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1) Discuss in the details the factors affecting drug metabolism

Answer

A number of factors may influence the metabolic rate of a drug. Some of them are:

1) Chemical factors

a) Enzyme induction

b) Enzyme inhibition

c) Environmentalchemicals

2) Biological factors

a) Age

b) Diet

c) Sex diffefence

d) Species difference

e) Strain difference

f) Altered physiological factor

3) Physiochemical properties of the drug

CHEMICAL FACTORS

1) Enzymem induction: The phenomenom of increased drug metabolism ability of enzymes by several drugs and chemicals is called enzyme induction and the agents which bring about such an effect are called enzyme inducers.

Mechanisms of enzyme induction:

a) Increase inn both liver size and liver blood flow

b) Increase in both total and microsomal protein content

c) Increased stability of enzymes

d) Increased stability of cytochrome P-450

e) Proliferation of smooth endoplasmic reticulum

BIOLOGICAL FACTORS

1) Age: The drug metabollic rate in the different age groups differs mainly due to variation in the enzyme content, enzyme activity and haemodynamics

\* In neonates(upto 2 months) and infants (2 months to 1 year) the microsomal enzyme system is not fully developed. So many drugs are metabolized slowly. For e.g. Caffeine has a half life of 4 days in neonate in comparison to 4hrs in adults

\* Children (between 1 year and 12 years) metabolize several drugs much more rapidly than adults as the rate of metabolism reaches a maximum somewhere between 6 months and 12 years. As a result they require large mg/kg dose in comparison to adults

\* In elderly persons, the liver size is reduced, the microsomal 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. For example, chlomethaziole shows a high bioavailability within the elderly, therefore they require a lower dose.

2) Diet: 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 as enzyme synthesis is promoted by protein diet and also raise the amino acids for conjugation with drugs.

\* Fat free diet depresses cytochrome P-450 levels since phospholipids, which are important components of microsomes become deficient.

\* Grapeful inhibits metabolism of many drugs and improve their oral bioavailability.

\* 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 amount of glucuronides formed than under normal conditions

3) Sex difference: Since variations between male and female are observed following puberty. So , sex related difference in the rate of metabolism may be due to sex hormones. Such sex differences are widely studied in rats where male rats have greater drug metabolizing capacity. In humans, women metabolize benzodiazepines slowly than men. Several studies have shown that women on contraceptive pills metabolize a number of drugs at a slow rate.