Drug-Induced Cognitive Impairment in the Elderly

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Objectives
- Identify risk factors in the elderly that make them more susceptible to drug-induced cognitive impairment
- List medications associated with cognitive impairment in the elderly
- Develop strategies to improve pharmacotherapy and decrease the burden of the cognitive load

Background
- Elderly are at increased risk of medication side effects, including drug-induced cognitive impairment
  - Changes in pharmacokinetics and pharmacodynamics
  - Higher pill burden
  - Higher incidence of co-morbid conditions

Background
- Cognitive impairment is associated with:
  - Medication non-adherence
    - Increased hospitalizations
    - Increased costs
  - Even mild cognitive impairment may negatively affect medication adherence in elderly

Pharmacokinetic Changes
- Decreased renal elimination of drugs
  - Reduced renal mass
  - Decreased renal blood flow, tubular secretion, and GFR

Risk Factors
- Low weight
- Multiple comorbid conditions
  - Diabetes mellitus
  - Hypertension
  - Chronic kidney disease
  - HIV
- Polypharmacy
Drug-Induced Delirium vs. Dementia

- **Delirium**
  - Rapid onset, acute condition
  - Fluctuations in cognitive function
  - Disorientation, short-term memory impairment, altered consciousness and attention

- **Dementia**
  - Chronic impairment of cognition and memory

Medications Associated with Cognitive Impairment

Anticholinergic Medications

- **H₂ antagonists**
  - Cimetidine (Tagamet®)
  - Ranitidine (Zantac®)

- Scopolamine (Transderm Scop®)

- Oxybutynin (Ditropan®)

Tricyclic Antidepressants

- Avoid tertiary amines
  - Strong anticholinergic activity
  - Amitriptyline (Elavil®)

- Secondary amines are safer options for elderly
  - Desipramine (Norpramin®)
  - Nortriptyline (Pamelor®)

Antipsychotics

- Clozapine (Clozaril®)
- Olanzapine (Zyprexa®)
- Quetiapine (Seroquel®)
Hypnotics/ Sedatives

- Benzodiazepines
  - Higher risk with longer acting agents
    - Flurazepam (Dalmane®)
    - Diazepam (Valium®)
  - Increased risk with higher doses (>5 mg diazepam daily or equivalent)
- Barbiturates
  - Phenobarbital (Luminal®)

Cardiovascular Agents

- Digoxin (Lanoxin®)
- Class 1A antiarrhythmics
  - Disopyramide (Norpace®)
  - Quinidine (Quinidex®)
  - Procainamide (Pronestyl®)
- Diuretics
  - Hydrochlorothiazide (Microzide®)
  - Furosemide (Lasix®)

Pain Medications

- Opioids
  - Meperidine (Demerol®)
- Skeletal muscle relaxants
  - Carisoprodol (Soma®)
  - Cyclobenzaprine (Flexeril®)

Tools and Strategies to Improve Pharmacotherapy

- Beers Criteria
- Medication Appropriateness Index (MAI)
- Cognitive tests
  - CLOX
  - Trail Making Tests

Hypoglycemic Agents

- Sulfonylureas
  - Highest risk with long-acting agents
    - Glyburide (Diabeta®, Glynase®, Micronase®)
- Meglitinides
  - Repaglinide (Prandin®)
  - Nateglinide (Starlix®)
- Insulin
  - Highest risk may be with sliding scale

Improving Pharmacotherapy

- Beers Criteria
- Medication Appropriateness Index (MAI)
- Cognitive tests
  - CLOX
  - Trail Making Tests
Beers Criteria

- Criteria for determining potentially inappropriate medication (PIM) use
  - Independent of diagnosis
  - Dependent on diagnosis

CLOX Examples

MAI

- Questions to consider
  1. Is there an indication for the drug?
  2. Is the medication effective for the condition?
  3. Is the dosage correct?
  4. Are the directions correct?
  5. Are the directions practical?
  6. Are there drug-drug interactions?
  7. Are there drug-disease interactions?
  8. Is there unnecessary duplication?
  9. Is the duration of therapy acceptable?
  10. Is this drug the least expensive alternative?

Cognitive Tests

- Trail Making Tests
  - Part A
    - Circles labeled 1-25
    - Patient draws lines to connect circles in ascending order
  - Part B
    - Circles labeled with numbers (1-13) and letters (A-L)
    - Patient draws lines to connect circles in ascending order, alternating between numbers and letters

Cognitive Tests

- CLOX
  - “Draw me a clock that says 1:45. Set the hands and numbers on the face so that a child could read them.”
  - CLOX 1: Patient draws clock based on directions
  - CLOX 2: Patient observes provider drawing clock, and given opportunity to copy drawing
True/False Questions

1. Renal mass decreases with age, leading to a decreased excretion of drugs, and an increased risk of drug and metabolite accumulation in the elderly.
2. Desipramine would be expected to cause more cognitive impairment in an elderly patient than amitriptyline.
3. The Beers Criteria is a tool to identify medications that could potentially increase cognitive impairment in the elderly.

