Medication Dynamics and Polypharmacy Issues in Vulnerable Populations

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Objectives

1. Describe the basic principles of how drugs work in the body and with one another.
2. Identify the four most important ways that drugs impact the body in both positive and negative ways.
3. Describe three reasons why individuals in vulnerable populations, particularly individuals with I/DD and or aging have increased risks for reactions to polypharmacy.
4. Describe how to use the HRST to identify drug risk issues.
**Drug Management Issues**

- Drug ineffectiveness (FDA 1938)
- Adverse Drug Events
  - Over-sedation, falls, increased bleeding
- Over-dosage
- Under-dosage
- Drug Interactions
- Increased potential side effects
- Increased costs and hospitalizations

**Challenges of Pharmacotherapy**

- New drugs available each year
- FDA approved and off-label indications are expanding
- Changing managed-care formularies
- Advanced understanding of drug-drug interactions
- Increasing popularity of “nutricionals”
- Multiple co-morbid states
- Polypharmacy
- Medication compliance
- Effects of aging physiology on drug therapy
- Medication cost

**Pharmacokinetics (PK)**

- Half Life: The time it takes for half the drug to be eliminated from the body
- Protein Binding: Binding to blood protein, albumin. Only free drug is available for clinical activity.
  - Total drug load
  - Bound
  - Unbound
- Onset: Time interval that starts when the drug is administered and ends when therapeutic effects actually begin.
- Peak: Highest level of blood concentration
- Duration: Length of time drug produces its therapeutic effect
- Steady State: Occurs when the rate of drug administration equals the rate of drug elimination. Occurs after five half lives
Pharmacokinetics (PK)

- **Absorption**
  - Bioavailability: the fraction of a drug dose reaching the systemic circulation
- **Distribution**
  - Locations in the body a drug penetrates expressed as volume per weight (e.g. L/kg)
- **Metabolism**
  - Drug conversion to alternate compounds which may be pharmacologically active or inactive
- **Elimination**
  - A drug’s final route(s) of exit from the body expressed in terms of half-life or clearance

I/DD population and Drug Dynamics

- I/DD population:
  - Age earlier and differently
  - More incidence of multiple disease states
  - Assault on liver and kidneys due to lifetime use of medications
    - Anti-seizure medications
    - Few medications extensively excreted in kidneys ex: gabapentin
  - Not as many functioning brain neurons
    - Affects psychotropic medications ex: antipsychotics, antidepressants

I/DD population and Drug Dynamics

- I/DD population:
  - Non-ambulatory status slows metabolism
    - Oral dosing slowed
    - May be incomplete
    - GERD and hyper acidic states
  - Swallowing issues and g-tube absorption issues
    - What can be crushed
    - Adherence to g tube
    - Medications administered alone vs together
The Aging Imperative

- Persons aged 65y and older constitute 13% of the population and purchase 33% of all prescription medications.
- By 2040, 25% of the population will purchase 50% of all prescription drugs.

Effects of Aging on Rx use (Absorption)

- Reduced gastric acid production
  - Raises gastric pH
  - May alter solubility of some drugs (ASA etc)
- Longer gastric emptying
  - Delay or reduce absorption
- Decreased esophageal motility
  - Capsules more difficult to swallow
- Loss of subcutaneous fat
  - Increased rate of absorption of topical medications
- Increased fragility of veins
  - IV administration more difficult

Effects of Aging on Absorption

- Rate of absorption may be delayed
  - Lower peak concentration
  - Delayed time to peak concentration
- Overall amount absorbed (bioavailability) is unchanged
Factors Affecting Absorption

- Route of administration
- What it taken with the drug
  - Divalent cations (Ca, Mg, Fe)
  - Food, enteral feedings
  - Drugs that influence gastric pH
  - Drugs that promote or delay GI motility
- Comorbid conditions
- Increased GI pH
- Decreased gastric emptying
- Dysphagia

Effects of Aging on Rx use (Distribution)

- Decreased cardiac output/circulation changes
  - May delay onset or extend effect of medications
  - Decrease of lean body mass/increase of fatty tissue where medications are stored
  - Prolong medication’s action
  - Increase sensitivity
  - Increase toxic effects
  - Higher plasma levels/more erratic distribution

Effects of Aging on Volume of Distribution (Vd)

<table>
<thead>
<tr>
<th>Aging Effect</th>
<th>Vd Effect</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased body water</td>
<td>Vd for hydrophilic drugs</td>
<td>ethanol, lithium</td>
</tr>
<tr>
<td>Decreased lean body mass</td>
<td>Vd for drugs that bind to muscle</td>
<td>digoxin</td>
</tr>
<tr>
<td>Decreased fat stores</td>
<td>Vd for lipophilic drugs</td>
<td>diazepam, trazodone</td>
</tr>
<tr>
<td>Decreased plasma protein (albumin)</td>
<td>% of unbound or free drug (active)</td>
<td>diazepam, valproic acid, clozapine, warfarin</td>
</tr>
<tr>
<td>Decreased plasma protein (α1-acid glycoprotein)</td>
<td>% of unbound or free drug (active)</td>
<td>mandine, propranolol, erythromycin, enalapril</td>
</tr>
</tbody>
</table>
Effects of Aging on Rx use (Metabolism)

- Difficult to predict, depends on
  - General health & nutritional status
  - Use of alcohol, medications
  - Long term exposure to environmental toxins/pollutants

- Aging causes decreased liver mass/hepatic blood flow
  - Delayed/reduced metabolism of drugs
  - Higher plasma levels

- Lower serum protein levels
  - Loss of protein binding

- Idiosyncratic reactions

Hepatic First-Pass Metabolism

- For drugs with extensive first-pass metabolism, bioavailability may increase because less drug is extracted by the liver
  - Decreased liver mass
  - Decreased liver blood flow

Aging Effects on Hepatic Metabolism

- Metabolic clearance of drugs by the liver may be reduced due to:
  - decreased hepatic blood flow
  - decreased liver size and mass

- Examples: morphine, meperidine, metoprolol, propranolol, verapamil, amitryptiline, nortriptyline
Other Factors Affecting Drug Metabolism

- Gender
- Comorbid conditions
- Smoking
- Diet
- Drug interactions
- Race
- Frailty

Metabolic Pathways

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Effect</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I: oxidation,</td>
<td>Conversion to metabolites of lesser,</td>
<td>Diazepam, quinidine,</td>
</tr>
<tr>
<td>hydroxylation,</td>
<td>equal, or greater</td>
<td>piroxicam, (Feldene)</td>
</tr>
<tr>
<td>dealkylation, reduction</td>
<td></td>
<td>theophylline</td>
</tr>
<tr>
<td>Phase II: glucuronidation,</td>
<td>Conversion to inactive metabolites</td>
<td>Lorazepam, oxazepam,</td>
</tr>
<tr>
<td>conjugation, or</td>
<td></td>
<td>temazepam (Restoril)</td>
</tr>
<tr>
<td>acetylation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** NOTE: Medications undergoing Phase II hepatic metabolism are generally preferred in the elderly due to inactive metabolites (no accumulation)**

Effects of Aging on Rx use (Excretion)

- Reduction in number of functioning nephrons/decreased glomerular filtration rate
- Longer half-life of medications
- Increased side effects
- Increased potential for toxicity
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Concepts in Drug Elimination

- Half-life: time for serum concentration of drug to decline by 50% (expressed in hours)
- Clearance: volume of serum from which the drug is removed per unit of time (mL/min or L/hr)
- Reduced elimination ⇒ drug accumulation and toxicity

Effects of Aging on the Kidney

- Decreased kidney size
- Decreased renal blood flow
- Decreased number of functional nephrons
- Decreased tubular secretion
- Result: ↓ glomerular filtration rate (GFR)
- Decreased drug clearance: atenolol, gabapentin, H2 blockers, digoxin, allopurinol, quinolones (Cipro, Floxin, Levaquin)
Pharmacodynamics (PD)

