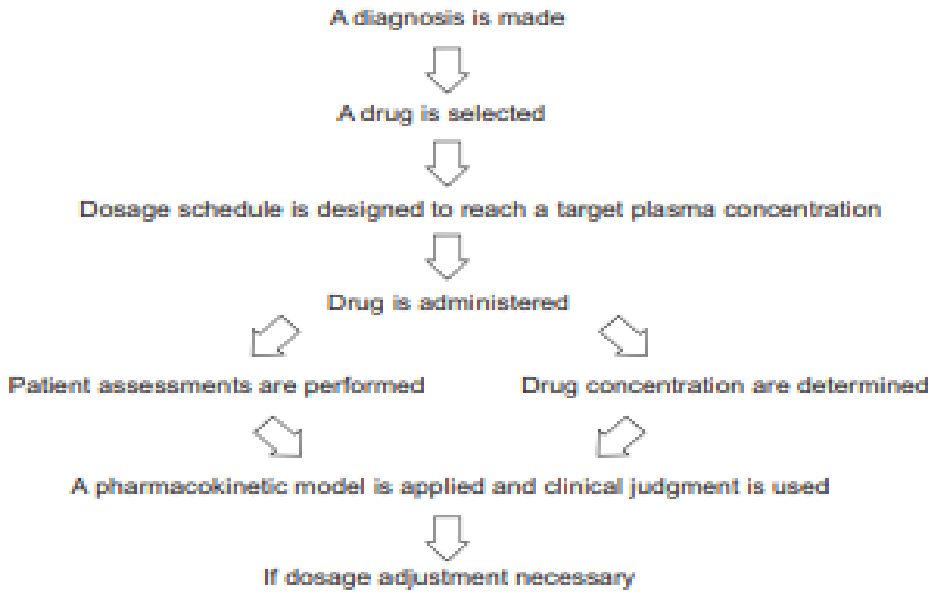

Figure 1. Process for reaching dosage decisions with therapeutic drug monitoring.

ROLE OF PHARMACIST

A reliable and responsive TDM service depends on team work between nurses, doctors, pharmacist, scientist and technical staff. The clinical pharmacist should provide advice to

medical staff on the appropriate use and timing of TDM and assist with the interpretation of results. In addition the pharmacist maybe involved in :

• Initial selection of drug regimen.this may involve decisions about drug choice, dose, dosing interval, route of administration and dosage form of the drug, taking into account factors such as sex, age, body weight, race, metabolism status, renal function, plasma albumin concentration, use of other drugs and laboratory results.

• Adjustment of the dosage regimen based on TDM results and the patients clinical response,.

• Assessment of possible causes for unexpected results, such as non- compliance, bioavailability problems, medication errors, drug interactions or pharmacogenetic variability.

• Dose adjustment for patients on haemodialysis or peritoneal dialysis.

• Provision of poisons information

Example of drugs for which TDM is performed

- Carbamazepine
- Ciclosporin
- Digoxin
- Gentamicin
- Lithium
- Phenytoin
- Theophylline (aminophylline)
- Vancomycin

TDM detail of Ciclosporin

3. Ciclosporin

Therapeutics	**Sampling**
Dosage forms: Oral, intravenous infusion (over 2 to 6 hours). **Loading and maintenance doses:** Different doses are applicable for different clinical indications. Please refer to manufacturer Summary of Product Characteristics or Pharmacy Department for full details. **Time to steady state:** 72 hours. **Therapeutic range:** Depends on indication for treatment. **Toxic effects:** Nephrotoxicity, hepatotoxicity, muscle tremor, nausea, gingival hyperplasia, hypertension, hyperkalaemia.	**Volume of blood:** Fill to line. **Tube to use:** Lavender top. **Lab performing assay:** Referred out from Wirral Clinical Biochemistry. **Emergency service:** No. Samples taken outside hours should be sent to the laboratory. **Sampling time:** Trough level immediately before next dose; peak level not usually done for renal transplants. **Reporting procedure:** Available via PCIS.
Pharmacokinetics	**Additional Information**
Elimination half-life: 6 to 21 hours. **Major route of excretion:** Biliary. **Volume of distribution:** 3.9L/kg. **Factors affecting plasma concentration:** ***Increased*** by fluconazole, ketoconazole, itraconazole, erythromycin and verapamil. ***Decreased*** by hepatic enzyme inducers.	**1.** Dosage and plasma concentrations are variable depending on the type of transplant or other indication. **2.** Due to differences in bioavailability, the prescriber should specify the brand of ciclosporin. **3.** In general, the recommended intravenous dose is one third of the oral dose. **4.** The injection contains polyethoxylated castor oil that may lead to anaphylactic reactions when injected too rapidly.