Summary

- Elderly are at an increased risk of drug-induced cognitive impairment
- Pharmacists can play vital role in identifying and preventing drug-induced cognitive impairment

References

Treatment of Insomnia, Anxiety, and Aggression in the Elderly: How many benzodiazepines is too much?

William Olsufka, PharmD
PGY2 Psychiatric Pharmacy Resident
Miami VA Healthcare System
January 26, 2015

Objectives
- Define and identify diagnostic criteria for insomnia, anxiety, and aggression per DSM-5
- Discuss the use of benzodiazepines in the treatment of insomnia, anxiety, and aggression
- Discuss the associated risks and benefits of using benzodiazepines in the elderly

Insomnia Diagnostic Criteria
- The sleep disturbance causes clinically significant distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning
- Sleep difficulty:
  - Occurs at least 3 nights per week
  - Present for at least 3 months
  - Occurs despite adequate opportunity for sleep

Insomnia Diagnostic Criteria Continued
- A predominant complaint of dissatisfaction with sleep quantity or quality, associated with one (or more) of the following symptoms:
  - Difficulty initiating sleep
  - Difficulty maintaining sleep
  - Early-morning awakening with inability to return to sleep

Anxiety Diagnostic Criteria
- Excessive anxiety and worry
- Difficult to control
- Associated with three (or more) of the following six symptoms:
  - Restlessness or feeling keyed up or on edge
  - Being easily fatigued
  - Difficulty concentrating or mind going blank
  - Irritability
  - Muscle tension
  - Sleep disturbance

Diagnostic Criteria Continued
- The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
- The disturbance is not attributable to the physiological effects of a substance or another medical condition
- The disturbance is not better explained by another mental disorder
Aggression Diagnostic Criteria

General definition:
Disruptive, impulse-control, and conduct disorder that cause clinically significant distress or impairment

Study Inclusion Criteria

Three criteria defined:
- Ever use
- Cumulative dose (Prescribed Daily Doses; PDD)
- Drug elimination half-life

Benzodiazepine (BDZ):
Brief Review

How BDZ Work

- Keep calm and eat your benzodiazepines

Study Results

- BDZ \( \rightarrow \) increased risk of Alzheimer’s Disease
  - OR 1.51 [95% CI 1.36 - 1.69]
  - Adjustment OR 1.43 [95% CI 1.28 - 1.60]
- Cumulative dose exposure
  - 1-90 PDDs: 1.09 [95% CI 0.92 - 1.28]
  - 91-180 PDDs: 1.32 [95% CI 1.01 - 1.74]
  - >180 PDDs: 1.84 [95% CI 1.62 - 2.08]
- Alzheimer’s disease more likely with Long-acting BDZ (LB)
  - LB: 1.70 [95% CI 1.46 - 1.98]
  - SB: 1.43 [95% CI 1.27 - 1.61]

Alzheimer’s Disease and BDZ Correlation?

- Case-control study
  - 1796 Alzheimer’s disease
  - 7184 controls
- All participants ≥ 66 years of age
- Followed patients 6 years prior to diagnosis

Study Conclusion

- Alzheimer’s disease risk: \( \uparrow \) 43-51%
- Risk increased with longer exposure and use of LB

Strengths

- Assessed BDZ use >5 years
- Explored dose-effect relations
- Generalizable study to the elderly

Weaknesses

- Used claims databases
- Delay between onset and diagnosis of Alzheimer’s Disease
**BDZ and Fall Risk**

- Major issue in the elderly
- 1/3 of elderly experience at least 1 fall/year
  - 15% fall 2x or more
  - 10% → serious consequences (fractures)
- Primary Risk Factors
  Impaired cognition, gait, vision, & balance

**Beer’s Criteria**

- Purpose
  - Intended to improve the care of the elderly
  - Provide a list of potentially inappropriate medications (PIMs)
  - Improve quality of life and cost
  - Reviews evidence for appropriate recommendation

**STOPP**

- Screening Tool of Older Persons’ potentially inappropriate Prescriptions
- Explicit Medicine Review Tool
- Long-term BDZ inappropriate
  - Prolonged sedation, confusion, impaired balance, and falls
- Does half-life of BDZ influence fall risk?
- Short-acting up to 24 hours

**Graded Recommendation**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Description</th>
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<tbody>
<tr>
<td>Quality of evidence</td>
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<td>Evidence includes evidence-based randomized or controlled studies in representative populations that directly assess effects on health outcomes (0.2 meta-analyses; higher quality randomized controlled trials or multiple, consistent observational studies with no significant methodological flaws showing high effect)</td>
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**Short-Acting VS. Long-Acting**

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<tbody>
<tr>
<td>Lorazepam</td>
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<tr>
<td>Oxazepam</td>
<td>Bromazepam</td>
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<tr>
<td>Temazepam</td>
<td>Chlordiazepoxide</td>
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<tr>
<td>Triazolam</td>
<td>Clonazepam</td>
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<tr>
<td>Zolpidem</td>
<td>Diazepam</td>
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<tr>
<td>Zopiclone</td>
<td>Flurazepam</td>
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<tr>
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<tr>
<td>Temazepam</td>
<td>Lorazepam</td>
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<tr>
<td>Zopkicline</td>
<td>Nortriptyline</td>
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**BEER’s Criteria**

