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Drug Absorption

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Definition/Introduction

The study of drug absorption, distribution, metabolism, excretion, and how the body affects the drug is known pharmacokinetics. The application of pharmacokinetic methods to ensure patients are treated safely and effec known as clinical pharmacokinetics. The introduction of pharmacokinetics as a discipline has facilitated the development of rational drug therapy, the understanding of drug action and metabolism, understand of concer effect relationship, and the establishment of dosage regimens.[1]

The most important principle in pharmacokinetics theory is drug absorption which is defined as the transporta the unmetabolized drug from the site of administration to the body circulation system.[2] Several mechanisms absorption have been identified including passive diffusion, carrier-mediated membrane transport such as acti facilitated diffusion, and other nonspecific drug transporters, such as P-glycoprotein. Different factors can aff absorption, these factors can be classified as drug-specific and patient-specific factors. Therefore, the percenta drug absorption is varied among different routes of administration, such as oral, subcutaneous (SQ), transderr intravenous (IV), and intramuscular (IM). Since the oral route is the major route of administration, the major emphasis of this article will be on gastrointestinal (GI) drug absorption. The bioavailability of a drug product known as the rate and extent of its absorption. A better understanding of the drug absorption process and affe factors play an important role in achieving better bioavailability and thus better therapeutic effect.[3] This arti going to discuss the different mechanisms of drug absorption and the affecting factors; and their correlation to bioavailability.

Issues of Concern

Regardless of the absorption site, the drug must cross the cell membrane to reach the systemic circulation. Th occur primarily in one of two ways, either through passive (simple) diffusion or through carrier-mediated mer transporters.

The most common mechanism of absorption for drugs is passive diffusion. This process can be explained thro Fick law of diffusion in which the drug molecule moves according to the concentration gradient from a highe concentration to lower concentration until equilibrium is reached. Passive diffusion can occur in an aqueous c environment. Aqueous diffusion occurs in the aqueous compartment of the body, such as interstitial space or t aqueous pores in the endothelium of blood vessels. Drugs that are bound to albumin or other large plasma pro cannot permeate most aqueous pores. On the other hand, lipid diffusion occurs through the lipid compartment body. Therefore it is considered as the most important factor for drug permeability due to the greater number lipid barriers which separate the compartment of the body. The lipid-aqueous partition coefficient of the drug used to determine how rapidly the drug moves between lipid and aqueous mediums.

Another mechanism of absorption is via carrier-mediated membrane transporters. Numerous specialized carri mediated membrane transport systems are present in the body for the transportation of ions and nutrients, part

in the intestine. Such systems include active and facilitated diffusion. Active diffusion is an energy-consumin that is essential for GI absorption; and renal and biliary excretion of many drugs. This process facilitates the absorption of some lipid insoluble drugs, which mimics natural physiological metabolites such as 5-fluoroura the GI tract. In contrast to passive diffusion, active diffusion enables the movement of drugs from regions wit drug concentrations to regions with higher drug concentrations. In active diffusion, the carrier binds to form a complex with the drug. This complex facilitates the transportation of the drug across the membrane and then disassociate on the other side. The carrier molecule may be highly specific to the drug molecule. Drugs sharir similar structures can compete with each other for the carrier in absorption sites. Since there are only a small of carrier molecules available, the binding sites on the carrier may become saturated if the drug concentration high at which the dose increases do not affect the concentration of the drug. While some transporters facilitate absorption, other transporters such as P-glycoprotein (P-gp) can effectively impede drug absorption. P-gp (als as MDR1) is an energy-dependent efflux transporter that facilitates the secretion of molecules back into the in lumen, thereby restricting overall absorption. Facilitated diffusion is another transporter system that appears t minor role in terms of drug absorption. It is similar to the active diffusion system in that both are saturable, ar exhibit drug selectivity and competition kinetics. However, the main differences are that facilitated diffusion require energy, and unlike active transport does not enable the movement against a concentration gradient. An example of a facilitated diffusion system is the organic cation transporter 1 (OCT1), which facilitates the mov of some drugs such as metformin, an antidiabetic agent.[4]

Drug-specific factors that affect drug absorption include the physicochemical and the pharmaceutical variable drugs. One example of the physicochemical variables is the drug solubility and the effect of pH and pKa in w most drugs act as weak acids or bases in solutions in both ionized and non-ionized forms. The ionized drugs a hydrophilic and cannot cross the membrane of the cell. Whereas the non-ionized drugs appear to be lipophilic penetrate the cell membrane easily by simple diffusion. The distribution of weak electrolytes across membran would be a result of the pH gradient across the membrane and the drug's pKa. Weakly acidic drugs are easily in low pH medium such as the stomach. Whereas weakly basic drugs are not absorbed until they reach the hig medium in the small intestine.[5][6]

