Physiologic Changes with Aging

Led as a 12-15 minute group discussion with active participation from the trainees.

Objectives

1. Define pharmacokinetics and pharmacodynamics
2. Understand physiologic changes and potential effects on drug pharmacokinetics
3. Identify high-risk medications in the geriatric population due to pharmacokinetic and pharmacodynamics changes

Definitions

- Pharmacokinetics: The portion of pharmacology concerned with the movement of drugs within the body in terms of their absorption, distribution, metabolism, and excretion.
- Pharmacodynamics: The portion of pharmacology concerned with the effects of drugs on the body and their mechanism of action.
- Volume of distribution: Distribution of a medication between plasma and the rest of the body after a dose of a medication.
- Half-life (t ½): The amount of time required for the amount of a given drug in the body to fall to half its initial value.

Teaching Pearls for Physiologic Changes with Age That May Effect Drug Pharmacokinetics

Organ System	Physiologic Change with Aging	Effect on Pharmacokinetics
Gastrointestinal	↑in stomach pH ↓GI blood flow Slowed gastric emptying Slowed GI transit	• Reduced absorption of some drugs and nutrients that require an acidic environment • Absorption rate may be slowed
Skin	Thinning of dermis Loss of subcutaneous fat	• Decreased drug reservoir formation with transdermal formulation
Body Composition	↓total body water ↓lean body mass ↑body fat ↓ serum albumin ↑a1-acid glycoprotein	• Increase in volume of distribution and accumulation of lipid-soluble drugs • Reduced volume of distribution of water-soluble drugs • Increase in free fraction of highly protein-bound drugs
Liver	↓in liver mass ↓blood flow to liver ↓in CYP enzymes	• Reduced first pass metabolism • Increased half-life and decreased clearance of drugs with a high first-pass metabolism • Reduction in phase I metabolism
Renal	↓in eGFR ↓renal blood flow ↓tubular secretion ↓renal mass	• Reduced renal elimination of many medications • Increased half-life of renally eliminated drugs and metabolites

Hutchison LC. ACCP Updates in Therapeutics: Geriatrics. 2015.

Pharmacokinetic Changes Common with Aging

- Absorption
    - Iron, B12, calcium absorption decreased
    - Slowed gastric emptying may increase risk of ulceration with aspirin, NSAIDS, KCl

    - Transdermal formulations should be used with caution
- Distribution
    - Lipid-soluble benzodiazepines have an increased half-life
    - Decrease in P-glycoprotein transporters, which may lead to higher concentrations in the brain of some medications
- Metabolism
    - Morphine and propranolol clearance are substantially reduced due to decrease in first-pass metabolism
    - Changes in phase I metabolism and CYP enzymes is variable and based on age, sex, and genetics
- Elimination
    - Drugs eliminated renally must be appropriately adjusted
    - Creatinine Clearance (CrCl) calculation using the Cockcroft-Gault equation is a validated method for drug dosing in older adults

Pharmacodynamic Changes Common with Aging

- Increased Sensitivity
    - Benzodiazepines
    - Opioids
    - Antipsychotics
    - TCAs
    - Antihypertensives, α-blockers
    - Warfarin
    - NSAIDs
    - Anticholinergic agents
        - Side effects of anticholinergic agents: “Anticholinergic Toxidrome” may cause blurred vision, altered mental status, confusion, delirium, flushed skin, hyperthermia, dry skin, urinary retention, constipation
- Decreased Sensitivity
    - β-blockers
    - β -agonists
- Impaired homeostasis
    - Diuretics

References

1. Bowie, M. W. and P. W. Slattum. Pharmacodynamics in older adults: a review. Am J Geriatr Pharmacother 2007:5(3):263-303.
2. Cusack, B. J. Pharmacokinetics in older persons. Am J Geriatr Pharmacother 2004:2(4): 274-302.
3. Turnheim, K. When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. Experimental Gerontology 2003:38(8): 843-853.