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Assignment

Discuss the factors affecting drug metabolism.

Answer

DRUG METABOLISM

This is the metabolic breakdown of drugs by living organism, usually through specialized enzymatic systems. There are various ways physiological and pathological factors that affect drug metabolism.

1. Physiological/Biological Factors

   These factors include;

   a) AGE

   The drug metabolic rate in the different age groups differs due to variation in the enzyme content, enzyme activity and haemodynamics.

   - In neonates (up to 2months) and infants (2months to 1yr), the microsomal enzyme system is not fully developed so many drugs metabolize slowly. For example, caffeine has a half life of 4days in neonates in comparison to 4hrs in adults.
   - Children (1yr to 12yrs) metabolize several drugs much more rapidly than adults as the rate of metabolism reaches a maximum somewhere between 6months and 12yrs. As a result they require large mg/kg dose in comparison to adults.

- In elderly persons, the liver size is reduced, microsomal 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. For example, chlomethiazole shows a high bioavailabity within the elderly, therefore they require a lower dose.

b) DIET/NUTRITION

The enzyme content and activity is altered by a number of dietary components. Generally,

- Low protein diet decreases and high protein diet increases the drug metabolizing ability enzyme synthesis is promoted by protein diet and also raises the level of amino acids conjugation with drugs.
- Fat free diet depresses cytochrome P-450 levels since phospholipids, which are important components of microsomes become deficient.
- Grapefruit inhibits metabolism of many drugs and improve their oral bioavailability.
- Dietary deficiency of vitamins like vitamin A, B_2, B_3, C and E and minerals such as Fe, Ca, Mg, and Zn retard the metabolic activity of enzymes.
- Starvation results in decreased amount of glucoronides formed than normal conditions.

c) SEX DIFFERENCE

Sex related differences in the rate of diffusion maybe as a result of sex hormones. Women metabolize benzodiazepines slowly than men. Several studies have shown that women on contraceptive pills metabolize a number of drugs at a slow rate.

d) STRAIN DIFFERENCE

The differences are observed between strains of same species, it may be studied under two headings;

- Pharmacogenetics; a study of inter-subject variability in drugs response is called pharmacogentics. The inter-subject variations in metabolism may either be monogenetically or polygenetically controlled. A polygenetic control is observed in twins. In identical twins (monozygotic), very little or no difference in metabolism of halothane, phenylbutazone, dicoumaral and antipyrine was detected but large variations were observed in fraternal twins (dizygotic).
- Ethnic Variations; differences observed in the metabolism of drug among different races are called Ethnic Variations. Such variations may be monomorphic or polymorphic. Example; approximately equal percent of slow and rapid acetylators are found among whites and blacks whereas the slow acetylators dominate Japanese and Eskimo population.

e) ALTERED PHYSIOLOGICAL FACTORS

- Pregnancy; affects hepatic drug metabolism and this may be due to the physiological changes during pregnancy. These include elevated concentration of various hormones such as estrogen, progesterone, placental growth hormones and prolactin.
- Disease State; some of these diseases are cirrhosis of liver, alcoholic liver disease, cholestatic jaundice. Other factors responsible for variation in drug metabolism are the endocrine disorders, such as diabetes mellitus, hypo and hyperthyroidism, pituitary disorders and various types of infections (bacterial, viral, malaria).

2. Environmental Factors

These are usually considered to be those influences in our surroundings that can affect drug metabolism. These environmental factors include a large number of environmental chemicals that potentially could affect drug biotransformation, usually grouped into heavy metals, industrial pollutants and pesticides.

The most important industrial pollutants are typically aromatic or aromatic polycyclic compound and poly chlorinated biphenyls and they have various effects like inductive enzyme effects, procarcinogenic effects, etc.

Pesticides are also of various types (insecticides, herbicides,) and are considered environmental contaminants in air, soil, water and food.