Introduction to Pharmacokinetics

Abstract

Pharmacology is an area many nurse prescribers tell me that they worry about. This is whether they are prescribing students or qualified prescribers. They are very aware of the importance of pharmacological knowledge and its impact on safe prescribing. They typically want to know how much information they need to know and what depth and breadth that information should take. Another area they worry about is how many drugs they need to be familiar with? This series of pharmacology articles will explore some concepts in pharmacology to support the prescriber in developing that knowledge. This article begins by examining the basic concepts of pharmacokinetics to allow the reader to improve their understanding of drug handling within the body. It will explore the processes of absorption, distribution, metabolism and excretion to chart a drugs 'route' from administration to elimination.

Welcome to the first in a series of 'bite-sized' pharmacology articles. We are going to begin with some of the basic concepts of pharmacology.

Pharmacology is the study of drugs (chemicals) and their interactions with the body.

The word pharmacology comes from the Greek word *pharmakon* which can mean both remedy and poison. There are two ways we can study the interactions of drugs with the body, those being pharmacokinetics and pharmacodynamics.

Pharmacokinetics can be defined in its simplest terms as the effect that the body has on the drugs. It can also be referred to as drug handling. Pharmacokinetics can be broken down into four processes and are known by the acronym ADME.

A- Absorption of the drug
D- Distribution of the drug molecules

M- Metabolism of the parent drug
E- Excretion or Elimination of the drug and its metabolites

These pharmacokinetic processes can only occur after drug administration by the chosen route.

Absorption of Drugs

Before a drug can begin to exert any effect on the body it has to be absorbed into the body systems. This absorption process can be affected by many things but the main factor relating to absorption is the route of administration. All routes of drug administration require the drug to be absorbed from the administration site with one exception. The main purpose of the absorption step is to get the drug into the blood stream for distribution. The giving of a drug intravenously (I.V.) means that the drug is delivered into the blood stream and the absorption step is bypassed.

Some routes of administration of drugs can allow for faster onset of action. This is almost always due to an accelerated absorption. It is important for a nurse prescriber to be aware this so that choice of route of administration for drugs can be considered as part of the prescribing process.

Factors that affect the rate and reliability of drug absorption can be can be categorised as physiological or physico-chemical.

Physiological Factors;

- Blood flow to absorbing site

  A good blood flow will allow for good and reliable absorption. For example, the blood flow to the upper gastrointestinal tract (the site of absorption for orally administered medication) is extremely good in a healthy individual, making oral administration a good choice from the perspective of blood flow.

- Total surface area for absorption

A larger surface area will increase the rate and reliability of absorption. For example, the alveoli of the lungs are tightly bundled to give a large surface area within the chest. This makes it a very good site for drug absorption

- Time of arrival and contact time at absorption site.

  The quicker a drug arrives at and the longer it remains at its absorbing site, the better the absorption of the drug will be. Intramuscular injections of drugs are delivered straight to the absorbing site and remain there until absorbed, making this a good route of administration

Physico-chemical Factors;

- Solubility- a drug that is soluble in body fluids will be more rapidly absorbed than those that do not go into solution easily
- Chemical stability- a more chemically stable drug will take longer to be absorbed than one that breaks down readily into its constituent parts, for example, on contact with gastric acid
- Lipid to water partition coefficient- is it more fat soluble than water soluble. Drugs need to be water soluble to be absorbed into the blood stream but also need to have a degree of lipid solubility to cross cell membranes
- Degree of ionisation- the chemical charge of a drug (positive or negative) can affect its rate of absorption dependant on the charge of the site of absorption.

EXERCISE

Choose a drug from your area of practice and identify the routes of administration for the drug. Using a pharmacology text or online resources (such as the Electronic Medicines Compendium) find out the absorption properties of the drug by each route.

Distribution of Drugs

After administered and absorption, drugs are distributed to their site of action. For some drugs that site is known and drugs are available to give locally or topically. For systemically acting drugs, they need to be distributed within the blood stream, to the cells and/or tissues where they can have their effect.

How does this happen?

Distribution occurs firstly into body fluids. These are plasma, extracellular fluid and intracellular fluid. The drug molecules are then taken up into body tissues/organs. Specific tissues take up some drugs, e.g. iodine and thyroid gland, but most drugs will be taken up by all tissues and act at their sites within.

These processes can be affected by the extent of plasma protein binding. Plasma proteins such as albumin bind drug molecules. Drugs bound to plasma proteins are pharmacologically inert, only drugs 'free' in the plasma are active.

Drugs often have to pass through physiological barriers. The 2 main examples are the placenta and the blood brain barrier (BBB). Drugs must be highly lipid soluble to pass across these barriers. If not, they may not be able to reach their site of action.

The factors which affect drug distribution are taken into consideration by drug companies when developing and formulating medications.

The drug has now reached its site of action and is having its effect on the body. The body however continues to act on the drug in the following ways.

EXERCISE

Choose a drug from your area of practice and identify the extent of plasma protein binding of the drug. Using a pharmacology text or online resources (such as the Electronic Medicines Compendium) to find out how well the drug is distributed.

Metabolism

This is the process of metabolising the parent drug compound and occurs mainly in the liver (also known as biotransformation) to different compounds called metabolites. There are many routes of metabolism but they fall into two phases within the live (see table). The molecules are altered by chemical processes into metabolites The drug metabolite may have a decreased or increased pharmacological activity. It may also have a different activity. Some drugs are what are termed **pro-drugs** where the parent drug is inactive *until* it is metabolised by the liver, a good example is codeine, which is metabolised to the active form morphine by the body. The metabolite is made more polar (chemically charged), than the parent drug and this allows for easier excretion by the kidney. Drug metabolism can influence dose and frequency of dosing.

Hepatic Metabolism

Phase	Process
Phase I metabolism	oxidation
	reduction
	hydrolysis
Phase II metabolism	conjugation

Box 1- These terms are different chemical reactions to change the properties of the drugs to facilitate their removal from the body by excretion. Most drugs undergo phase I oxidation followed by phase II conjugation.

EXERCISE

Choose a drug from your area of practice and identify the metabolic process for the drug. Using a pharmacology text or online resources (such as the Electronic Medicines Compendium).

Excretion of Drugs

Once drugs have been metabolised by the liver, they are excreted from the body. The main route of drug excretion is by renal elimination and clearance. As previously outlined, some drug metabolites are also active. If these, and any remaining parent drug were not eliminated, they would accumulate in the body and could cause toxic and unwanted effects.

Renal elimination starts with active glomerular filtration. This is where ionised drugs are actively secreted to the proximal tubule of the nephron, the functional unit of the kidney. These are recognised by the kidney as ready to be excreted and are "pushed" out into the forming urine. A more passive form of drug movement occurs in the distal tubule of the nephron. Here there is passive movement of drugs molecules and metabolites according to a concentration gradient. This applies to unionised compounds and prevents the entire dose of a drug being excreted at once. allows drug effect to continue between doses.

EXERCISE

Choose a drug from your area of practice and identify the extent of renal elimination of the drug. Using a pharmacology text or online resources (such as the Electronic Medicines Compendium).

This has been a brief introduction to the concepts in pharmacokinetic handling of a drug. In future articles in this series we will explore aspects of pharmacokinetics in more detail before moving on to pharmacodynamic actions.

Further Reading

https://www.medicines.org.uk/emc/

Barber and Robertson (2015) *Essentials of Pharmacology for Nurses* 3rd Edition McGraw Hill London