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Learn@Lunch
Geriatric Education Series
Kathryn Hyer, PhD, MPP
Principal Investigator

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Making Life Better®
Polypharmacy and Common Drug Interactions in Geriatric Patients

Jasmine Cutler, Pharm.D., CPh
USF Health Byrd Alzheimer’s Institute
Assistant Professor, USF College of Pharmacy
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Today’s 4 Objectives

- Review basic pharmacodynamics (PD) and pharmacokinetics (PK) in the elderly population
- Discuss clinical effects of common drug interactions
- Discuss common drug interactions in the elderly population
- Discuss ways to identify and resolve common drug interactions
What is Polypharmacy?

Polypharmacy is defined as the simultaneous use of multiple medications by a single person or patient.

- Potentially inappropriate drug
- Presence of six or more concurrent medications
Geriatric Population

• In 2014, represented 14.5% of the U.S. population, totaling 46.2 million people
• Uses more than 30% of all prescription medications
• Consumes more than 40% of nonprescription medications
• More than 80% of this population has at least one chronic disease
Little Known Facts

• Florida has highest percentage of total population (19.4%) aged 65 years and over

• Sumter County has the oldest median age of any US County.
Where to First?

- Review basic pharmacodynamics (PD) and pharmacokinetics (PK) in the elderly population
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PD and PK

- Pharmacodynamics (PD) deals with how the body handles the medication from administration to eliminations with particular emphasis on the relationship between drug concentration and effect.
- Pharmacokinetics (PK) deals with the movement of drugs within the body and concentrates on drug absorption, distribution, metabolism, and excretion.
Pharmacokinetic Changes

Absorption

Distribution

Metabolism

Excretion
Pharmacokinetic Changes

Absorption

- **Age-related changes**
  - Increased gastric pH
  - Decreased gastric emptying
  - Decreased GI motility
- **Result**
  - Decreased absorption of acidic drugs
  - Increased “contact time” of drugs in the stomach
Pharmacokinetic Changes

Absorption

- **Age-related changes**
  - Decreased intestinal blood flow and poor blood perfusion
  - Thinning of skin
  - Reduction of muscle mass
  - Impairment of active and passive transport

- **Result**
  - Possible slowing of *rate* of absorption, but little effect on *extent* of absorption
  - Transdermal drug absorption is impaired
Pharmacokinetic Changes

Distribution

• **Age-related changes**
  • Decrease in total body water and lean body mass
  • Increase in total fat content

• **Result**
  • Decreased volume of distribution (Vd) of drugs primarily distributed in water and lean mass (higher blood levels of the drug)
  • Increased Vd of lipid-soluble drugs (delayed effect or accumulation of the drug)
Pharmacokinetic Changes

Distribution

- Age-related changes
  - Decrease in serum albumin concentrations, especially in malnourished or frail patients
  - Decreased circulation
- Result
  - Increased serum concentrations of drugs highly bound to albumin
Pharmacokinetic Changes

- **Age-related changes**
  - Decline in liver mass
  - Decrease in hepatic blood flow, function, and first-pass metabolism

- **Result**
  - Decreased clearance and hepatic metabolism of certain medications
  - Changes in bioavailability of certain drugs
  - Phase II metabolism *not* affected

See Table 5-2 in Murphy Text
Common Hepatically Metabolized Medications

- Morphine
- Meperidine
- Verapamil
- Amitriptyline
- Nortriptyline
- Nifedipine
Pharmacokinetic Changes

Excretion

• **Age-related changes**
  - Decreased kidney mass, renal perfusion, and glomerular filtration
  - Decline in ability to concentrate urine
  - Reduced creatinine clearance

• **Result**
  - Prolonged half-life for renally-excreted drugs, *results in more adverse events than any other age-related alteration!*
Common Renally Eliminated Medications

- Allopurinol
- Aminoglycosides
- Atenolol
- Baclofen
- Ciprofloxacin
- Digoxin
- Diltiazem
- Gabapentin
- Lithium
- Metformin
- Methotrexate
- Ranitidine
- Tetracycline
Where to Next?

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What is a Drug Interaction?

