Pharmacology

Lecture 3

Zeenah Frihat
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Passion Batch

Pharmacokinetics start from first step which is absorption.

Absorption is the first limiting step of all Pharmacokinetics and the most important in determining the action and the final action of the drug. The most important factor here is the bioavailability

The amount of drug absorbed on or in or over the amount of drug administered is bioavailability

Route of administration, what they varies in (difference in) is onset of action which depends on absorption

-no absorption = no action

When you give a patient 2 drugs, one can inhibit the other and cause to fail the treatment (treatment failure)

When we give tetracycline or iron tablets with milk this is zero absorption (NO ACTION)

Bioavailability referred by "F"

F=1 for IV (means all the drug is in your blood stream) absorption=100%

F= the fraction of drug absorbed per /drug administered

If absorbed 80 of drug in blood str am / 100 mg dministered, so bioavailability is 80% or other wa is 0 .

Bioavailability is tested for each drug, so how they can know it's value for each drug?

1) F = 1 for IV, so they administered the drug by IV and found the concentration in the plasma .

2) They administered the drug by orally and the find conc. In the plasma,

3) Then divide the conc. of the plasma by oral on the plasma conc. of the IV and find the percentage

Absorption: is transferring of drug from site of administration to blood stream.

It means if you took it orally the site of absorption will be mostly stomach and intestine, which is better? The intestine

We have 4 types of absorption, can be for drugs:

1)Passive diffusion of irons and minerals (from higher concentration to lower conc.) so when patient take the medication. He doesn't need anything, any energy or carriers. So it's done very easy

2)Carriers if the drug is high molecular weight so it need carrier (carry it from lumen of GIT to blood stream), still no need for energy,

ex: degoxin

3)Active diffusion which needs energy and carrier, against conc. gradient (from low conc. to high conc.), why?

First it will be absorbed inside , so inside will have more drug than outside so first few particles can be absorbed but by the time they build up conc. in blood stream the cant continue…

so how they can continue absorbed ?

- They'll need energy &carriers (that's why most drugs are absorbed by this interaction)

Drugs are mostly weak acids , small group of drugs is weak base so because they are transported by same channel and same carriers that are competitors

(when you give 2 drugs they will compete, and one will transfer and the other can't be absorbed) this way of drug-drug interaction and absorption level

2 drugs (A+B) = A inhibits absorption of B so A will act, B none

4)Endocytosis and exocytosis we use them a lot especially in nerves, neurotransmitters, hormones (hormonal glands) some of drugs done by this.

A lot of our body analog are drugs (drugs like ones what in our body) for example epinephrine is a drug and also secreted by exocytosis and taken to cell by endocytosis

This happen for highly large molecular weight (they can't be absorbed by plasma membrane)

Plasma membrane is lipophilic but we have in between the protein in the plasma membrane some hydrophilic.

the perfect drug absorbed easily : high lipophilic (not very very lipophilic) with low hydrophilic

"like dissolves like" polar dissolve polar , non polar like non polar , acid absorbs acids , bases absorb basic

$HA \leftrightarrow H^+ + A^-$

HA is a weak acid , consider it a drug , which one will be absorbed more ? HA or A-

HA is non ionized (lipophilic) but ions are hydrophilic (dissolve easily in water), so HA will be absorbed in plasma membrane , BUT A- will be more in urine .

The role : any drug like to be non ionized like to be absorbed but ionized to be secreted

Ka = [A-] [H+] / HA (equilibrium equation)

Low pH means high [H+] so it will transfer to right (more HA)

So HA stays HA when the media is acidic

When we say acidic like acidic this mean for example we give aspirin which is acidic (like HA)
it will be absorbed in your stomach because of low pH but in intestine it will be less absorbed because pH = 5.5 (less acidic)

Conclusion :Your stomach(pH) is a good area for absorption of acidic drug

if you give basic drug it need high pH to be absorbed so it will be more absorbed in intestine

في ادوية في حال اعطيناها مع مضاد الحموضة رح يقلل امتصاصها

Ex: aspirin with famodar (both anti acidic) , famodar will increase the pH so the aspirin will not be absorbed (because it need low pH) and won't do the action

Ex: ketoconazole (anti fungus) is a basic drug will be absorbed most in intestine

Other factors for absorption: intestine has 2 factors , more surface area(1000 fold more than stomach) and more blood flow

Notes:

- GIT lining has more blood flow than muscle lining
- intestine has more blood flow than stomach
- More blood supply capillaries = absorbs more

If the patient have diarrhea, it increases GIT motility (peristalsis),and the absorption will not happen and the drug will go to large intestine because there is no contact time for the drug to be absorbed and build up conc.

(diarrhea = no contact time = no absorption)

If a patient took 2 tablet of panadol and need fast onset of action he can take anti vomiting like clobram which decreases the peristalsis of the intestine (relax the intestine) so it will help the paracetamol reach the contact time . we use drug-drug interaction to make more therapeutic effect

Drug-drug interaction is not always wrong or not used or bad ,sometimes we use it to make *synergism*

Synergism mean 1 + 1 = 4 it means , we give 2 drugs and the effect will be more than the total of both .

p-glycoprotein eliminate the drug from blood stream (exporting drugs out of the cell) so it work against absorption, found in liver and kidney

for example the placenta to carry the fetus (for maternal blood supply) it export the drug out of the fetus by p-glycoprotein .

We have drugs to inhibits p-glycoprotien in intestine to improve absorption.

Bioavailability

No bioavailability = no absorption

Factors that influence bioavalability :

-first pass hepatic metabolism

After the drug inters blood stream(after absorption) it goes to hepatic circulation or portal circulation it goes directley to the liver without distribution to other organs , and metabolism occurs which mean it change it from active to non active or from polar to non polar or ionize the non ionization, finally it has 2 ways either secreted to bile or secreted by kidney

-Other factors on bioavalability is solubility of drug mean if should be ionized or non ionized ,we have to moderate what our ion hydrophilicity with moderate lipophilicity

-Chemical instability (before absorption) if the drug is unstable in your stomach it will not be absorbed

The drug is a chemical structure , if you destroyed this chemical structure(like breaking cycle form) it will affect absorption and bioavailability like : insulin(destroyed by enzymes because it is a protein), penicillin G (unstable because of pH , destroyed because of acidic) , heparin

Smaller particle size easily absorbed. higher particle size less absorbed (we can solve this problem by *interic coated* is a form of dosage form to decrese the effect of pH on the tablet for ex we want the drug to be absorbed in certain areas) like to open in intestine NOT stomach

Still couldn't find a way for enzymes , only pH

So drug formation, molecular weight aslo affect bioavailability and absorption

Ex : drug formed as specific powder will be absorbed readily

Also high amount of binders = no disintegration = absorption

***If 2 drug have the same bioavailability are they therapeutic(bio) equivalence?**

No because there is other factors like dynamics

Ex : famotidin and ranitidine (anti acidic) both are same bioavailability BUT not bio equivalent on the same dose , that's why we find famotidin the pill is 20 mg and the ranitidine 150 mg

The factor here is potency

GOODLUCK