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Study 1 Methods
- COHORT study → 1,509 participants
- “Fall calendar”
- Definition: “An unintentional change in position resulting in coming to rest at a lower level or on the ground.”
- Assessed 7 major categories of chronic somatic diseases

Study 2 Methods
- Prospective Observation Study → 564 participants
- >65 yo and went to the ED or PCP after a fall
- Exclusion:
  - No Fall History
  - MMSE <24
  - Fall secondary to traffic or work
- Medium high and very high fall-risk

Study 1 Results
- During 1-year follow-up
  - 468/1509 (31%) fell at least once
  - 174/1509 (11.5%) fell 2x or more
- Fall risk → BDZ use
  - HR 1.58 [95% CI 1.10 – 2.29]
  - Adjustment HR 1.46 [95% CI 1.00 - 2.15]
- No statistical or clinically significant difference between short and long BDZ

Study 2 Results
- 131 (23.2%) used BDZ or BDZ-like drugs
- 82 (14.5%) → Short BDZ
- 55 (9.8%) → Long BDZ
- 1-year follow-up:
  - 249 (44.1%) fell at least once
  - 130 (23.0%) fell 2x or more
- BDZ-like drugs:
  - HR 1.37 [95% CI 1.03 – 1.84]
  - Short BDZ
    - HR 1.56 [95% CI 1.13 - 2.15]

BDZ and Fracture Risk
- Meta-Analysis
  - 19 case-control and 6 cohort studies
  - Relative fracture risk ↑25%
  - Commonly seen in short BDZ
- Theories
  - Prescribed more frequently
  - Started on short and then switched to long BDZ
- Short BDZ more severe?

BDZ and Fracture Risk
- Unknown why this may occur
  - Increase in falls?
- Hip fractures most common
- More research needed
  - Elderly at higher risk of fractures
  - Bone mineral density reduction
  - Participants were >65 years
  - Did not study different doses or duration
  - Large prospective studies needed
Patient Case: MB

- 87 year old woman
  - “I’ve never had joy in my life—just tried to get through day by day.”
  - “I know it’s an addiction, but I had to clear my mind to keep living. So many times, I felt like jumping into the pit of a subway station to get it over with.”
- Carisoprodol for 15 years
- Alprazolam for 15 years (anxiety)
  - Alprazolam 1 mg four times daily
  - Denies all adverse effects

What else used? (for taper)

- Fluoxetine 20 mg daily
- Buspirone 20 mg BID
  - Adverse effects: gas, fatigue, dry skin, akathisia
- Nefazodone 50 mg at bedtime
  - Adverse effects: “Daytime hangover”
- Paroxetine 10 to 20 mg daily
  - Able to reduce to alprazolam 0.5 mg BID

Patient Case Continued

- PMH:
  - HTN
  - Pacemaker
  - Hysterectomy
  - Arthritis
- SH:
  - Non-smoker
  - Drinks minimally
- No FH of major illness

What do you think?

- Were the medications chosen appropriate?
- Were the doses appropriate?
- Should any other agents be tried?
- Should the alprazolam even be discontinued?

Current Medications

- Alprazolam 0.5 mg BID
- Diltiazem ER 120 mg
- Enalapril 10 mg daily
- Paroxetine 10 mg daily
- Diphenhydramine 50 mg as needed

Sleep Function

Changes due to older age:
- Less restorative deep sleep
- Fragmented sleep pattern
- Numerous factors associated with increased age
Sleep and BDZ

- Why do they get started?
  - Time to fall asleep
  - Sleep duration
- What do they do?
  - Suppress deep sleep stages

<table>
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<th>Long-Term Use</th>
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<tbody>
<tr>
<td>Alertness</td>
<td>Tolerance</td>
</tr>
<tr>
<td>Falls</td>
<td>Physical &amp; psychological</td>
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<tr>
<td>Anterograde Amnesia</td>
<td>dependence</td>
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<tr>
<td></td>
<td>Cognitive impairment</td>
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True/False Questions

- The Beers criteria is the most widely cited criteria used to assess inappropriate medications used in the elderly?
  - True
- Benzodiazepines are a safe long-term treatment option for insomnia and anxiety in the elderly?
  - False
- Benzodiazepines could potentially pose a risk for dementia and/or Alzheimer’s disease?
  - True

Conclusion

BENZODIAZEPINES: YOU SHALL NOT PASS!!!!
Medication-Related Falls in the Elderly

Estefania Idarraga, PharmD
PGY1 Pharmacy Resident
Mercy Hospital,
A Campus of Plantation General Hospital
Miami, FL

The Aging Population and Falls

- Between 2000 and 2050, the number of people aged 60 years and over is expected to increase from 605 million to 2 billion
- Approximately 28-35% of people age 65 and over fall each year
- As the number of older adults continues to grow, so will the number of falls

