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Biochemistry Assignment.

Discuss in details the factors affecting drug metabolism.

Drug metabolism is the metabolic breakdown of drugs by living organisms, usually through specialized enzymatic systems. The study of drug metabolism is called pharmacokinetics. The metabolism of pharmaceutical drugs is an important aspect of pharmacology and medicine. For example, the rate of metabolism determines the duration and intensity of a drug's pharmacologic action. And the rate of metabolism can be affected by various factors which include;

1. Muscle Mass:

Muscle tissues have high metabolic activity than fat tissue, so a high amount of muscle tissue improves the rate of drug metabolism. But individuals with more fat tissues than muscle tissue would eventually have a lower metabolic rate than individuals with more muscle tissue to fat tissue.

2. Age:

In general, drugs are metabolized more slowly in fetal, neonatal and elderly than in adults. As an individual gets older their metabolic rate generally slows, this is as a result of muscle loss and changes in hepatic, hormonal and neuronal activities. For neonatal their metabolic rate is also relatively slow, this could be due to lack of certain enzymes needed. During development children going through peiods of growth undergo extreme rate of metabolism.

3. Gender:

Sex differences in metabolism (phase I and II) are believed to be the major cause of differential pharmacokinetics between men and women. Many CYP450 enzymes (phase I metabolism) show a sex-dependent difference in activity. Most of the phase II enzymes have a higher activity in men than in women. The CYP450 superfamily of enzymes is responsible for metabolizing 70% to 80% of all prescribed drugs.14 A total of 18 CYP gene families have been identified, and the majority of drug metabolism is mediated by CYP1, CYP2, and CYP3.

CYP1A2, the primary enzyme for metabolizing the antipsychotic drugs olanzapine and clozapine, shows a higher activity in men. CYP2B6 expression and activity are higher in women than in men. Among the extensive metabolizers, CYP2D6 activity is higher in women than in men,21 and increased activity is seen during pregnancy. CYP3A4 is the most abundantly expressed CYP in the liver and is the predominant enzyme for phase I metabolism, Its expression (protein and mRNA) and activity are higher in women than in men.

4.Hormonal factors:

Hormonal changes during pregnancy, menopause, puberty, malnutrition, obesity, diabetes mellitus, hypothyroidism, hyperthyroidism, systemic inflammation, and conditions of altered extracellular fluid volume or osmolality has been seen to have effects on drug metabolism. Testosterone has been noted to have an effect on drug metabolism, that is why at times some drugs are moteblised slower in Male than female and vis versa.

5. Deit:

Foods can enhance, delay, or decrease drug absorption. Foods impair absorption of many antibiotics. They can alter metabolism of drugs; eg, high-protein diets can accelerate metabolism of certain drugs by stimulating cytochrome P-450.

6. Species:

Animal studies are commonly used to predict metabolism and toxicity of potential new human drugs. However, it is important to realize that humans differ from animals in isoform composition, expression and catalytic activities of enzymes involved in drug metabolism. In fact, even small changes in the amino acid sequences of these enzymes can give rise to profound differences in substrate specificity and catalytic activity. Therefore, differences in expression between species of the most important family of drug metabolizing enzymes, the cytochrome P450s are a major cause of species differences in drug metabolism.

7. Environmental factors:

In terms of the weather, it is noted that drug metabolism is faster during extreme weathers. During a hot day the heart beats faster than normal and the body works had to cool the body temperature, it increases metabolism. Also during cold weathers the body works to increase the temperature and the heart and vessel are at work to improve blood flow, this also increases metabolism.

8. Pathological factors:

The activity of drug-metabolizing enzymes is altered by several pathological states, such as diseases of the liver, heart or kidney. As the liver is the major site for metabolism with various enzymes available for metabolizing varieties of drugs an alternation to the normal physiology of the liver causes a drastic effect in drug metabolism. So as the heart (dealing with the drug transportation) and the kidneys (elimination of drug metabolites).

9. Dose of the Drugs:

A dose is a measured quantity of a medicine delivered as a unit. The greater the quantity delivered, the larger the dose. Some substances are meant to be taken in small doses over large periods of time to maintain a constant level in the body, while others are meant to have a large impact once and be expelled from the body after its work is done. Prescription drug dosage is based typically on body weight, this is to determine the safe dose to be given to prevent overdose or under dose.

10. Route of administration:

There are various routes of administering drugs, it has been noted that the intravenous route is the fastest route because it goes straight to the blood stream and nasal route has been noted to be that fastest route for absorption. Although oral administration is sslow the metabolic rate of the drugs administered could be faster than any other route, in the gastrointestinal tract the drugs undergoes metabolic activities before reaching the blood stream at times some drugs a activated (meaning the drug was administered a prodrug).