FACTORS AFFECTING DOSE AND ACTION OF A DRUG

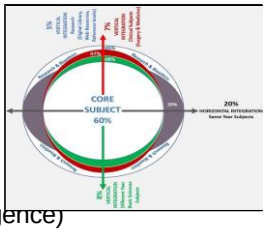
SOURCES:

- BERTRAM G. KATZUNG BASIC & CLINICAL PHARMACOLOGY 15TH EDITION
- GOODMAN AND GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS 13TH EDITION.

Sequence Of Lecture

- Spiral Integration
- Horizontal Integration
- Vertical integration
- Core Subject
- EOLA(End of lecture assessment)
- Digital Library References

(Research, Bioethics, Artificial Intelligence)



LEARNING OBJECTIVES

- At the end of session, the students of 3rd year should be able to:
- Discuss different factors affecting drug dose and action regarding Physiological, Pathological,Psychological,Genetic, Drug related (drug interactions) and Environmental factors
- Explain Synergism, Summation and Potentiation , Accumulation

Which of the following factors primarily affects the absorption of a drug?

A) Blood pressure
B) Route of administration
C) Liver function
D) Plasma protein binding
E) Renal function

Which of the following factors increases the rate of drug metabolism?

A) Age
B) Drug interactions
C) Liver disease
D) Genetic polymorphisms
E) All of the above

Which of the following can happen when two drugs compete for protein-binding sites?

A) Increased drug clearance
B) Decreased drug absorption
C) Increased free drug concentration of one drug
D) Decreased drug metabolism
E) Increased drug excretion

How does a high-fat meal affect drug absorption?

A) Increases absorption of lipophilic drugs
B) Decreases absorption of hydrophilic drugs
C) Has no effect on drug absorption
D) Increases the clearance of drugs
E) Increases the rate of renal elimination

Which of the following describes functional/ physiological antagonism?

A) Two drugs bind to the same receptor but do not compete for the same binding site

B) A drug binds to a receptor and prevents another drug from binding

C) Two drugs produce opposite effects through different mechanisms in the body

D) One drug chemically neutralizes the other

E) One drug changes the pH to reduce the activity of another drug

In which type of drug antagonism does one drug reduce the effects of another by binding to a different site on the receptor?

A) Competitive antagonism
B) Non-competitive antagonism
C) Functional antagonism
D) Chemical antagonism
E) Physiological antagonism

What effect does drug tolerance have on drug action?

A) Increases drug effectiveness
B) Decreases drug effectiveness
C) Has no effect on drug effectiveness
D) Makes the drug less toxic
E) None of the above

What type of drug interaction occurs when two drugs with similar effects are taken together, and the combined effect is equal to the sum of the individual effects?

A) Synergism
B) Antagonism
C) Additive effect
D) Potentiation
E) Sensitization

In which type of drug interaction do two drugs produce a combined effect greater than the sum of their individual effects?

A) Antagonism
B) Synergism
C) Additive effect
D) Potentiation
E) Chemical antagonism

What is the primary characteristic of drug summation?

A) The effects of drugs are opposite and cancel each other out.
B) The effects of drugs combine to produce a response greater than the sum of their effects.
C) The drugs do not interact and their effects are simply added together.
D) One drug enhances the effects of the other drug.
E) The drugs block each other from producing their effects.

Factors Modifying Doses and Action of Drugs

1. **Physiological Factors**
2. **Pathological Factors**
3. **Environmental factors**
4. **Psychological factors**
5. **Genetic Factors**
6. **Interaction with other drugs** (drug-drug interactions)

Physiological Factors

1. **Age**
2. **Gender**
3. **Pregnancy & Lactation**
4. **Body size**
5. **Racial Difference**
6. **Food**

1. **AGE**

- Formula for calculating dose in infants & children
- YOUNG'S FORMULA:

Child Dose = (Age/ Age + 12) adult dose

➢ **DRUG ABUSE:**

" An overpowering desire (compulsion) to continue taking drug, a tendency to increase dose & a high tendency for withdrawal symptoms."

10. DRUG INTERACTION

"When one drug alters concentration or action of another drug, a drug interaction is said to occur."