Other physicochemical variables such as particle size and surface area, dissolution rate, amorphism, and polymorphism characteristics, and nature of the dosage form will also affect systemic drug absorption. The ra dissolution is the amount of the solid substance that turns into a solution per time at standard conditions of pH composition, and temperature and, at a constant surface area. For example, cisapride, a gastroprokinetic agent low aqueous solubility. However, it has good oral bioavailability due to its rapid rate of dissolution in GI fluic particle size is inversely related to the dissolution rate. Thus, reducing particle size increases surface area and consequently, a higher dissolution rate. Micronizing of the drug particles increases the dissolution rate and so For example, digoxin is found to have 100% bioavailability in the micronized tablet. Furthermore, the interna structure of the drug can be either in a crystalline or amorphous form. Polymorph is a term in which the solid substance has more than one crystalline form. The polymorphs can vary in their physical properties such as so hardness, and melting point. For example, chloramphenicol palmitate has three polymorphic forms A, B, & C all these, form B is found to have the highest absorption and bioavailability. Pharmaceutical variables include presence of different excipients (inactive ingredients), which may increase or decrease the absorption rate dep on the added ingredient. There are several dosage forms in which the drug can be administered. Each dosage a different absorption rate depending on many factors, including the nature of the dosage form and the site of administration. Generally, for orally administered dosage forms, solutions have a higher rate of absorption. O pharmaceutical variables include drug expiration and storage condition.[5]

Patient-specific factors affecting the drug absorption (physiological variables) include age, gastric emptying t intestinal transit time, disease status, blood flow at the absorption site, pre-systemic metabolism, and GI conte With increased age, many physiological changes occur, which may lead to decreased drug absorption. Critica patients may have reduced blood flow to the GI tract, which will result in reduced drug absorption. Generally, intestinal absorption is more critical for most drugs than any other site in the GI tract due to the increased surf

of the intestinal mucosa. The duodenal mucosa has the quickest drug absorption because of such anatomical characteristics as villi and microvilli, which provide a large surface area. However, these villi are much less a in other parts of the GI tract. Drugs may be absorbed from the GI tract at a different rate. For orally administe drugs, before they reach the circulation, they can be metabolized within the gut wall or the liver. This is know first-pass metabolism, which will result in a decreased amount of active drug absorbed. Food content appears the absorption rate of many orally administered drugs. For example, the absorption rate of levodopa, an antiparkinsonian drug, is decreased when administered with protein-containing food. While the absorption of albendazole, an antiprotozoal agent, is enhanced with lipid-containing food.[7]

Clinical Significance

The benefit and toxicity of a drug are determined by its concentration in the plasma. The bioavailability plays essential role in maintaining drug plasma concentration within the therapeutic range. Since the bioavailability drug is directly dependent on the rate and extent of drug absorption at the site of administration, factors affect absorption, including the route of administration directly affect the bioavailability of that drug. For a drug wit optimal physicochemical absorption properties under normal physiological conditions, the rate and extent of absorption are directly affected by the route by which the drug is administered.

Generally, the order of bioavailability among different routes of administration ranked highest to lowest, is pa rectal, oral, and topical, respectively.[2] Drugs administered intravenously (IV) achieve 100 percent bioavaila which they can reach the systemic circulation directly without the absorption process. IV drugs are usually administered when a rapid onset of response is required, such as in emergency cases. Other situations where I are required include patients who are unconsciousness, those who have a non-functional GI tract, when there unavailability of oral the form, or when there is a need for tissue penetration that is not achievable by oral the [8] Although the bioavailability of orally administered drugs is complex and variable depending on the factor affecting the absorption process, it is more convenient for many patients, and it is the most common route of administration used for most drugs.[9] Bioavailability and pharmacokinetic studies are aimed to identify a sui dosage regimen for a new drug candidate to ensure its therapeutic effectiveness and safety, to identify new formulations of the existing drugs, compare the bioavailability for a drug with different dosage forms or the s dosage form of a different manufacturer, and to control the quality of a drug product during the early stages o marketing by the determination of the effect of different physicochemical and physiological factors on absorp

Absolute bioavailability is a test in which the bioavailability of an orally administered drug is determined in comparison to its IV administration. It is useful in the identification of the absorption characteristics of a drug administered orally. Another type of bioavailability test is called relative bioavailability in which the bioavail an orally administered drug is compared with that of an oral standard of the same drug. It is also known as comparative bioavailability. In contrast to absolute bioavailability, it is used to identify the absorption charact of a drug from different formulations. Bioequivalence studies are conducted to differentiate between two drug products having the same active ingredients. It is useful in the comparison between a brand and generic formu [10]

Drug absorption and bioavailability are essential aspects of pharmacokinetics. They influence drug effectiven safety. They can also affect the onset, intensity, and sometimes the duration of action. Many factors can affect absorption and bioavailability of drugs; some of them are drug-specific while the others are patient-specific. Bioavailability and pharmacokinetic studies aim to optimize drug use by maintaining the drug concentration the therapeutic range.

Nursing, Allied Health, and Interprofessional Team Interventions

Medication management requires an interprofessional team of healthcare professionals that includes a nurse, laboratory technologists, pharmacists, and physicians. Without proper medication management, the morbidity

mortality from various health conditions can be high. An adequate understanding of drug absorption can facil interprofessional collaborations to improve patient health outcomes.

Continuing Education / Review Questions

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