Monitoring drug levels

Therapeutic Drug Monitoring (TDM) is a means of finding the optimal dosing interval with the aim of the greatest possible **reduction of toxicity** while simultaneously **maintaining the effect**. This is the determination of the concentration of drug levels in biological samples, which are evaluated in connection with the clinical condition.

Indication for TDM

- Difficult to monitor the effect of the drug;
- complex mechanism of action;
- toxicity (low therapeutic index – digoxin, cytostatics);
- assumption of a significant drug interaction;
- suspicion of reduced effectiveness of the drug in a specific patient;
- intoxication, prevention of intoxication;
- genetic polymorphism (rapid and slow metabolizers, large inter-individual differences in effect - theophylline);
- prophylactic drug administration;
- doubt about patient compliance (cooperation).

Individualization of dosage

The purpose of TDM is also to design a dosage regimen for a specific patient. Fluctuations in plasma drug levels may be due to medical conditions, polymorbidity, drug interactions, in the critically ill, the elderly, neonates, or the chronically ill.

Strategy

First, the **therapeutic concentration** to be achieved is determined. The lower limit is a therapeutic effect, the upper limit already shows toxic effects. Therefore, approximately the middle of this range is chosen. Medicines are usually administered in the form of repeated doses or continuous infusions. Therefore, the goal is to determine an appropriate **maintenance dose**. Sometimes, however, it is necessary that the target concentration (c_{ss} concentration in the steady state) be reached already at the beginning of the therapy - an **initiation** (introductory, impact, loading) **dose**. This is particularly appropriate for drugs that would take too long to reach a steady-state concentration considering the purpose of the treatment (e.g. lidocaine). Steady-state plasma concentration, with constant supply and elimination of the drug, is reached in approximately 4-5 elimination half-lives (the level will be 95-97% c_{ss}).

Sampling

The collection of biological samples for TDM has its own rules. Samples should be collected after the previous dose and before the next scheduled dose. However, some drugs are eliminated very quickly after administration, so it is appropriate to take a sample after administration of the dose. The first sample is to be taken after two elimination halves. Although the condition has not yet stabilized, we can thus prevent damage to the patient during the administration of toxic drugs. If the measured concentration is 90% of the expected concentration, we can halve the dosing rate.

TDM is suitable for these drugs

- **Antibiotics**: *aminoglycosides (gentamicin, amikacin), vancomycin*.
- **Antiepileptic drugs**: *ethosuximide, phenobarbital, phenytoin, carbamazepine, valproic acid, lamotrigine, primidone*.
- **Thymoprophylaxis**: *lithium*.
- **Bronchodilation**: *theophylline*.
- **Cytostatics**: *busulfan, methotrexate*.
- **Immunosuppressants**: *cyclosporin-A, mycophenolate mofetil, sirolimus, tacrolimus*.
- **Cardiovascular drugs**: *digoxin, antiarrhythmics, warfarin, heparin*.

Links

References

- LINCOVÁ, Dagmar – FARGHALI, Hassan, et al. *Základní a aplikovaná farmakologie.* 2. edition. Praha : Galén, 2007. ISBN 978-80-7262-373-0.

Recommended reading

- MARTÍNKOVÁ, Dahlia – CHLADEK, Jaroslav, et al. *General Pharmacology.* 1. edition. Hradec Králové : Olga Cermáková, 2001. ISBN 80-902883-4-0.