➢ 2 TYPES:
- Pharmacokinetic Interaction
- Pharmacodynamic Interaction

Pharmacokinetic interaction

Interaction of Absorption:

- A dg may increase or decrease absorption of another dg from intestinal lumen
- Ranitidine, H_2 receptors blocker, raises gastrointestinal pH & increase absorption of basic drugs such as triazolam
- Ca^{2+} & Fe^{2+} each form insoluble complexes with **tetracycline** that retard their absorption
- ***Cholestyramine***, a bile acid-binding resin, binds several dgs (e.g. warfarin, digoxin) preventing their absorption if administered simultaneously
- Addition of **epinephrine** to local anesthetic injections; resulting vasoconstriction slows absorption of anesthetic, thus prolonging its local effect

Drug-Drug Interaction

Pharmacodynamic interactions

- Are derived from modification of action of one dg at target site by another dg, independent of a change in its concentration

This may result

- In an enhanced response (synergism)
- Decreased response (antagonism)

11. SYNERGISM

"This is when two drugs are used together to enhance the therapeutic response."

TYPES:

➢ **SUMMATION:** This is when the combined effect of two drugs is equal to sum of individual drugs. i.e. 2+2=4

e.g. Aspirin + Paracetamol
Ephedrine + Theophylline

- **POTENTIATION**

This is when combined effect is greater than sum of individual drugs, i.e. 2+2=5 or more

e.g. Co-trimoxazole= Sulfamethoxazole + Trimethoprim

Captopril + Furosemide

- Potentiation also occurs when one drug that has no action of its own, enhances action of another, i.e. 0+2=5

- E.g. Carbidopa plus Levodopa

12. ANTAGONISM

Antagonism: One drug opposes or inhibit the action of another drug

TYPES:

- Chemical Antagonism
- Physical antagonism
- Physiological Antagonism
- Pharmacological Antagonism
  - ✓ Competitive (Reversible)
  - ✓ Non-competitive (Irreversible)

13. ACCUMULATION

- Any drug will accumulate in body if the rate of administration is greater than rate of elimination.

- Most of drug is eliminated after 4-5 half lives. This means that if dosing interval is shorter than 4-5 half lives, accumulation will occur.

- Accumulation is inversely proportional to fraction of dose lost in each dosing interval. The fraction lost is 1 minus fraction remaining just before next dose.

- Fraction remaining can be predicted from dosing interval & half life.

- A good index of accumulation is Accumulation factor.

- Accumulation factor= 1 / fraction lost in 1 dosing interval

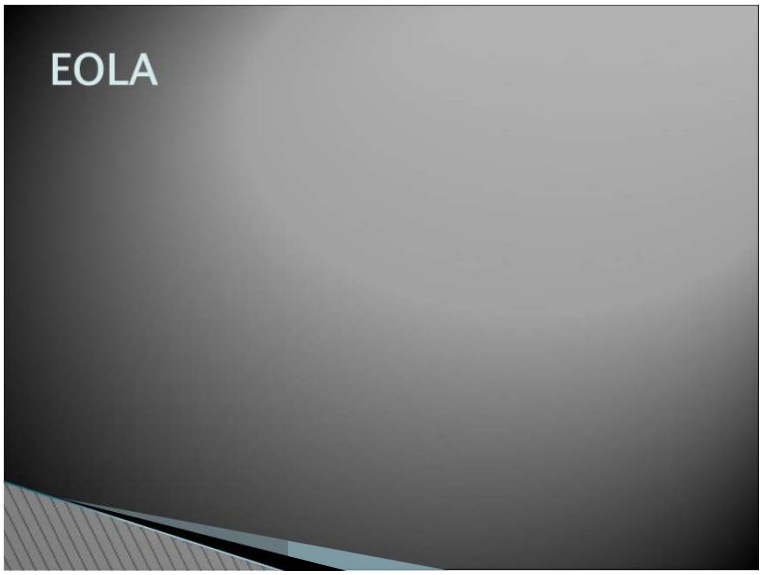
  = 1/1- fraction Remaining

➢ **So for a drug given once every half life, accumulation factor= 1/0.5=2**

- **16. MISCELLANEOUS FACTORS**
- Wrong diagnosis or incomplete diagnosis.
- Poor patient compliance or over compliance.

EXAMPLE

- To improve patients compliance, we use (DOTs)



- Trimethoprim and sulfamethaxazole are bacteriostatic drugs when given alone. However the combination is bactericidal. Which of the following term best defines this drug interaction:
- 1. Additive effect
- 2. Summation
- 3. Potentiation
- 4. Sensitization
- 5. Tolerance

- Chen C, Liu F, Ren Y, Suttner L, Sun Z, Shentu Y, Schmidt EV. Independent drug action and its statistical implications for development of combination therapies. Contemporary Clinical Trials. 2020 Nov 1;98:106126.
- D'Alessandro C, Benedetti A, Di Paolo A, Giannese D, Cupisti A. Interactions between food and drugs, and nutritional status in renal patients: a narrative review. Nutrients. 2022 Jan 4;14(1):212.