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

<table>
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<th>Organ System</th>
<th>Physiologic Change with Aging</th>
<th>Effect on Pharmacokinetics</th>
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| 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 |

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**