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MECHANISM OF DRUG ACTION

INTRODUCTION

In pharmacology, the term mechanism of action (MOA) refers to the specific biochemical interaction through which a drug substance produces its pharmacological effect. A mechanism of action usually includes mention of the specific molecular targets to which the drug binds, such as an enzyme or receptor.Receptor sites have specific affinities for drugs based on the chemical structure of the drug, as well as the specific action that occurs there.

Drugs that do not bind to receptors produce their corresponding therapeutic effect by simply interacting with chemical or physical properties in the body. Common examples of drugs that work in this way are antacids and laxatives.

In contrast, a mode of action (MoA) describes functional or anatomical changes, at the cellular level, resulting from the exposure of a living organism to a substance.

This differs from a mechanism of action, as it is a more specific term that focuses on the interaction between the drug itself and an enzyme or receptor and its particular form of interaction, whether through inhibition, activation, agonism, or antagonism.

(a) Agonists

Ligands that bind to a receptor and produce an appropriate response are called agonists. For example, the catecholamine adrenaline is an agonist at β -adrenoceptors. When it binds to β -adrenoceptors in the heart, it increases the heart rate.

(b) Antagonists

Ligands that prevent an agonist from binding to a receptor and thus prevent its effects are called antagonists. Antagonists do not themselves have any pharmacological actions mediated by receptors. For example, propranolol, a β -adrenoceptor antagonist, binds to β -adrenoceptors in the heart and prevents catecholamine-induced tachycardia (for example in response to exercise).However, in the absence of an agonist propranolol has no effect via adrenoceptors.

C) Competitive agonist and antagonist:

A competitive antagonist binds to the same site as the agonist but does not activate it, thus blocks the agonist's action. A non-competitive antagonist binds to an allosteric (non-agonist) site on the receptor to prevent activation of the receptor.

FACTORS MODIFYING DRUG ACTION

Body weight/size:

It influences the concentration of drug attained at the site of action

Average adult dose refers to individuals of

medium built.

Age:

Infants and Children:

The dose of drug for children often calculated from the adult dose.
However, infants and children are having important physiological differences

- Higher proportion of water
- Lower plasma protein levels
- More available drug
- Immature liver/kidneys
- Liver often metabolizes more slowly
- Kidneys may excrete more slowly

Elders:

In elderly, renal function progressively declines
(intact nephron loss) and drug doses need reduction

- Chronic disease states
- Decreased plasma protein binding
- Slower metabolism
- Slower excretion
- Dietary deficiencies
- Use of multiple medications
- Lack of compliance

Sex:

Females have smaller body size, and so require doses of drugs on the lower side of dose range.
They should not be given uterine stimulants during menstruation, quinine during pregnancy and sedatives during lactation.

Pregnancy:

Profound physiological changes which may affect
drug responses:

- GI motility reduced – delayed absorption of

orally administered drugs

- Plasma and ECF volume expands
- Albumin level falls
- Renal blood flow increases markedly
- Hepatic microsomal enzyme induction

Food:

- Delays gastric emptying, delays absorption

(ampicillin)

- Calcium in milk – interferes with absorption of

tetracyclines and iron by chelation

- Protein malnutrition
- Loss of BW
- Reduced hepatic metabolizing capacity
- Hypoproteinemia

Route of drug administration:

I.V route dose smaller than oral route
Magnesium sulfate:

- Orally – purgative
- Parenterally – sedative/hypotension
- Locally – reduces inflammation

Psychological state:

- Efficacy of drugs can be effected by patients beliefs, attitudes and expectations
- Particularly applicable to centrally acting drugs
- In some patients inert drugs (placebo) may produce beneficial effects equivalent to the drug, and may induce sleep in insomnia.

Presence of diseases/pathological states:

Drug may aggravate underlying pathology

- Hepatic disease may slow drug metabolism
- Renal disease may slow drug elimination
- Acid/base abnormalities may change drug absorption or elimination
- Severe shock with vasoconstriction delays absorption of drugs from s.c. or i.m

Drug metabolism in:

- Hyperthyroidism –enhanced
- Hypothyroidism - diminished.

Genetic factors:

- Lack of specific enzymes
- Lower metabolic rate
- Acetylation
- Plasma cholinesterase (Atypical pseudo cholinesterase)
- G-6PD
- Glucuronide conjugation

Tolerance:

- It means requirement of a higher dose of drug toproduce an effect, which is ordinarily produced by normal therapeutic dose of the drug

Drug tolerance may be:

- Natural
- Acquired
- Cross tolerance
- Tachyphylaxis (ephedrine, tyramine, nicotine)
- Drug resistance.