17/MHS06/049

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Bch 313: Medical biochemistry IV

1. Discuss in details the factors affecting drug metabolism

Factors affecting drug metabolism include both the internal factors and the external factors. The internal factors include:

1. Disease
2. Age
3. Sex
4. Specie
5. Hormones
6. Genetics

a. Disease- there are many diseases that affect the metabolism of drugs. Some of which include alcohol liver disease, cirrhosis of the liver , jaundice, diabetes mellitus, malaria, acromegaly and various bacterial and viral diseases. It is see that the major disease affects a scene in the liver and the liver is qualitatively the most important side for me to follow them. Some of the possible causes in the effect Of metabolism due to diseases may be:

-altered hepatic flow

-decrease in some activity in the liver

-Hypoalbuminaemia (leading to lower plasma binding of the drugs).

b. Age- drug metabolism rate in different age groups to family due to variations in the enzyme content in some activity and the haemodynamics. and the development of systems in general.

- In elderly persons there is a reduction in liver size, the microtonal enzyme activity is decreased and hepatic blood flow also declines as a result of reduced cardiac output, all of which contributes to decreased metabolism of drugs.

- Between the ages 6-12- metabolism of drugs or cause more rapidly as the rates of metabolism which is a maximum summer between six months and 12 years of age they require large doses of drugs

- In infants: do you do on the development of systems especially the enzyme system drug metabolism is really slow.

c. Sex- this is largely due to the difference of sex hormones presents in both males and females. Such as observed in rats where it is seen that male rats metabolize drugs faster than female rats. In humans, it is said that women metabolize benzodiazepines slower than men. On average, men are larger than women. Body size differences results in larger distribution volumes and faster total clearance of most medications in men compared to women. Greater body fat in women (until older ages) may increase distribution volumes for lipophilic drugs in women. Total drug absorption does not appear to be significantly affected by sex although absorption rates may be slightly slower in women..

d. Species- both qualitative and quantitative variations in the enzyme and the activity contributes to the difference in drug metabolism and different species. Qualitative differences generally results from the presence or absence or specific enzymes in those species. Quantitative differences result from variations in the months and localization of enzymes in the amount of natural inhibitors is a competition of enzymes for substrates ( for specific substrates). The human liver contains less cytochrome p-450 per gram of tissue then do the liver of some other species.

e. Hormones- The presence of some species either increase or decrease the rate of metabolism that is to say higher level of some hormones may inhibit the activity of CU enzymes were inducing the activity of others. It’s typical example is seen in the pituitary growth hormone and stress related changes in ACTH levels ( adrenocorticotropin hormone)

F. Genetics- Due to the different genetic makeup of every human being, there is a rapidly expanding list of genetic variants that affect the function of drug metabolizing enzymes and lead to altered drug responses. With this, it is possible to see why on identical exposure, certain individuals tend to fall sick while some others do not. Genetic factors can account for 20 to 95 percent of patient variability and because of their genetic makeup, some people metabolize) drugs slowly. As a result, a drug may accumulate in the body, causing toxicity. Other people metabolize drugs so quickly that after they take a usual dose, drug levels in the blood never become high enough for the drug to be effective.

External factors

1. Diet
2. Economy
3. Environment

Diet- in human beings, the enzyme content, site and activity is altered by a number of dietary components. Generally

* Low protein diet decreases the drug metabolism while high protein diets increases drug metabolizing activity as enzyme synthesis is promoted by protein diet and also in addition, raises the amount of amino acids for conjugation with drugs.
* Dietary deficiencies of vitamins such as vitamin A, B2, B3, C, E and of minerals such as Fe, Ca, Mg, Zn retards the metabolic activity of enzymes.
* Fat free diet depresses cytochrome P-450 levels since phospholipids which are important components of microsomes become more deficient
* Starvation results in decreased amount of glucuronides formed under normal conditions. .