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Course:

ASSIGNMENT

Write on the factors affect drug metabolism

Factors that affect drug metabolism include:

1. Chemical factors
 - a. Enzyme induction
 - b. Enzyme inhibition
 - c. Environmental chemicals
2. Biological factors
 - a. Age
 - b. Diet
 - c. Sex difference
 - d. Specie difference
 - e. Strain difference

BIOLOGICAL FACTORS

a. AGE: the drug metabolic rate in different age group differs mainly due to variations in the enzyme content, enzyme activity and aerodynamics.

In neonates(upto 2 months) and in infants(months to 1 year), the microsomal enzyme system is not fully developed. So many drugs metabolize slowly. For example, caffeine has a half life of 4 days in neonates in comparison to 4hours in adult.

Children(between 1year and 12 years) metabolize several drugs much more rapidly than adults as the rate of metabolism reaches a maximum somewhere between 6months and 12 years.

In elderly persons, the liver size is reduced, microsomal enzyme activity is decreased and hepatic blood flow also declines as a results of reduced cardiac output, all of which contributes to decreased

metabolism of drugs. For example, chlorthalidone allows a high bioavailability within the elderly therefore they are required in a lower dose.

b. DIET: the enzyme content and activity is altered by a number of dietary components. Generally;

Low protein diet decreases and high protein diet increases drug metabolizing ability as enzyme synthesis is promoted by protein diet and also raises the level of amino acids for conjugation of drug.

Fat free diet depresses cytochrome p450 levels since phospholipids which are important components of microsomes becomes deficient.

Dietary deficiency of vitamins like vitamin A, B2, B3, C and E and minerals such as Fe, Ca, Mg, Zn retard the metabolic activity of enzymes.

Starvation results in decreased amounts of glucuronides formed than under normal conditions.

c. SEX DIFFERENCE: since variations between Male and female are observed following puberty. So sex differences in rate of metabolism may be due to sex hormones. It has been studied that Male rats have greater metabolizing capacity. In humans, women metabolize benzodiazepines slowly than men. Several studies have shown that women on contraceptive pills metabolize a number of drug at slow rate.

d. SPECIE DIFFERENCE: have been observed in both phase 1 and phase2 reactions. In phase 1 reaction both qualitative and quantitative variations in enzyme and their activity have been observed. Qualitative differences result from variations in the amount and localisation of enzymes, the amount of natural inhibitors and the competition of enzymes for a specific substrate.

CHEMICAL FACTORS

ENZYME INDUCTION

The phenomenon of increased drug destabilizing ability of enzymes by several drugs and chemicals is called enzyme induction and the agents which bring about such effects are called enzyme indicators.

Mechanisms of enzymes induction are:

increase in both liver size and liver blood flow

Increase in both total and microsomal proteins content

Increased stability of enzymes

Increased stability of cytochrome p450

Decreased degradation of cytochrome p450

Consequences of enzyme induction include:

1. Decrease in pharmacology activity of drugs

2. Altered physiological status due to enhanced metabolism of endogenous compounds such as sex hormones.

ENZYME INHIBITION

A decrease in drug metabolizing activity of an enzyme is called enzyme inhibition. The process of inhibition may be direct or indirect process.

A. Direct inhibition; it may result interaction at the enzyme site, the next outcome being a change in enzyme activity.

ENVIRONMENTAL CHEMICALS: several environmental agents influence the drug metabolizing ability of enzymes, for example; halogenated pesticides such as DDT and polycyclic aromatic hydrocarbons contained in cigarette smoke have induction effects.