Relationship between dose, plasma level and effect

Effects of drugs

The application of an active substance induces a response in the organism (biochemical, physiological, morphological change) - it produces an effect.

The changes can be:

- **temporary** (*reversible*),
- **permanent** (*irreversible*)

Depending on the route of administration and the dosage form, the effects may be:

- **local** (*topical*) i.e. at the site of application or in the immediate vicinity,
- **total** (*resorptive*) i.e. developing in the body after absorption.

The effects for which drugs are applied are called the main (desired) effects. However, most drugs also have side (undesirable) effects.

In general terms, we can distinguish:

Stimulation of function

1. Stimulation - stimulation of the functions of any organ within physiological limits.
2. Analeptic effect - stimulation of blood circulation, CNS, breathing.
3. Excitation - strong stimulation or irritation.

Attenuation of function

1. Inhibition - temporary reduction of function within physiological range.
2. Paralytic effect - complete cessation of function (may progress to complete paralysis).

After high doses, the effects may be toxic, poisoning occurs, which may be lethal.

Drug doses

The effect for most substances depends in direct proportion to the size of the dose.

Dose distribution of drugs

- Dosis maxima singula - maximum single dose (for 1 administration).
- Dosis maxima pro die - the maximum daily dose (if necessary the doctor may exceed the maximum daily dose) .
- Dosis therapeutica - therapeutic dose.
- Dosis plena - full dose (if the drug is given in 1 dose).
- Dosis pro cura - dose for the entire treatment period.
- Dosis therapeutica pro die - recommended therapeutic dose per day.
- Dosis toxica - after administration of toxic symptoms.
- Dosis lethalis - lethal dose.

Shock dose

We administer an impact dose (bolus) when we want to achieve a high concentration of the drug in the body and maximum effect.

Saturation dose

A saturation dose is a dose at which a certain concentration in the body must be reached before the drug has an effect. It is usually divided into individual sub-doses. Once the body is saturated with the drug, the level is maintained at a constant level by maintenance doses.

Dose-effect relationship

There are two basic types of dose-effect relationship, namely quantitative and qualitative.

Quantitative type

Determines the relationship between the dose of a drug and the magnitude of response measured on a single biological unit. The response is given by an observable, measurable characteristic (number), e.g., weight change, urine output volume, drop in BP,...

The range of effect is given by

- **subthreshold dose** - no measurable effect,
- **Threshold dose** - produces a measurable response,
- **střední efektivní dávkou** ED_{50} – vyvolá účinek o velikosti 50 % maximálního účinku,
- a **maximální dávkou** – nejmenší dávka, při které je dosahováno maximálního možného účinku.

Quantal type

Defines the relationship between the dose of a drug and the number of biological objects exhibiting the pharmacological effect of interest. The response either occurs or does not occur (e.g. animal death, sleep, convulsions...). These relationships can be expressed:

1. method

On a set of animals, we individually determine the minimum dose that elicited the observed response. The dose is not the same in all animals and the results give a distribution curve of minimum doses.

2. method

The experimental animals are divided into several groups and each group receives the same dose. For each group, the dose will be gradually increased. The number of responders in each group over a period of time will be determined. From the results, a graph is obtained from which the LD50 i.e. the dose for which the probability of death (response) is equal to 50% (mean lethal effective dose) can be read.

Therapeutic index

The therapeutic index (TI) provides information on the relative safety of the drug. It is given by the ratio between the dose that is toxic for 50% of the population and the dose that is effective for 50% of the population.

TI = TD50 / ED50

The higher the TI, the greater the relative safety of the drug (because the toxicity dose is therefore higher than the efficacy dose - this is advantageous).

Drugs with a high TI - e.g. penicillin

Low TI drugs - e.g. digoxin, warfarin

Therapeutic breadth

Therapeutic breadth (efficacy) is determined by the difference between TD50 and ED50. It determines how much the dose can be raised. It informs about the absolute value of the difference between the doses given, but not about the relative ability of the substance to induce therapeutic and toxic symptoms.

Refences

Used sources

- EYBL, Vladislav. *Vybrané kapitoly z obecné farmakologie.* 2007. edition. 2007. ISBN 978-80-246-0679-8.