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Medi Quest BRS Hospital

A monthly News letter from BRS Hospital

Pharmacokinetics and Pharmacodynamics for the Practitioner

Part 1 - Pharmacokinetics

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In order to prescribe rationally a knowledge of the Pharmacokinetics and the Pharmacodynamics of the drug is essential

Pharmacokinetics

1. What is pharmacokinetics ?
Pharmacokinetics is what the body does to the drug. It refers to movement of drug into the body , through the body and out of it.

The major processes involved in pharmacokinetics are absorption, distribution, metabolism and excretion also known by the acronym ADME.

2. What is absorption of drugs ?
Absorption is the transfer of drug from its site of administration (we refer to the GI tract) to the blood stream. However this process is bypassed when a drug is injected IV

3.What are the methods of transport of drug from GI tract ?

1) Passive diffusion Most drugs are absorbed by passive diffusion obeying the Fick's Law of diffusion. Passive diffusion is by lipid diffusion and or aqueous diffusion

Lipid diffusion is a process by which the drug dissolves in the lipid components of the cell membranes. This process is facilitated by a high degree of lipid solubility of the drug. Aqueous diffusion occurs by passage through aqueous pores in cell membranes. Because aqueous diffusion is restricted to drugs with low molecular weights, many drugs are too large to be absorbed by this process.

2) Active transport

3) Pinocytosis

4.What is another important factor one should remember in the absorbtion of drugs ?

Many drugs are weak acids or bases that exist in both ionized and nonionized forms in the body. Only the nonionized form of these drugs is sufficiently soluble in membrane lipids to cross cell membranes

Need to know: Ideally a drug should be lipid soluble , nonionized , hydrophobic and yet have the capacity to penetrate aqueous pores to favour maximum absorbtion

5.Where does drug absorption takes place ?

Drug absorption takes place predominantly in the small intestine because of a larger surface area, more permeable membranes and better blood supply.

6. What is the role of gastric emptying time in drug absorption ?

As drugs are poorly absorbed in the stomach , gastric emptying time becomes the rate limiting step in absorption.
If gastric emptying time is rapid as in a fasting state the rate of absorption is speeded up , conversely fatty food slows gastric emptying and the rate of absorption.

7. Why should oral Penicillin be given in an empty stomach or in between meals ?

Oral Penicillin G (Pentids) is degraded by gastric enzymes hence it is given on an empty stomach . On the other hand Oral Penicillin V (Kaypen) is more stable in the presence of gastric enzymes , although it may be taken with meals , higher serum levels are achieved if it is taken on an empty stomach.

8. What is bioavailability ?

Bioavailability is expressed a fraction of the administered drug that reaches systemic circulation in a chemically unchanged form (used in reference to drugs administered other than IV route ,when a drug is administered IV the bioavailability is 100%).

For example , if 100 mg of a drug is administered orally and 70 mg of this drug reaches systemic circulation unchanged , the bio availability is 70 %

9. What is first pass hepatic metabolism ?

When a drug is absorbed across the G1 tract it enters portal circulation before it enters systemic circulation. If the drug is rapidly metabolized by liver, the amount of unchanged drug that gain access to the systemic circulation is decreased i e the bioavailability is decreased. Drugs like propranolol or lidocaine undergo significant biotransformation during a single passage through the liver.

What it means – For eg. There is a wide variation in the IV and oral dose of Propranolol.

The oral dose of Propranolol is 1 mg/kg whereas iv dose 0.1 mg /kg

10.What is drug distribution?
Drug distribution is the process by which a drug reversibly leaves the plasma and enters the extra vascular space which is interstitial space or intra cellular space

11. What are the factors which influence distribution ?
1) Blood flow
2) Capillary permeability
3) Drug structure
4) Binding of drug to protein

12. What is the volume of distribution of a drug (Vd) ?

The volume of distribution is a hypothetical volume of into which the drug is disseminating

13. What are the body water compartments the drug can distribute in

Drugs can distribute plasma, interstitium and intra cellular fluids.
A drug that has a low molecular weight and is hydrophobic can distribute across all body water compartment which constitutes about 60% of body weight
The volume of distribution is given by the formula

$$\frac{\text{Total concentration of drug in the body}}{\text{Concentration of drug in plasma}}$$

14. What is the significance of Volume of distribution ?

a. It helps you to calculate the loading dose

b. Higher the volume of distribution , greater the half life of a drug.

15. What do M & E stand in acronym ADME (which represents Pharmacokinetics)

M stands for metabolism and E for excretion of the drug. Both together account for the elimination of the drug. Note : Metabolism and elimination are used interchangeably . Metabolism or biotransformation per se is the enzymatic process by which a drug is altered , but the process of metabolism is the first step in the elimination of drug from the body.

16. What is drug Metabolism ?
Drugs are eliminated or inactivated by biotransformation / metabolism. Liver is the major site of biotransformation.

17. What are the 2 important terminologies you should know in drug elimination ?

a) First order kinetics: Here the rate of drug elimination is directly proportional to the concentration of free drug. This means a constant fraction of drug is eliminated per unit time
b) ie the amount eliminated is proportional to the amount available to be eliminated.
c) Stated another way greater the drug concentration, the greater the amount cleared per unit time

Most drugs follow first order kinetics and half life of a drug is calculated based on first order kinetics (refer below)

d) Zero order kinetics :
With a few drugs like Asprin, Eptoin and alcohol, a constant amount of drug is eliminated / unit time

(Readers are advised to watch you tube tutorials by Dr.Areo Saffar Zadeh for a clear explanation on this topic)

18.What do you mean by half life of a drug ?
The half-life is the time required for the plasma drug concentration to decrease by 50% by the process of elimination.

For example if plasma concentration of a drug is 100 mg/l , then at the end of one half life T1/2 the plasma concentration will be 50mg/l , and the end of two half lifes. It would be 25mg/l , at the end of 3 half lives it would be 12.5mg/l and at the end of 4 half lives it would be 6.25mg/l and at the end of 5 half lives it would be 3.125 mg/l ie at the end of 5 half lives nearly 97 % percent of the drug is eliminated.
Note: 5 half lives are required for most of the drug to be eliminated

19.In what way is the half life of a drug influence prescribing practices ?

An important use of half-life information is in chronic drug use where doses are repeated prior to the complete disappearance of the previous dose. Drug dosing in this manner leads to accumulation of the drug, meaning that the maximum concentration of the drug does not occur until the amount administered and the amount eliminated are equal. Knowing the time it will take to reach this maximum concentration plateau (also known as steady state concentration) and the expected fluctuations in drug concentration between doses (and about that plateau) is of considerable utility to the physician bent on rationally using drugs.

To be Continued in next Issue

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