Goals and Objectives

- Understand the impact of medication-related falls in the elderly
- Identify medications associated with falls in the elderly
- Describe the role of the pharmacist in the prevention of falls

Defining a Fall

- Older people tend to describe a fall as a loss of balance
- Health care professionals generally refer to events leading to injuries and ill health
- World Health Organization (WHO) defines a fall as an event which results in a person coming to rest inadvertently on the ground or floor or other lower level

Rate of Nonfatal, Medically Consulted Fall Injury Episodes, by Age Group in 2010

- Rate per 1,000 population

Falls in Institutions

- Each year, between 700,000 and 1,000,000 people in the United States fall in the hospital
- A fall may lead to increased length of stay, poor patient outcomes and decreased reimbursement
- Centers for Medicare & Medicaid Services does not reimburse hospitals for certain types of traumatic injuries that occur in the hospital
Impact of Falls in The Elderly

- Approximately 20-30% of people who fall suffer moderate to severe injuries such as lacerations, hip fractures, and head traumas
- ~50% of elderly people who fall cannot get up without help
- In 2011, about 22,900 older adults died from an unintentional fall injury

Cost of Falls in the Elderly

Risk Factors

Socioeconomic

- Limited access to health and social services
- Inadequate housing and medical equipment
- Lack of social interactions

Environmental

- Slippery floors and stairs, throw rugs, electrical cords
- Insufficient lighting

TRUE OR FALSE

- Falls are common in the elderly and contribute to morbidity and mortality.

Risk Factors

Biological

- Decrease in homeostatic response
- Physical, cognitive, and affective capacities decline
- Decrease in baroreceptor response leading to orthostatic hypotension

Risk Factors

Pharmacokinetic Changes

- Decrease in muscle mass, renal and hepatic function, and serum albumin
- Increased half life and lower clearance of drugs with a high first-pass metabolism
- Increased rate of adverse effects for both lipophilic and hydrophilic medications
Medications and Falls

Polypharmacy and Inappropriate Medications
- Multiple pharmacies and prescribing
- Inappropriate indications
- Overprescribing
- American Geriatrics Society (AGS) Beers Criteria identifies inappropriate medication that may increase risk for falls

Non-benzodiazepine Hypnotics

Concerns
- Cognitive impairment, delirium, unsteady gait, syncope, fractures
- Similar affects to benzodiazepines seen

Considerations
- Minimal benefit
- Avoid chronic use >90 days
- Alternatives: non-drug therapy, low-dose trazodone (Desyrel®), low-dose doxepin (Sinequan®), ramelteon (Rozerem®)

Benzodiazepines

Concerns
- Sensitivity and decreased metabolism
- Risk of cognitive impairment, delirium, and fractures

Considerations
- May be appropriate for severe anxiety, seizure disorders, alcohol withdrawal
- Avoid use for treatment of insomnia, agitation, or delirium
- Shorter-acting agents not safer than long-acting ones

Fall Risk with Non-benzodiazepine Hypnotics

- Retrospective cohort study evaluated rate of fractures with the use of zolpidem (Ambien®) and benzodiazepines
- Risk of fractures with zolpidem (Ambien®) exceeded that with alprazolam (Xanax®) and lorazepam (Ativan®) and was similar to that with diazepam
- Fracture rates increased rapidly with zolpidem (Ambien®) in patients age 65 and over

True or False

- Using short-acting benzodiazepine for occasional insomnia is not likely to potentiate a fall.

Prospective observational studies evaluated the elimination half-life and fall risk
Use of short acting agents was not associated with a lower fall risk compared to long acting
Use of all benzodiazepines should be strongly discouraged in elderly patients
Concerns
- Electrolyte imbalances
- Hypotension

Considerations
- Mild chronic hyponatremia has been linked to high incidence of falls
- Adequate hydration
- Timing of diuretics
- Monitoring blood pressure


Self-matched case-crossover analysis of 1,785 long term care residents looked at relationship between change in diuretic prescription and falls
Fall risk was elevated more than 2-fold within 1 day of receiving a new prescription for a diuretic or an increase in diuretic dosage
Estimated that for every 271 loop diuretic drug changes, one excess fall occurred


Concerns
- Increased orthostatic hypotension and anticholinergic affects
- Unsteady gait, cognitive impairment, syncope
- Potential for extrapyramidal disturbances

Considerations
- Orthostatic hypotension particularly with chlorpromazine (Thorazine®), thioridazine (Mellaril®), and clozapine (Clozaril®)
- Alternatives (less anticholinergic): quetiapine (Seroquel®), risperidone (Risperdal®), ziprasidone (Geodon®)


Concerns
- Common side effects: bradycardia, hypotension
- Changes in body fat and water composition can significantly alter volume of distribution

Considerations
- Avoid antiarrythmics with vasodilator properties: procainamide (Procanbid®), quinidine (Quindine®), sotalol (Betapace®)
- Postural hypotension common with beta and calcium channel blockers
- Most antiarrythmic drugs will need dosage adjustments


