Routes of drug administration, first-pass effect

We usually divide routes of drug administration that produce systemic effect in Enteral or Parenteral. From Greek *Enteros = Intestine* and *Para = Beside*. Thus either it passes through the intestinal tract or it avoids it. This is extremely important as some drugs are poorly absorbed in the intestines, others are well absorbed however are metabolized almost completely by **first-pass effect**.

Enteral

Are entering the intestinal tract.

Oral

Given by mouth is the most common route of drug administration, however it also the one with the most complicated pathway to the target tissues. Most drugs are absorbed in the intestinal tract by passive transfer and usually end up in the portal circulation encountering the liver and thus high chance of passing the first-pass effect.

Rectal

Rectal administration can be used for producing local or systemic effects. It is quite unreliable however. 75% of drainage of the rectal region bypasses the portal circulation and thus minimizing first-pass effect. The inferior and middle rectal veins are linked to the systemic circulation whereas the superior rectal vein joins the inferior mesentering vein and from there onto the portal vein. It can be very useful during vomiting and in patients that are unable to take medications by mouth.

Sublingual

Sublingual administration can be classified into Parenteral as well, it does not enter the lower GastroIntestinal Tract, however it is placed under the tongue thus going oral. The drug diffuses into the capillary network and enters the system circulation directly. It is very rapidly absorbed, low infection risk, avoiding the rough environment of the GIT and no first-pass metabolism.

Parenteral

This route of administration avoids the GIT, and is used for drugs that are poorly absorbed or unstable in the GIT, for unconscious patients and when acute onset is required.

Intravenous (IV)

Injection straight into the systemic circulation is the most common parenteral route. It is the fastest and most certain and controlled way. It bypasses absorption barriers and first-pass metabolism. It is used when a rapid effect is required, continuous administraction and large volumes. The disadvantages are that one cannot recall injected drugs, introduction of bacteria through contamination as well as too rapid delivery or too high concentration may produce strong adverse effects.

Intramuscular (IM)

Produces a faster effect than oral administration, however the rate of absorption depends greatly on the site of injection and on local blood flow. The drug can be aqueous solutions or depot preparations (in a form of ester or salt). The absorption of the aqueous is fast and the depot form is slow. The advantage of the depot form is that it can provide a sustained dose over an extend period of time.

Subcutaneous (SC)

The absoroption of subcutaneous injections is slower than that of IV route and it needs absorption similar to Intramuscular injection. However it minimizes the risks associated with IV injections.

Other routes

- **Inhalation**

This route is used for gaseous drugs or those that can be dispersed in an aerosol, and is produces an effect almost as fast as with IV. It provides rapid delivery across the mucous membranes of the respirateory tract. It is used for asthmatic drugs, and anesthetics.

- **Intranasal**

Drug administration directly into the nose. Includes agents such as nasal decongestants or cocaine by abusers.

- **Topical**

As the name implies, it is applied where and when a local effect of the drug is desired.

- **Transdermal**

Drug administration through the skin. It can achieve systemic effects but rate of absorption can vary markedly depending on the physical characteristics of the skin at application.

- **Intrathecal / Intravetricular**

Drug administration into the cerebrospinal fluid (CSF). Used in cases of CNS cancers, cryptococcal meningitis etc.

First-pass effect

First-pass effect or also known as *first-pass metabolism* or *presystemic metabolism* is when an administered drug enters the liver and undergoes extensive biotransformation and thus decreasing the concentration rapidly before it reaches its target.

Mechanism

It happens most commonly when the drug is administered orally. The drug then is absorbed in the GIT and enters enters the portal circulation before entering the systemic circulation. Via the portal circulation it enters the liver where some drugs undergo extensive biotransformation and the drug concentration is decreased.

Thus it is the fraction of lost drug during the process of absorption generally related to the liver. This happens most commonly through oral intake. Noteable drugs undergoing significant first-pass metabolism include: Propanolol, Lidocaine, Diazepam

Beneficial effect

Some drugs take benefit of the liver biotransformation. These drugs are administered as *prodrugs* and are converted from inactive to active form. E.g. Codeine is administered and demethylated (biotransformation in liver) into its active form Morphine proper

Links

Related articles

- Drug absorption
- Bioavailability

Sources

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