Assignment 2.1 First Pass Metabolism

First pass metabolism is the way in which ligands get metabolized at a certain location in the body that results in reduced concentration of the active drug when it reaches the area of action or the blood stream. First pass effect is associated with the liver, due to it being a major site of drug metabolism. First pass can also take place in other areas of the body such as the gastrointestinal tract, the lungs and other tissues that are active metabolically in the body.[1]

Orally administered drugs must pass from the intestine to the liver before reaching the blood stream.[2] Because of this, for several drugs, most of the dosage is reduced by what is called xenobiotic metabolism which is the chemical transformation that converts lipophilic compounds into more readily excreted hydrophilic metabolites.[2 3] The first pass effect refers to the combination of the metabolism in the liver and the digestive enzymes in the gut since some drugs are also metabolized by gut flora. [2] An issue of concern with first pass effect is the differences among individual patients must be considered when dosing. It is important to understand that human metabolism differs from patient to patient in areas such as gender and age so the amount the drugs prescribed must vary in order to ensure that patients remain them the drugs therapeutic window.[1]

In contrast to oral administration, other routes such as intravenous (IV) inhalation, sublingual and intramuscular, undergo a less significant first pass effect as they enter the blood stream prior to entering the liver. When looking at oral vs. IV administration, we can view two related terms which are bioavailability and hepatic extraction ratio. Bioavailability is the portion of the drug that reaches the systemic circulation (blood stream) and hepatic extraction ratio is the portion of the drug that is extracted from the blood by the liver. When a drug is given via an IV, its bioavailability is near 100% since it is entering the blood stream directly.[4]

We can conclude that drugs administered intravenously would have an initially higher blood plasma concentration (Cmax) than drugs orally administered since IV drugs go directly into the blood stream and oral drugs, due to the first pass metabolism, enter the circulatory until after they have been metabolized in the liver.

Resources

[1]Herman TF. First Pass Effect. StatPearls [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK551679/. Published September 3, 2020. Accessed November 27, 2020.

[2]Pelley PhD JW. First Pass Effect. First Pass Effect - an overview | ScienceDirect Topics. https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/first-pass-effect. Published 2007. Accessed November 27, 2020.

[3]McGinnity DF, Grime K. Xenobiotic Metabolism. Xenobiotic Metabolism - an overview | ScienceDirect Topics. https://www.sciencedirect.com/topics/medicine-and-dentistry/xenobiotic-metabolism. Published 2017. Accessed November 27, 2020.

[4]Winn A, Freeman,MD BS. Anesthesiology Core Review: Part One Basic Exam. AccessAnesthesiology. https://accessanesthesiology.mhmedical.com/content.aspx?bookid=974. Published 2014. Accessed November 27, 2020.