Concerns
- Hypotension may potentiate falls
- Risk for orthostatic hypotension

Considerations
- Avoid alpha blockers, alpha agonists (recommended for routine treatment of hypertension)
- Avoid clonidine (Catapres®) as first-line agent
- Assess blood pressure goals/treatment duration
- Monitor blood pressure/report readings
- Counsel patient to stand up slowly

Antihypertensives

Concerns
- Fall Risk with Diuretics
- Antipsychotics
- Antihypertensives

Concerns
- Hypotension may potentiate falls
- Risk for orthostatic hypotension

Considerations
- Avoid alpha blockers, alpha agonists (recommended for routine treatment of hypertension)
- Avoid clonidine (Catapres®) as first-line agent
- Assess blood pressure goals/treatment duration
- Monitor blood pressure/report readings
- Counsel patient to stand up slowly

Cohort of 4,961 community-living adults 70 years and older, associated antihypertensive medication use with risk of serious fall injury
Subsequent injury was twice as likely among a subgroup of persons with a fall injury in the prior year
Assess potential harms vs benefits of antihypertensive medications

**Anticonvulsants**

**Concerns**
- Increased risk of falls due to central nervous system effects such as sedation, dizziness, and impaired postural control
- May activate latent psychosis, confusion, or agitation

**Considerations**
- Avoid except for use in seizures or if safer alternatives cannot be used
- Alternatives for neuropathic pain: duloxetine (Cymbalta®), venlafaxine (Effexor®), pregabalin (Lyrica®), gabapentin (Neurontin®), topicals

**Fall Risk with Anticonvulsants**
- **Ensrud, et al.**
  - Prospective cohort
  - 8,127 community-dwelling women on psychoactive medications
  - 75% more likely than non-users to fall at least once and were twice as likely to experience subsequent falls
- **Pickett, et al.**
  - Case control study
  - Older patients using anticonvulsants were more likely to present to the emergency department for injurious falls

**Antidepressants**

**Concerns**
- Tricyclic antidepressants (TCAs): orthostatic hypotension (alpha blockade), cardiac arrhythmias, and anticholinergic effects
- Selective serotonin receptor inhibitors (SSRIs): associated with similar or even larger risks, role in bone physiology

**Considerations**
- TCAs: (less anticholinergic effects) nortriptyline (Pamelor®), desipramine (Norpramin®), low-dose doxepin (Sinequan®), trazodone (Desyrel®)
- Alternatives to SSRIs: SNRIs, mirtazapine (Remeron®), bupropion (Wellbutrin®)

**Fall Risk with SSRIs and TCAs**
- **Ensrud, et al.** Case control study investigated the risk of hip fractures in 8,239 cases of community-dwelling seniors treated in hospitals
- Risk of hip fracture among those exposed to SSRIs was greater than with TCAs
- Dose effect of SSRIs on fractures was reported in Richards et al., thus underlying the importance of “starting low, going slow”

**Anticholinergics**

**Concerns**
- More sensitive to anticholinergic effects
- Increased visual impairment, confusion, delirium

**Considerations**
- First generation antihistamines, skeletal muscle relaxants, antispasmodics
- Recommend alternatives
- Anticholinergics: second generation antihistamines
- Skeletal muscle relaxants: applying heat or cold; correct seating and footwear
- Antispasmodics: fiber, fluids, polyethylene glycol (Miralax®)

**Antidepressants**

**Concerns**
- Increased sensitivity may increase falls risk by causing sedation, dizziness and psychomotor impairment

**Considerations**
- Alternatives for mild to moderate pain: acetaminophen (Tylenol®), short-term NSAID, or topicals
- Counsel patients to consult provider for dosage increases when needed

**Opioids**

**Concerns**
- Within low-potency opioids, codeine combinations demonstrated to have the highest risk of injury, a 127% greater risk per one adult dose equivalent increase
True or False

- The use of serotonin reuptake inhibitors (SSRIs) in the elderly is not associated with falls.

The Role of the Pharmacist

**Non-pharmacological recommendations**

- Proper lighting, reduction of clutter, electrical cords, throw rugs
- Suggest vision and bone health screening
- Recommend physical therapy/exercise programs
- Recommend proper shoes with low heel height and high surface contact area

Decrease polypharmacy

- Determine risk versus benefit when starting a drug or changing its dosage
- Encourage the use of one provider and one pharmacy
- Screen for medications with duplicate indications and contact the provider

Impact of a Pharmacist

- Pharmacist reviewing medications at Morton Plant Mease (MPM) Rehabilitation resulted in 47% fewer falls elderly patients
- Changes involved lower dosages or frequencies in psychoactive drugs, hypnotics, cardiovascular medication and analgesics
- Resulted in an estimated $308,000 annual savings for the facility

The Role of the Pharmacist

**Medication therapy management**

- Create a schedule with optimal timing of medications
- Evaluate for proper dosage and duration of therapy
- Assess for possible drug interactions (food, over-the-counter supplements and herbals)
- Address calcium and vitamin D supplementation

Conclusion

- As the aging population continues to grow, so will the number of medications to manage their multiple co-morbidities
- Identifying and avoiding the medications associated with falls in the elderly is an important modifiable risk factor
- Pharmacists have an important role in optimizing regimens and educating patients to reduce the occurrence of falls
Incontinence in the Elderly (It Depends!!)