A drug interaction occurs when a substance affects the activity of a drug when both are administered concomitantly. It can lead to a beneficial, synergistic, or detrimental clinical outcome.
Drug-Drug Interactions

• Cytochrome P450 system
  – Isoenzymes: 1A2, 2C19, 3A4, 2C9
  – Drugs are either substrates, inducers, or inhibitors of these isoenzymes

• Antagonistic

• Additive or synergistic
Factors Influencing Cytochrome P450 System

- Age
- Gender
- Ethnicity/race
- Liver function
- Circadian rhythms
- Comorbid conditions
Modifiable Factors Influencing Cytochrome P450 System

- Diet
- Weight
- Physical activity

- Cigarette smoking
- Alcohol abuse
In relation to the cytochrome P450 system, cigarettes act as an:
A. Inducer
B. Inhibitor
C. Substrate
D. Has no effect
Knowledge Check

In relation to the cytochrome P450 system, cigarettes act as an:

A. Inducer
B. Inhibitor
C. Substrate
D. Has no effect
Common Inducers

- Anticonvulsants
  - Phenytoin
  - Phenobarbital
  - Carbamazepine
- Barbiturates
- Carbamazepine
- Cigarettes
- Ethanol
- Glucocorticoids
- Primidone
- Rifampin
- St. John’s Wort
Common Inhibitors

- Amiodarone
- Antibiotics
  - Ciprofloxacin
  - Erythromycin
  - Metronidazole
- Antidepressants
  - Fluoxetine
- Antihypertensives
  - Verapamil
- Clopidogrel
- Grapefruit juice
- Antifungals
  - Ketoconazole
  - Itraconazole
Effects of Grapefruit Juice

Contains furanocoumarins

Irreversibly inhibits intestinal CYP-450 3A4

Increase plasma serum levels of drugs with high first-pass metabolism

Common Medications with Significant Interactions with Grapefruit Juice

- Felodipine
- Carbamazepine
- Amiodarone
- Oxycodone
- Simvastatin
- Sildenafil
“Red Flag” Medications

• First generation anticonvulsants (carbamazepine, phenytoin, phenobarbital)
• Selective serotonin reuptake inhibitors (SSRIs)
• Antifungals (ketoconazole)
“Red Flag” Medications

• Digoxin
• Erythromycin/Clarithromycin
• Hormones
• Lithium
• Theophylline
• Warfarin
Over-the-Counter Medications and Drug Interactions

- Antacids/laxatives
- Cimetidine
- Vitamin K
- Iron
- Cranberry

- Herbals
  - St. John’s Wort
  - Ginkgo biloba
- Sleep aids
- Cough/cold products
- Diet aids
Drug-Food Interactions

- Caffeine
- Charbroiled foods
- Cheeses
- Cranberry juice
- Dairy
- Grapefruit juice

- Green, leafy vegetables
- Salt substitutes
- Tyramine-containing foods
Where To Next?

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Consequences of Drug Interactions

- Drug toxicity
- Therapeutic failure
- Additive effects
Drugs that Increase QT Interval

- Amiodarone
- Amitriptyline
- Diphenhydramine
- Dofetilide (Tikosyn)
- Citalopram
- Clarithromycin
- Droperidol (Inapsine)
- Haloperidol
- Quinidine
- Mirtazapine
- Trazodone
- Vandetanib (Caprelsa)
Knowledge Check

Which of the following medication(s) interact with warfarin? (Select all that apply)

A. Bactrim DS
B. Cephalexin
C. Ibuprofen
D. Vodka
Knowledge Check

Which of the following medication(s) interact with warfarin? (Select all that apply)

A. Bactrim DS
B. Cephalexin
C. Ibuprofen
D. Vodka
Knowledge Check

Which of the following medication(s) can cause photosensitivity?

A. Aspirin
B. Furosemide
C. Meloxicam
D. B & C only
E. All of the above
Knowledge Check

Which of the following medication(s) can cause photosensitivity?

