Basic pharmacokinetic parameters affecting steady-state drug levels

Elimination constants

Elimination constants have different meaning in first and zero order kinetics. Most substances are eliminated according to first order kinetics, the elimination constant corresponds to the relative fraction of substance eliminated per unit time and is dimensionless. Some substances (e.g. ethanol, high doses of acetylsalicylic acid) are eliminated according to zero-order kinetics. The elimination constant corresponds to the absolute amount of substance eliminated per unit time.

The actual elimination constants are parameters of the respective compartmental model and are not usually used by themselves.

Volume of distribution

The volume of distribution Vd is the apparent volume of blood that would be required for a given amount of a substance to reach the same concentration in it as it reaches in the blood. All is clear from the principle of measurement - a certain amount of a substance is given and after a while, when it has been evenly dispersed but only a negligible amount has been excreted, the concentration of the substance in the blood is measured. The higher the Vd, the more the substance is distributed into the tissues. The Vd is particularly important for estimating the impact (saturation) dose.

Half-life

Half-life is a quantity that tells us how long it takes for the concentration of a substance to drop by half. For substances with zero-order kinetics, it is of little importance. It is related to the elimination statement of the pharmacokinetic model for substances with first-order kinetics by the following relationship:

$$t_{1/2} = \frac{\ln 2}{k_e}$$

In simple dosing, the steady state, that is, the state where the amount of substance taken in is equal to the amount of substance excreted, is approached in about four to five half-lives.

Clearance

Clearance is a parameter representing the volume of plasma that is completely cleared of a given substance per unit time. The total clearance of a drug can be determined as follows from a single administration of dose D:

$$CL_{TOT} = \frac{D}{AUC}$$

where ***AUC*** (area under curve) is defined as the time integral of the plasma concentration after a single administration:

$$AUC = \int_0^\infty c(t)\,\mathrm{d}t$$

However, total clearance is not indicative of the mechanism of excretion, so a distinction is usually made between renal and non-renal. **Renal clearance** can be determined as the proportion of the total drug excreted in the urine. Except for certain groups of drugs (e.g. general inhalation anaesthetics), other non-renal forms of excretion are not very significant, so **hepatic clearance** is usually calculated as the difference between total and renal clearance.

References

Related articles

- Pharmacokinetics and its use in clinical practice
- Physicochemical basis of pharmacokinetics
- Mathematical description of pharmacokinetic processes

Použitá literatura

- JANKŮ, Ivo. *Farmakokinetické základy dávkování léků.* 1. edition. Praha : Avicenum, 1986. 305 pp.

- LINCOVÁ, Dagmar – FARGHALI, Hassan, et al. *Základní a aplikovaná farmakologie.* 1. edition. Praha : Galén, Karolinum, 2002. 601 pp. ISBN 80-246-0538-4.

- LÜLLMANN, Heinz, et al. *Farmakologie a toxikologie.* 2. české edition. Praha : Grada, 2004. 725 pp. ISBN 80-247-0836-1.