Ajambar Rayamazhi
Miami VA PGY1 Pharmacy Practice Resident
DCPA 2015 Presentation

Objectives

- Discuss age and disease-related incontinence in the elderly population
- Review other causes of incontinence
- Explain treatment options for incontinence in the elderly

Urinary Incontinence Etiology

Process of micturition (process of urination)

- Micturition is controlled by the sacral micturition center of the spinal cord (S2-4)
- Sensory input is received from bladder and corresponding structures
- Motor input is then sent back to bladder via parasympathetic nerve fibers as well as to the urethral sphincter
- Bladder also receives sympathetic response to contract external sphincter. Also responsible for relaxing bladder as it fills, and relaxing outlet of the bladder as micturition is achieved

Urinary Incontinence Etiology

Process of micturition (process of urination)

- Inhibitory effects of micturition are predominantly controlled by central nervous system
- Urge to void felt between 150cc to 250cc of fluid in the bladder
- Voiding urge inhibited by central nervous system until aforementioned cholinergic stimulation occurs from voluntary voiding
- Any disruptions in any of these processes due to anatomical, physiological, psychological, or drug-induced causes may lead to urinary incontinence
- Aging process can weaken detrusor muscles and may impede complete emptying.

What is Elderly Incontinence?

- The involuntary leakage of urine or fecal matter
  - A common and often debilitating problem.
  - Causes a myriad of psychosocial, medical, and economic issues.
  - Those who suffer tend to become isolated and withdraw from social activities.

Epidemiology

- In the case of the elderly, urinary incontinence is most prevalent.
- Effects 21.1 percent of men older than 65 years and 17 to 55 percent in older females.

Types of Urinary Incontinence

Incontinence categorized as:

- Established Incontinence
  Chronic incontinence that typically involves structural or autonomic issues
- Transient Incontinence
  Intermittent or temporary incontinence caused by various other processes
Types of Established Incontinence

Four (4) main types of incontinence
- Urge Incontinence
- Stress Incontinence
- Mixed incontinence
- Overflow Incontinence

Stress Incontinence

Involuntary leakage followed by urgency
- Prolapse of pelvic structures (women)
- Damage of the sphincter
- Possibly involvement of uninhibited bladder contractions
- Can occur with effort or exertion such as coughing or laughing
- Very common

Urge Incontinence

Urinary leakage due to inability to delay voiding until reaching lavatory facilities upon perception of voiding
- Uninhibited bladder contractions
- Related to central nervous system dysfunction
  - Stroke
  - Parkinson’s Disease
  - Multiple Sclerosis
  - Obstruction of prostate
  - Status-post Prostatic Resection
- Very common

Overflow Incontinence

Leakage of urine without the urge to void or inability to void normal volumes of urine
- Anatomical obstruction (of prostatic or urethral origin)
- Hypotonic bladder condition (syphilis, diabetes, compression of spinal cord)

Uninhibited Bladder

- Also called detrusor over activity/hyperreflexia
- May be due to the following dysfunctions:
  - Defect in afferent sensory signals from urinary tract
  - Central processing of sensory signals
  - Dysfunction of detrusor muscle
- Often occurs at low bladder volumes
- 50–75% prevalence

Transient Incontinence

Associated with acute medical conditions
- UTI
- Acute illness causing fatigue, immobilization and confusion
- Drugs (notably anticholinergics)
- Psychological issues (depression accompanied by regression and dependence)
Medications with Possible Effects on Continence

<table>
<thead>
<tr>
<th>Medication</th>
<th>Incontinence Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergics</td>
<td>Impairment of emptying, retention</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Anticholinergic effects (see above)</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>Urge Incontinence</td>
</tr>
<tr>
<td>Lithium</td>
<td>Polyuria</td>
</tr>
<tr>
<td>Alpha-adrenergic agonists</td>
<td>Stress leakage (women)</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Pedal edema resulting in nocturnal polyuria</td>
</tr>
<tr>
<td>Calcium Channels Blockers</td>
<td>Impaired activity of detrusor muscle (DHPs can cause pedal edema leading to nocturnal polyuria)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Polyuria</td>
</tr>
</tbody>
</table>

Screening and Diagnosis for Elderly Incontinence

- Typically includes history and physical
- Abdominal more so with overflow incontinence due to possible distended bladder
- Neurological examination is important to identify signs of cord compression or sensation and reflex issues in the lower extremities
- Often undetected by clinicians

Postvoid Residual Studies
- Determination of amount of residual urine after voiding
  - More than 20cc - 30cc within a few minutes of postvoidance considered abnormal
  - Abnormal findings should prompt evaluation of outflow obstruction or hypotonic bladder