A. Aspirin
B. Furosemide
C. Meloxicam
D. B & C only
E. All of the above
Case Scenario

Mr. N.B. is a 80-year old African-American male. His medical conditions include hypertension, angina pectoris, GERD, diabetes mellitus, hyperlipidemia, and occasional migraine headaches. He is currently on the following medications:

<table>
<thead>
<tr>
<th>Medication List</th>
</tr>
</thead>
<tbody>
<tr>
<td>chlorothiazide 500 mg daily</td>
</tr>
<tr>
<td>amlodipine 5 mg daily</td>
</tr>
<tr>
<td>metoprolol succinate XL 50 mg daily</td>
</tr>
<tr>
<td>simvastatin 20 mg every night</td>
</tr>
<tr>
<td>Nitrostat 0.3 sublingual tablet as needed</td>
</tr>
<tr>
<td>Aspirin 81 mg daily</td>
</tr>
</tbody>
</table>
You May Ask…

How Do We Avoid Drug Interactions?
Discuss ways to identify and resolve common drug interactions

Discuss clinical effects of common drug interactions

Review basic pharmacodynamics (PD) and pharmacokinetics (PK) in the elderly population

Discuss common drug interactions in the elderly population

...Perfect Question
Healthcare Professional’s Role

- First, do no HARM
- Patient-centered care and education
- Ensure each medication has an indication
Healthcare Professional’s Role

• Advantage of an interdisciplinary health team approach
• Importance of patient follow-up and transitions of care
• Assess for mental health conditions
• Screen for use of multiple pharmacies and prescribers
Healthcare Professional’s Role

- Screen for potential differential diagnosis
- Make one medication change at a time
- Start slow and titrate dosages
- Inquire about non-prescription and herbal medication use
- Be familiar with indications, side effects, properties, and formulations of each medication
Healthcare Professional’s Role

Be familiar with the monitoring parameters associated with each medication

- K+ levels
- Na+ levels
- GFR and sCr
- LFTs
- GI bleeding
- TSH/T3/T4
- Behavioral changes
Healthcare Professional’s Role

• Identify and eliminate duplicate therapies
• Assess medication adherence
• Ensure medications are taken properly and adverse drug events are avoided
• Use appropriate doses and be aware of best timing of administration
• Some medications should be taken with or without food
In Practice: Drug Reactions Similar to Common Complaints of Elderly

- Unsteadiness
- Dizziness
- Drowsiness
- Falls
- Dysphagia
- Anorexia

- Fatigue
- Malaise
- Incontinence
- Insomnia
- Depression
## Suggested Administration Times for Select Medications

<table>
<thead>
<tr>
<th>Drug Categories</th>
<th>Ideal Time of Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure lowering agents</td>
<td>Morning</td>
</tr>
<tr>
<td>Lipid lowering agents</td>
<td>Evening</td>
</tr>
<tr>
<td>Bisphosphonates (ex. Actonel, Fosamax, Boniva)</td>
<td>Morning, on an empty stomach &gt;30/60 minutes away from other medications and food with a full glass of plain water; swallow tablet whole; remain in upright position</td>
</tr>
<tr>
<td>Synthroid</td>
<td>Morning, on an empty stomach &gt;30 minutes away from other medications and food with a full glass of water</td>
</tr>
<tr>
<td>Sex Hormones</td>
<td>Morning</td>
</tr>
<tr>
<td>Antiplatelets (not Coumadin)</td>
<td>Morning</td>
</tr>
<tr>
<td>Acid Secretion inhibitors</td>
<td>Evening</td>
</tr>
<tr>
<td>Sedating agents/Sleep aids</td>
<td>Evening</td>
</tr>
<tr>
<td>Diuretics (ex. HCTZ)</td>
<td>Morning</td>
</tr>
<tr>
<td>Stimulating Drugs</td>
<td>Morning</td>
</tr>
<tr>
<td>Coumadin</td>
<td>Evening</td>
</tr>
</tbody>
</table>
Resources

- Beers Criteria
- Screening Tool to Alert Doctors to Right Treatment (START)
- Screening Tool of Older Persons’ Prescriptions (STOPTP)
- Appropriate Medication Use in Vulnerable Elders (ACOVE)
Recent Literature

• Feasibility Trial (DEFEAT-polypharmacy)
• Development of the Tool to Reduce Inappropriate Medications (TRIM)
• Reducing Inappropriate Polypharmacy: The Process of Deprescribing
References


References

References


Questions?

“The more I live, the more I learn. The more I learn, the more I realize, the less I know.”

--Michel Legrand
Jasmine Cutler, Pharm.D., CPh
USF College of Pharmacy (813) 974-3935
Byrd Alzheimer’s Institute (813) 396-0623
Jcutler@health.usf.edu
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Jasmine Cutler, Pharm.D., CPh
Pharmacists, USF Health Byrd Alzheimer’s Institute
Assistant Professor, USF College of Pharmacy
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