- Definition: the time course and intensity of pharmacologic effect of a drug
- Age-related changes:
  - ↑ sensitivity to sedation and psychomotor impairment with benzodiazepines
  - ↑ level and duration of pain relief with narcotic agents
  - ↑ drowsiness and lateral sway with alcohol
  - ↓ HR response to beta-blockers
  - ↑ sensitivity to anti-cholinergic agents
  - ↑ cardiac sensitivity to digoxin

PK and PD Summary

- PK and PD changes generally result in decreased clearance and increased sensitivity to medications in older adults and those with I/DD
- Use of lower doses, longer intervals, slower titration are helpful in decreasing the risk of drug intolerance and toxicity
- Careful monitoring is necessary to ensure successful outcomes

Polling Question

- The absorption, distribution, metabolism and excretion of a drug is called pharmacokinetics.
  - A. True
  - B. False
Consequences of Overprescribing
- Adverse drug events (ADEs)
- Drug interactions
- Duplication of drug therapy
- Decreased quality of life
- Unnecessary cost
- Medication non-adherence

Optimal Pharmacotherapy
- Balance between overprescribing and underprescribing
  - Correct drug
  - Correct dose
  - Targets appropriate condition
  - Is appropriate for the patient
- Avoid “a pill for every ill”
- Always consider non-pharmacologic therapy

Adverse Drug Events (ADEs)
- Responsible for 5-28% of acute geriatric hospital admissions
- Greater than 95% of ADEs in the elderly are considered predictable and approximately 50% are considered preventable
- Most errors occur at the ordering and monitoring stages
Most Common Medications Associated with ADEs in the Elderly

- Opioid analgesics
- NSAIDs
- Anticholinergics
- Benzodiazepines
- Also: cardiovascular agents, CNS agents, and musculoskeletal agents


The Beers Criteria

<table>
<thead>
<tr>
<th>High Potential for Severe ADE</th>
<th>High Potential for Less Severe ADE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline (Elavil)</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>Digoxin &gt;0.125mg/d</td>
<td>diphenhydramine</td>
</tr>
<tr>
<td>Disopyramide (Norpace)</td>
<td>Dipyrudamole (Persantine)</td>
</tr>
<tr>
<td>GI antispasmodics</td>
<td>Indomethacin</td>
</tr>
<tr>
<td>Meperidine</td>
<td>Muscle relaxants</td>
</tr>
<tr>
<td>Pentazocine (Talwin)</td>
<td></td>
</tr>
</tbody>
</table>

Patient Risk Factors for ADEs

- Polypharmacy
- Multiple co-morbid conditions
- Prior adverse drug event
- Low body weight or body mass index
- Age > 85 years
- Estimated CrCl <50 mL/min
Prescribing Cascade

Drug 1

ADE interpreted as new medical condition

Drug 2

ADE interpreted as new medical condition

Drug 3


Polypharmacy

- Concurrent use of multiple medications
  - >85 = 12% of population
  - Consume 30% of all prescription drugs [average person takes 4-5 prescription meds]
  - Consume 40% of OTCs

- Excessive use of drugs
- Overdose of a drug

Concepts in Drug-Drug Interactions

- Absorption may be $\uparrow$ or $\downarrow$
- Drugs with similar effects can result in additive effects
- Drugs with opposite effects can antagonize each other
- Drug metabolism may be inhibited or induced
Pharmacodynamic Definitions
- Tolerance: Decreased response to a drug over time, requiring an increase in drug dosage to achieve the same therapeutic effect (pain medications)
- Additive effect: Two drugs with similar actions administered together. The effects are equivalent to the sum of either drug administered alone at higher dosages.
- Antagonism: Drug interaction which occurs when the combined response of two drugs is less than the response produced by either alone.

Pharmacodynamic Definitions
- Synergism: Two drugs that produce the same effect are given together and one enhances the effect of the other drug. This produces greater effects than either drug given alone.
- Protein Binding: When two drugs are given together they can compete for protein binding sites, leading to an increase in the effect of one drug as that drug is displaced from the protein and become a free unbound drug.

Pharmacotherapeutics
- Definition: The use of drugs to treat disease
- Examples:
  - Replacement therapy: to replenish or substitute for missing substances in the body (insulin, iron)
  - Excite or depress cells (brain neurons)
  - Alter tissues or cells (chemotherapy)
Polypharmacy

- Doctors more likely to prescribe medications for older clients than young ones

- Altered response to medications: cumulative effect on physiology of aged:
  - Aging
  - Disease
  - Stress
  - Trauma

Polypharmacy

- Elderly rely on various medications to control or relieve a range of age-related problems
  - Cardiovascular disease
  - Diabetes
  - Degenerative joint disease
  - Autoimmune disorders

Polypharmacy

- Risks of problems:
  - Medication errors
    - Wrong drug, time, route
  - Adverse effects from each drug
    - Polypharmacy primary reason for adverse reactions
  - Adverse interactions between drugs
Drug-Drug Interactions (DDIs)
- May lead to adverse drug events
- Likelihood ↑ as number of medications ↑
- Most common DDIs:
  - cardiovascular drugs
  - psychotropic drugs (antipsychotics, antidepressants, antianxiety medications)
  - Depends largely on mechanism of action (seizures, psychosis, depression, Alzheimer’s Disease)
- Most common drug interaction effects:
  - confusion
  - cognitive impairment
  - hypotension
  - acute renal failure

Common Drug-Drug Interactions

<table>
<thead>
<tr>
<th>Combination</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor + potassium</td>
<td>Hyperkalemia</td>
</tr>
<tr>
<td>ACE inhibitor + K sparing diuretic</td>
<td>Hyperkalemia, hypotension</td>
</tr>
<tr>
<td>Digoxin + antiarrhythmic</td>
<td>Bradycardia, arrhythmia</td>
</tr>
<tr>
<td>Digoxin + diuretic</td>
<td>Electrolyte imbalance; arrhythmia</td>
</tr>
<tr>
<td>Antiarrhythmic + diuretic</td>
<td>Electrolyte imbalance; dehydration</td>
</tr>
<tr>
<td>Diuretic + diuretic</td>
<td>Sedation; confusion; falls</td>
</tr>
<tr>
<td>Benzodiazepine + antidepressant</td>
<td></td>
</tr>
<tr>
<td>Benzodiazepine + antipsychotic</td>
<td></td>
</tr>
<tr>
<td>CCB/nitrate/vasodilator/diuretic</td>
<td>Hypotension</td>
</tr>
</tbody>
</table>

Drug-Disease Interactions
- Obesity alters Vd of lipophilic drugs
- Ascites alters Vd of hydrophilic drugs
- Dementia may ↑ sensitivity, induce paradoxical reactions to drugs with CNS or anticholinergic activity
- Renal or hepatic impairment may impair metabolism and excretions of drugs
- Drugs may exacerbate a medical condition
### Common Drug-Disease Interactions

<table>
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<tr>
<th>Combination</th>
<th>Risk</th>
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</thead>
<tbody>
<tr>
<td>NSAIDs + CHF</td>
<td>Fluid retention; CHF exacerbation</td>
</tr>
<tr>
<td>Thiazolidinediones + CHF</td>
<td></td>
</tr>
<tr>
<td>BPH + anticholinergics</td>
<td>Urinary retention</td>
</tr>
<tr>
<td>Narcotics + constipation</td>
<td>Exacerbation of constipation</td>
</tr>
<tr>
<td>Anticholinergics + constipation</td>
<td></td>
</tr>
<tr>
<td>Metformin + CHF</td>
<td>Hypoxia; increased risk of lactic acidosis</td>
</tr>
<tr>
<td>NSAIDs + gastropathy</td>
<td>Increased ulcer and bleeding risk</td>
</tr>
<tr>
<td>NSAIDs + HTN</td>
<td>Fluid retention; decreased effectiveness of diuretics</td>
</tr>
</tbody>
</table>

### Principles of Prescribing in the Elderly and Individuals with I/DD
- Avoid prescribing prior to diagnosis
- Start with a low dose and titrate slowly
- Avoid starting 2 agents at the same time
- Reach therapeutic dose before switching or adding agents
- Consider non-pharmacologic agents

### Prescribing Appropriately
- Determine therapeutic endpoints and plan for assessment
- Consider risk vs. benefit
- Avoid prescribing to treat side effect of another drug
- Use 1 medication to treat 2 conditions
- Consider drug-drug and drug-disease interactions
- Use simplest regimen possible
- Adjust doses for renal and hepatic impairment
- Avoid therapeutic duplication
- Use least expensive alternative
Preventing Polypharmacy

- Review medications regularly and each time a new medication started or dose is changed
- Maintain accurate medication records (include vitamins, OTCs, and herbals)

Polling Question

- Two antidepressants would never be appropriately prescribed to treat depression.
  - A. True
  - B. False

Troublesome medications

- Antacids
  - Acid-base imbalance (sodium bicarbonate)
  - Constipation (aluminum hydroxide)
- Anti-arrhythmics
  - Confusion
  - Slurred speech
  - Light-headedness, seizures
  - Hypotension
Troublesome medications

- Anticoagulants:
  - Bleeding
  - Watch food interactions

- Corticosteroids
  - Sodium retention (may worsen HTN & CHF)
  - Insomnia
  - Psychotic behavior
  - Osteoporosis

Troublesome medications

- Antipsychotics
  - Jaundice
  - Extrapyramidal symptoms
  - Sedation, dizziness (can lead to falls)
  - Orthostatic hypotension
  - Scaling skin on exposure to sunlight (phenothiazines)

Troublesome medications

- Anxiolytics
  - Confusion, lethargy
  - Slurred speech
  - Ataxia, falls
  - Blurred vision
Troublesome medications

- Laxatives
  - Intestinal malabsorption
  - Reduced absorption of fat-soluble vitamins (if taking mineral oil)
  - Magnesium toxicity (clients with renal insufficiency taking magnesium)

Troublesome medications

- Narcotic analgesics
  - Respiratory depression
  - Constipation
  - Urinary retention
  - Demerol:
    - Hypotension, dizziness
    - Confusion

Troublesome medications

- NSAIDs
  - Prolong bleeding
    - Gastric discomfort, bleeding
  - Increased risk of toxicity (with impaired renal function)
  - Avoid with Lithium
Troublesome medications

- Respiratory agents
  - Restlessness, nervousness
  - Confusion
  - Blood pressure disturbances
  - Palpitations, tachycardia
  - Chest pain

- Tricyclic antidepressants
  - Dry mouth
  - Constipation
  - Blurred vision
  - Postural hypotension
  - Dizziness
  - Tachycardia
  - Urinary retention

If client taking > five meds regularly

- Suggest physician prescribe combination drugs or long-acting forms
  - Fewer pills to remember
- Suggest re-evaluation of medications periodically
- New medications
  - Good information
  - Encourage follow up
Summary

• Successful pharmacotherapy means using the correct drug at the correct dose for the correct indication in an individual patient
• Age alters PK and PD
• ADEs are common among the elderly
• Risk of ADEs can be minimized by appropriate prescribing

Using the HRST in Polypharmacy and Medication Dynamics

Medication Purposes in the HRST

• The HRST allows for the classification of meds into 5 med purpose categories, with an additional Other category:
  • Anti-epileptic
  • Bowel
  • Emergency Drugs
  • Gastrointestinal
  • Psychotropic
  • Other
Medication Purposes

- Accurate selection is key!
- Selection reflects why the med was prescribed, regardless of original med intent
- Various reports can be pulled based off med purposes
- Data can be used to respond to polypharmacy issues on various levels within a state or client
- Allows for instant identification of those in a polypharmacy situation

Reporting on Polypharmacy in the HRST

- Reports are customizable
- Reports include:
  - Individuals on 3 or more Psychotropic Meds
  - Medications by Purpose
  - Individuals on Psychotropic Meds
  - Individuals on specifically identified meds
- More report options coming in the upgraded version, HRST 3.0!

Demonstrating the HRST Medication Reports

1. Log into the application using your login credentials
2. Click on Reports from the Menu bar at the top, then click Spreadsheets
3. Click the grey arrow next to the folder titled, Medications
4. Click on the desired report and desired report format
5. Click Generate
Getting Help

- For Clinical help:
  - Email: clinassist@hrstonline.com

- For Technical help:
  - Email: support@hrstonline.com

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