Laboratory testing
- Urinalysis testing may reveal underlying causes of incontinence, particularly in the case of UTI's
- In men, PSA testing is encouraged to help rule out possibility of BPH and/or prostate cancer

Urologic studies
- Cystoscopy is the most sensitive and specific urologic procedure
  - Provides direct visualization of the urethra and bladder.
  - Typically done in elderly patients who have no clear cause of transient incontinence
- Other urological studies include cystometrics, urine flow studies, urethral profilometry, and sphincter electromyography

Usefulness of some of these tests is controversial due to unknown level of specificity
Non-Pharmacological Treatment

- Readily available toilet substitutes
- Bladder retraining
- Absorbent Pads
- Pelvic floor muscle exercises
- Studies have found that these methods have questionable benefit
- Catheters
  - Indwelling catheters predispose male patients to UTI if not managed correctly
  - Used when no other form of treatment is feasible i.e. outflow obstruction that cannot be corrected surgically

Pharmacological Treatment

Stress Incontinence

- Currently nothing in the US is approved
- Duloxetine is indicated in some European countries
- Stimulates pudendal alpha-adrenergic and 5-hydroxytryptamine-2 receptors to improve urinary symptoms
- Randomized control trial of 112 men showed that effect of duloxetine quickly wore off after discontinuation and patients were more likely to discontinue due to nausea compared to placebo

Pharmacological Treatment

Urgency incontinence

- Antimuscarinic agents such as oxybutynin, tolterodine, darifenacin, solifenacin, fesoterodine, trospium
  - Reduce voluntary bladder contractions through blockage of muscarinic receptors in the wall of the detrusor muscle
  - Common adverse affects are dry mouth, constipation, blurry vision, impaired cognitive abilities and tachycardia

Pharmacological Treatment

Urgency incontinence in men with BPH

- Alpha blockers such as tamsulosin, alfuzosin, silodosin, terazosin, doxazosin
  - Enhance bladder emptying
  - Most common side effects are orthostatic hypotension and dizziness
- Antimuscarinic drugs such as oxybutynin, tolterodine, darifenacin, solifenacin, fesoterodine, trospium

Pharmacological Treatment

Stress Incontinence

- Transurethral bulking agents and perineal slings more effective in women
- Urinary sphincters more effective in men

Surgical Treatment

Indicated for patients who fail medication therapy

- Urgency Incontinence
  - Electrical stimulation, botulinum toxin via cystoscopy, augmentation cystoplasty
- Stress Incontinence
  - Transurethral bulking agents and perineal slings more effective in women
  - Urinary sphincters more effective in men

What is Fecal Incontinence?

- Involuntary loss of solid or liquid feces
- Significantly impacts patients socially and economically as well as impairs quality of life
- An underreported and rather prevalent condition, due to reluctance of patients to admit it
- Large community-based studies have shown fecal incontinence to range from 1 to 24 percent
Fecal Incontinence Etiology

Process of defecation
- Rectal distension leads to reflex relaxation of the internal anal sphincter
- As stool continues to enter the sigmoid colon, urge to defecate increases
- Upon desire to defecate, the anorectal angle is voluntarily straightened by squatting or sitting
- Increased abdominal pressure is facilitated by straining
- The resulting descent of the pelvic floor, contraction by the rectum and inhibition of the external anal sphincter results in the act of defecation

Loss of the normal process of defecation result by:
- Dysfunction of the anal sphincter
- Abnormal rectal compliance
- Decreased rectal sensation
- Altered stool consistency
- Can also be a combination

Subcategorized into two forms:
- Urge Incontinence
  Desire to defecate is present, but efforts to retain stool leads to incontinence
- Passive Incontinence
  Unaware of need to defecate before occurrence of an incontinent episode

Screening and Diagnosis of Fecal Incontinence

- History and Physical Examination
- Laboratory Measurements
  - Stool studies for patients presenting with diarrhea
- Endoscopy
  - Flexible sigmoidoscopy for patients under 40
    To rule out masses and mucosal inflammation
  - Colonoscopy for patients aged 40 and over
    To rule out inflammatory bowel disease and colorectal cancer

Anorectal manometry and endorectal ultrasound
Reserved screening for those who fail to respond to initial therapy

Defecography
Screening for patients with refractory symptoms

Screening and Diagnosis of Fecal Incontinence

- Dietary and life style modification
  - Avoiding foods and activities known to worsen symptoms (fructose, lactose and caffeine)
  - Increased physical activity
  - High fiber and low fat diet
- Medication management
  Loperamide or diphenoxylate plus atropine
  - Four randomized studies showed a reduction in fecal urgency, use of pads, episodes of incontinence and unformed stools
  Loperamide may be more effective and result in less central nervous system side effects
Treatment for Elderly Fecal Incontinence

- Biofeedback
  - Physical therapy and muscle re-training for patients refractory to lifestyle changes and medication management
- Injectable/bulking agents
  - Dextranomer stabilized with hyaluronic acid
  - Used in passive fecal incontinence
  - May enhance anal resting pressures and alleviate fecal incontinence

