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## **ASSIGNMENT**

Discuss in details the factors affecting drug metabolism

## **ANSWER**

### **FACTORS AFFECTING DRUG METABOLISM**

There are various factors that affect drug metabolism

These factors maybe internal or external.

**INTERNAL FACTORS;** these include species, genetic, gender, age, hormones and diseases

#### **AGE**

Age affects the metabolism of drugs. Metabolism of drug in the elderly is slow. This is because the enzymes in the liver which are responsible for metabolizing drugs are few. Hence, the half-life of drugs is greatly increased. Also, the age associated reduction of liver blood flow affects the ability of the liver to metabolize drugs. These factors make drugs have adverse effects on the elderly. In young children drug metabolism is slow because the required enzymes for metabolizing drugs are not fully developed and active.

#### **GENDER**

The gender of an individual influences how drugs are metabolized. Generally, drug metabolism is faster in males than in females this maybe due to some factors such as;

**Weight;** females have a higher percentage of body fat than males, this in turn directly affect the volume of distribution of drugs

**Renal factor;** men have a higher glomerular filtration rate than women hence, the volume of unchanged drugs excreted is higher.

*Enzymatic differences*; there is a more profound activity of cytochrome P450 and UGT enzymes in males than in females. This reduces the time taken to metabolize drugs in males

For these reasons there are differences in drug metabolism between sexes.

## **HORMONES**

Some steroid hormones may inhibit the action of cytochrome P450

## **DISEASE**

The effect of disease state has an impact on drug metabolism. The disease may be hepatic or non-hepatic.

A non-hepatic case such as thyroid dysfunction can influence the metabolism of drugs. For instance antipyrine have very short half-life during hypothyroidism and prolonged ones in hyperthyroidism. This is due to changes in metabolic rate because of the difference in circulating hormones of the thyroid.

Most diseases of the liver directly affect the metabolism of drugs. But there is no clear correlation because each hepatic disease vary in effect on drug metabolism. For instance cerebral sensitivity to opioids and sedatives is often enhanced in patients with chronic liver disease. Cirrhosis of the liver, alcoholic liver disease, cholestatic jaundice, liver carcinoma, viral hepatitis, hepatoma, tumour growths in the liver are all examples of hepatic diseases which have impact on drug metabolism.

## **GENETICS**

Genetic factors can influence drug metabolism. These factors account for (20-90)% of variability of drug metabolism in individuals. Genetic polymorphisms for many drug metabolizing enzymes and drug receptors have been identified, hence, genetics play a major role in affecting how drugs are metabolized. Pharmacogenetic studies the relationship between genetic factors and response to medication.

The genetic influences on drug metabolism interact with other intrinsic (i.e physiologic) and extrinsic (i.e cultural, behavioural, and environmental) characteristics of a person to determine the result of drug metabolism in such individual.

An example of where genetic factors greatly influence drug metabolism is in the rate of acetylation;

- Rapid acetylators have more hepatic acetyl N-transferase than the slow acetylators.
- 90% of Asians and Eskimos are rapid acetylators.
- Egyptians and Mediterranean are slow acetylators.

- The rate of acetylation is clinically important in terms of therapeutic response and toxicity.
- Also, genetic factors affect the rate of oxidation.

## **SPECIES**

The species of an organism directly affects the rate of metabolism of drug. This is because species differ in isoform composition, expression and catalytic activities of enzymes involved in drug metabolism. Hence drug metabolism rates differ.

An instance where this is obvious is in the rate of metabolism of hexobarbitone;

- It has a metabolism unit of 16.6 in mice, 3.7 in rat, 1 in dogs and cannot be metabolized by man. This is due to differences in Cytochrome P450

Therefore, differences in expression between species of the most important family of drug-metabolizing enzymes, the cytochrome P450s (CYPs) are a major cause of species differences in drug metabolism.

## **EXTERNAL FACTORS; diet and environment**

### **DIET**

The diet of an individual has great influence on the metabolism of drug.

Nutritional deficiencies can affect drug absorption and metabolism. Severe energy and protein deficiencies reduce enzyme tissue concentrations and may impair the response to drugs by reducing absorption or protein binding and causing liver dysfunction. Deficiency of vitamins and minerals have effect on drug metabolism e.g Vitamin C deficiency decreases activity of drug-metabolizing enzymes, especially in the elderly.

Food can alter metabolism of drugs; eg, high-protein diets can accelerate metabolism of certain drugs by stimulating cytochrome P-450. Eating grapefruit can inhibit cytochrome P-450 3A4, slowing metabolism of some drugs.