Elimination of drugs

The elimination of drug takes place mainly through the liver and kidneys, in some cases other organs also participate more significantly. The elimination of the drug does not mean only elimination, elimination is also the metabolic inactivation of the drug. The fundamental pharmacokinetic quantity used to characterize excretion is clearance. Drug elimination occurs as:

- Exclusion of the 1st order – the same % part is excluded for each time interval, i.e. always e.g. 10%
- Excretion of the 0th order – the same amount is excreted for each time interval, i.e. always e.g. 10 ml

Liver elimination

Hepatic elimination can be quantified using **hepatic clearance**:

$$CL_H = E \cdot Q_H,$$

where Q_H is hepatic blood flow and E is the extraction ratio defined using the respective drug concentrations in blood entering and leaving the liver as:

$$E = \frac{c_{in} - c_{out}}{c_{in}}.$$

According to the extraction ratio, it can be decided if liver blood flow or parenchyma function is critical for drug elimination:

- if $E < 0.3$, is the limiting function of the liver parenchyma,
- if $E > 0.7$, is the limiting flow of the liver.

Hepatic clearance can also significantly affect the enterohepatic circulation of the drug. If the drug is significantly excreted by the liver, but is reabsorbed from the intestine, the effective hepatic clearance is lower.

Renal elimination

Three events take place in the kidneys, each affecting a different group of substances:

1. glomerular filtration – has only a limited effect on protein-bound substances;
2. active tubular secretion - active transport of strong acids and bases in the proximal tubule;
3. passive tubular resorption - is only possible for non-ionized forms.

Renal elimination can be quantified using the relatively easy to measure **renal clearance**:

$$CL_R = \frac{V_U \cdot c_U}{c_P},$$

where V_U is the volume of urine for a given period of time, c_U is the drug concentration in urine and c_P *sub>* is the plasma concentration of the drug.

Other significant forms of elimination

Pulmonary elimination

Inhalation anaesthetics, partly also alcohol, are eliminated through the lungs, i.e. actually exhaled.

Elimination into milk

Excretion of the drug into breast milk does not play a major role in the actual elimination of the drug from the body, but it can be significant when assessing risks for a breastfed child.

Other routes of elimination of the drug are sweat, saliva, desquamating skin epithelium, etc. The pharmacokinetic significance of such excretion methods is not great, but sometimes it is possible to use the determination of the level of the drug, e.g. in saliva, for therapeutic monitoring of the concentration of the drug.

Total clearance

Total clearance characterizes the overall rate of drug excretion. It is defined as the sum of all partial clearances, in practice it is usually sufficient to assume that only the liver and kidneys are involved in elimination. Then you can put:

$$CL_{TOT} = CL_H + CL_R.$$

Links

References

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