Treatment for Elderly Fecal Incontinence

- Anal sphincteroplasty
  - Reserved for patients who are nonresponsive to regular treatment and show signs of damage to anatomic sphincter shortly after vaginal delivery
- Sacral nerve stimulation of the above
  - Reserved for patients who are refractory to all of the above
  - Involves electrical stimulation to the sacral nerve roots
- Dynamic Graciloplasty
  - Involves continuous electrical stimulation to the gracilis muscle which is transposed around the anal canal to increase resting tone

Colostomy

- Reserved for intractable incontinence not resolved by other methods
- Involves diversion of the fecal stream

Summary

- Both urinary and fecal incontinence within the elderly population are underreported yet strongly prevalent
- Can cause a severe detriment to sociological, economic, financial and personal burden and decrease quality of life
- The aging process can have a detrimental effect to the autonomic nervous system and cause dysfunction in both signaling and reflex, not to rule out disease, pharmacological, dietary and lifestyle related causes as well.
- Screening is largely based on history and physical, followed by laboratory testing and specific as well as nonspecific screening
- There exists many nonpharmacological and pharmacological treatment options for the elderly patient population, with treatment options for refractory and intractable cases.

True/False

1. The involuntary leakage of urine, or urinary incontinence, is often detected by clinicians.
2. As we age, bladder wall (detrusor) muscles lose strength and may impede complete emptying.
3. Although diuretics can cause increased urination, they are considered a direct cause of urinary incontinence.
The Prevention and Treatment of Decubitus Ulcer

Fei Wang, Pharm.D.
PGY-1 Pharmacy Resident
DCPA CE Presentation
January 24, 2015

Objectives

- Define decubitus ulcer and its prevalence
- Identify risk factors for decubitus ulcer
- Review clinical features for decubitus ulcer
- Evaluate decubitus ulcer prevention
- Discuss decubitus ulcer care and management
- Describe roles of pharmacists in decubitus ulcer management and prevention

Epidemiology

- An estimate of 2.5 million cases per year in the United States
- Elderly patients constitute single largest group (>60%) among all patients
- Associated with increase mortality and longer hospital length of stay
- Contributed $1.99 billions in excess health care costs between 2007 and 2009

Define Decubitus Ulcer

- Pressure ulcer/bed sore

Pathophysiology

- Ischemia/tissue hypoxia
  - External pressure exceed the capillary pressure of the tissue
  - ↓O₂ and nutrient delivery
  - ↑ waste and free radical
- Irreversible tissue damage
  - >70mmHg over 2 hours
- Tissue necrosis

Impact

- Avoidable harm!
- The Joint Commission selected pressure ulcer prevention as a National Patient Safety Goal
- Implementation of CMS nonpayment policy for hospital acquired stage 3-4 pressure ulcer
- HCAHPS scores
Most Common Sites for Ulcer Development

- Pressures are greatest over bony prominences
- Tissue with different susceptibility to the pressure induced injury

![Diagram showing muscle, subcutaneous fat, and dermis/epidermis]

Other Factors

- Shear force
  - Inclined position
  - Stretching of the tissue which further damages blood vessel
- Moisture
  - Primary result of superficial lesions
  - Little evidence suggests its contribution to pressure ulcer

Stage 1

- Intact skin with non-blanchable redness in a localized area
- The area may be painful, firm, or soft, warmer or cooler

Stage 2

- Partial-thickness dermal loss
  - Shiny or dry shallow open ulcer
  - Does not include skin tear
- With or without infection

Stage 3

- Full-thickness dermal loss
  - Subcutaneous fat may be visible
  - Does not expose bone, tendon, or muscle - no deep tissue loss
- Depth varies, with or without infection

Staging

- National Pressure Ulcer Advisory Panel (NPUAP)
- The European Pressure Ulcer Advisory Panel (EPUAP)*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Non-blanchable redness</td>
</tr>
<tr>
<td>II</td>
<td>Blister(s) or other break in the dermis, with or without infection</td>
</tr>
<tr>
<td>III</td>
<td>Full-thickness tissue loss without involvement of bone</td>
</tr>
<tr>
<td>IV</td>
<td>Full-thickness skin loss with involvement of supporting structure</td>
</tr>
<tr>
<td>Unstageable*</td>
<td>Base of the ulcer is covered by slough or eschar in the wound bed</td>
</tr>
<tr>
<td>Suspected deep tissue injury*</td>
<td>Purple of maroon localized skin or blood-filled blisters</td>
</tr>
</tbody>
</table>

*National Pressure Ulcer Advisory Panel.
Stage 4

- Full thickness skin loss
  - Exposed bone, tendon, or muscle
  - Extend into supporting structure
- Depth varies, with or without infection

Miscellaneous Stages

- Unstageable
  - Ulcer covered by slough or eschar therefore the true depth cannot be determined
  
- Suspected deep tissue injury
  - When there is discolored intact skin or blood-filled blisters

Complications

- Pain and discomfort
- