Drug-induced cognitive disorders in the elderly

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Objectives

➢ Explain why elderly patients are at higher risk for drug-induced cognitive disorders
➢ Review drug classes associated with cognitive disorders in the elderly
➢ Discuss common pharmacologic and non-pharmacologic approaches for treatment and/or prevention of delirium

Background

➢ 2010 U.S. Census Data
   • There are approximately 50 million people in the US 62 years of age and over
     ▪ Same number that was predicted to occur in 2020
     ▪ Increase of 21% since 2000
   • Florida has highest median ages
     ▪ Of the top 10 cities, 2 were located in South Florida
   • 3.6 million people ≥ 65 years old have an underlying cognitive disability

 WHY ARE THE ELDERLY AT RISK?

➢ Cognitive impairment and driving
   • Estimated 33 million licensed drivers ≥65 years old
   • 69% of AAA Foundation for Traffic Safety survey participants used one or more medication that may impair driving
     ▪ Of these, only 28% indicated they were aware of this risk

Background

➢ Adverse drug events have been linked to preventable problems in the elderly
   • Depression, falls, confusion
➢ 30% of hospital admissions are due to drug-related problems or drug toxicity in the elderly
➢ Delirium can increase the risk for medical complications
➢ In 2000, an estimated 106,000 deaths were medication related with an estimated healthcare cost of $85 billion

Arch Intern Med. 2003;163:2716-2724
### The “I’s” of geriatrics
- Immobility
- Isolation
- Incontinence
- Infection
- Inanition (malnutrition)
- Impaction
- Impaired senses
- Instability
- Intellectual impairment
- Impotence
- Immunodeficiency
- Insomnia
- Iatrogenesis

### Pharmacokinetics - absorption
- Changes in gastrointestinal physiology
- Most drugs are absorbed via passive diffusion and these changes may have little influence on bioavailability
- Decreased first-pass effect and/or gut wall metabolism
- Reduced subcutaneous fat results in altered absorption of transdermal medication

### Pharmacokinetics - distribution
- Dependent on blood flow, plasma protein binding, and body composition
- Age-related changes
  - ↓ Volume of distribution of water-soluble medications
  - ↓ Volume of distribution of lipophilic medications
  - Decrease in P-glycoprotein activity in the blood-brain barrier
  - Decreased albumin may lead to increased free fraction
  - Increased α1-acid glycoprotein may lead to decreased free fraction

### Pharmacokinetics - metabolism
- Liver is the major organ for drug metabolism
- Decreased phase I metabolism
  - Diazepam, piroxicam, theophylline, quinidine
- Relatively unaffected phase II metabolism
- Enzyme induction or inhibition does not appear to be affected

### Pharmacokinetics - elimination
- Renal excretion is the primary route of elimination
  - Age-related reduction in glomerular filtration
  - Cockcroft and Gault is a useful screening tool to assess renal function
    - Assumes stable renal function and actual body weight within 30% of ideal body weight
  - Modified Diet in Renal Disease (MDRD) equation

### Altered pharmacodynamics
- 4 possible mechanisms
  - Change in receptor numbers
  - Change in receptor affinity
  - Postreceptor alterations
  - Age-related changes in homeostatic response
Beer’s criteria

- Consensus criteria for medication use in older adults
  - Literature review
  - Expert panel- experts in psychopharmacology, pharmacoepidemiology, clinical geriatric pharmacology, and clinical geriatric medicine
- Adopted in 1999 by the Centers for Medicare and Medicaid Services (CMS) for nursing home regulation
  - Medications likely to cause problems in long-term care residents
  - Most commonly used medications causing cognitive impairment include analgesics, antidepressants, anticholinergics, and benzodiazepines (BZD)

Drugs-induced CNS depression/sedation

- Drowsiness
- Lethargy
- Decreased respiratory rate

Medications causing CNS depression/sedation

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drugs to avoid</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiolytic</td>
<td>Meprobamate</td>
<td>Shorter acting BZDs, buspirone</td>
</tr>
<tr>
<td>Long-acting BZD</td>
<td>Clorazepate</td>
<td>Anxiety: Shorter-acting BZDs</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>(insomnia use)</td>
<td>Temazepam, zolpidem, zaleplon, eszopiclone</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Chlorpheniramine</td>
<td>Cetirizine, fexofenadine, loratidine</td>
</tr>
<tr>
<td>Gastrointestinal antispasmod</td>
<td>Diphenoxylate</td>
<td>Change in diet, loperamide</td>
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<td>Carisoprodol</td>
<td>Baclofen, tizanidine</td>
</tr>
<tr>
<td>Urinary antispasmodics</td>
<td>Oxybutin</td>
<td>Behavioral therapy (urge incontinence)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Indomethacin</td>
<td>Acetaminophen (APAP), ibuprofen, COX II inhibitor (short term), allopurinol (gout)</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Amitriptyline</td>
<td>Norbuprtryline, desogronine, SSRI (except fluoxetine), bupropion, mirtazapine</td>
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MEDICATION-INDUCED COGNITIVE IMPAIRMENT

- CNS depression/sedation
- Delirium/confusion/alterted mental status (AMS)
- Extrapyramidal symptoms (EPS)

Drug-induced delirium/confusion/AMS

- Disturbance of consciousness with reduced ability to focus, sustain, or shift attention
- Change in cognition or the development of a perceptual disturbance not accounted for by dementia
- Disturbance developed over short period of time and fluctuates throughout the day
- Examination (labs, history, physical exam) finds the disturbance is caused by a medical condition, substance intoxication, or medication side effect

UpToDate, 2011. Diagnosis of delirium and confusional states. DSM IV Manual
Risk factors for medication-induced delirium

- Polypharmacy
  - ≥9 chronic medications
  - ≥12 doses of medications per day
- ≥6 concurrent chronic diagnoses
- Creatinine clearance <50 mL/min
- Low body weight
- Age >85 years old
- Prior medication-induced delirium

Medications causing delirium/confusion/AMS

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<td></td>
<td>Tolterodine</td>
<td>Flunixin or dorzolamide (benign prostate hypertrophy)</td>
</tr>
<tr>
<td>Analgesic</td>
<td>Pentazocine</td>
<td>Mid pain: APAP, ibuprofen</td>
</tr>
<tr>
<td></td>
<td>Cerivastatin</td>
<td>Moderate or severe pain: morphine,</td>
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<tr>
<td></td>
<td>Hydromorphone</td>
<td>hydrocodone/acetaminophen</td>
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<td>Diazepam</td>
<td>Sleep: temazepam, zolpidem, zaleplon, eszopiclone</td>
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Medications causing EPS

- Akathisia- motor restlessness with a compelling urge to move and the inability to sit still
- Parkinsonian syndrome- mask-like faces, resting tremor, cogwheel rigidity, shuffling gait, and bradykinesia
- Dystonias- involuntary contractions of major muscle groups
Optimal Pharmacotherapy

- Effective medications to treat conditions
- Correct doses
- Correct dosage forms
- Appropriate duration
- If appropriate, dose-adjusted for age-related and/or disease-related changes in pharmacokinetics and pharmacodynamics
- If possible avoid medication that can decrease patient function

American College of Clinical Pharmacy, 2010

Medication Appropriateness Index

- Is there an indication for the medication?
- Is the medication effective for the condition?
- Is the dosage correct?
- Are the directions correct?
- Are the directions practical?
- Are there clinically significant drug-drug interactions?
- Are there clinically significant drug-disease interactions?
- Is there unnecessary duplication with other medication(s)?
- Is the duration of therapy acceptable?
- Is this medication the least expensive alternative compared with others of equal utility?


Prevention- Avoiding polypharmacy

- Common and increasing problem in the elderly
- Increased use of dietary supplements
  - Herbals
  - Vitamins
  - Minerals
- Multiple medications have a strong correlation with adverse drug reactions
- Counsel patients/caregivers regarding this risk

Prevention- Inappropriate prescribing

- Inappropriate prescribing
  - Medications prescribed outside of accepted medical standards
  - Prescribing of medications which should be avoided because the risk outweighs the benefit
  - 92% of patients were taking at least one medication with one or more inappropriate reasons
- Avoid recommending medications on the Beer’s list
- After speaking with the patient/caregiver, match the medication with a diagnosis
- Question medications that may be a risk for your elderly patients and contact the physician

UpToDate, 2011. Drug prescribing in the elderly.
**Prevention- Medication adherence**

- Recommend cost-effective substitutions that are not at risk for causing cognitive impairment
- Counseling about most common adverse effects of medications and activities to avoid while on this medication
  - Warn patients about medications which may impair driving

**Non-pharmacologic approach**

- Improve balance and avoid falls
  - Tai Chi
  - Correction of vision problems
- Improve mental state
  - Reading
  - Playing games
  - Puzzles
  - Exercise
  - Sufficient sleep

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**Patient Case**

YC is a 70 year old woman who drives to 3 different pharmacies to pick up her medications. She is now at your pharmacy and tells you she has not been getting a sufficient amount of sleep due to her anxiety. Her elderly neighbor gave her some diphenhydramine capsules and told her “You won’t know what hit you after you take this.” She tells you it has helped her fall asleep but she doesn’t feel well rested in the morning.

**Patient Case**

Her current home medications include...

- Lisinopril 5 mg PO daily
- Simvastatin 20 mg PO qHS
- Fluoxetine 40 mg PO qHS
- Levothyroxine 88 mcg PO daily
- Diphenhydramine 50 mg PO qHS

What are some counseling points you can offer YC?

**Patient Case**

- Transfer all her prescriptions to 1 pharmacy
- Avoid diphenhydramine
  - Avoid driving when taking medications that may impair attention, focus, and coordination
- Fluoxetine should be taken in the morning or changed to a less activating SSRI

**True or False?**

- Risk factors for delirium include polypharmacy, creatinine clearance >50 mL/min, increased body mass index, and age >85 years old.
- The most common class of medications associated with cognitive impairment includes analgesics, benzodiazepines, anticholinergics, and antidepressants.
- Adverse outcomes associated with delirium include increased length of hospital stay and higher mortality rates.