MARTHA MOLKALE GAJERE

17/MHS01/134

MEDICINE AND HEALTH SCIENCES.

300 LEVEL

BIOCHEMISTY ASSIGNMENT

XENOBIOTICS ASSIGNMENT

QUESTION

Discuss in details the factors affecting drug metabolism.

ANSWERS

1. Sex: men have faster metabolism than women. This is due to sex hormones.
2. Age: in general, drugs are slowly metabolized in fetal, neonatal and elderly persons than in adults. As you grow older, metabolism slows down usually due to changes of hormonal and neurological processes.

In neonates and infants, the microsomal enzyme is no fully developed many drugs are metabolized slowly.

As they grow, higher doses are required till adulthood. But in elderly persons, the liver is reduced and also hepatic flow, therefore lower doses are required.

1. Body size: those with greater body mass have a larger body metabolic rate because they
2. Genetic variation: with N-acetyltransferases, individual variation creates a group of people who acetylate quickly, split roughly 50:50 in some populations. Slow acetylators are more prone to dose dependent toxicity.
3. Enzyme induction: phenomenon of increased drug metabolizing enzymes by several agents called enzyme inducers.

Mechanism of enzyme inducers include: increase in both liver size and liver blood flow, increase in both total and microsomal protein content, increased stability of cytochrome P-450, increased stability of enzymes, decreased degradation of cytochrome P-450, proliferation of smooth endoplasmic reticulum.

Consequences of enzyme induction include: decrease in pharmacological activity of drugs, increased activity where the metabolites are active, altered physiological status due to enhanced metabolism of endogenous compounds such as sex hormones.

1. Pathological factors: liver, kidney and heart diseases may influence drug metabolism.
2. Environmental chemicals: several environmental agents influence drug metabolizing ability of enzymes. Halogenated pesticides such as DDT and polycyclic aromatic hydrocarbons contained in cigarette smoke have enzyme induction effect. Organophosphate insecticides and heavy metals such as mercury, nickel, cobalt and arsenic inhibit drug metabolizing ability of enzymes. Other environmental factors that affect drug metabolism include temperature, pressure, altitude, atmosphere, etc.
3. Enzyme inhibition: decrease in drug metabolism of an enzyme is called enzyme inhibition. It may be direct or indirect.
4. Direct inhibition: may result from interaction of enzyme at a site an there would be a change in enzyme activity.
5. Competitive inhibition: occurs when structurally similar compounds compete in the same site on an enzyme.
6. Non-competitive inhibition: occurs when a structurally unrelated agent interacts with the enzyme and prevents the metabolism of drugs.
7. Product inhibition: occurs when the metabolic products competes with the substrate for the same enzyme.
8. Indirect inhibition: it is caused by either of the following;
9. Repression: It may be due to the fall in the rate of enzyme synthesis or rise in the rate of enzyme degradation.
10. Altered physiology: it may be due to nutritional deficiency or hormonal imbalance.
11. Dose, frequency, route of administration of a drug may affect metabolism.
12. Ethnic variations: differences observed in the metabolism of drugs among races. Such variants may be polymorphic or monomorphic. Approximately slow and rapid acetylators are found among whites and blacks whereas the slow acetylators dominate Japanese and Eskimo populations.
13. Nutrition: certain foods can enhance, delay or decrease drug absorption. High protein diets can accelerate metabolism of certain drugs by stimulating cytochrome P-450.

Fat free diet depresses cytochrome P-450

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

Starvation results in decreased amount of glucuronides formed then under normal conditions.

1. Hormonal imbalance: higher levels of one hormone may inhibit the activity of few enzymes while inducing others. Pituitary growth hormone and stress related changes in ACTH levels.
2. Species: metabolism of drugs is usually affected by the half-life and duration of such drugs in a specie. Specie differences occur in phase I and phase II reactions. They are usually quantitative (same metabolic route but different rates) or qualitative (different metabolic routes). Human liver contains less cytochrome P-450 per gram than liver of other species.
3. Pregnancy: pregnancy affects hepatic drug metabolism. This is due to the physiological changes associated with pregnancy such as elevated levels of hormones such as estrogen, progesterone, prolactin and placental growth hormone.
4. Disease: diseases that affect metabolism of drugs include cirrhosis of the liver, diabetes mellitus, acromegaly, alcoholic liver disease, malaria, viral infections, etc. the diseases cause either decreased enzyme activity in the liver, altered hepatic blood flow or hypoalbuminanemia. Oxidation of Vitamin D and hydrolysis of procaine are impaired to kidney diseases.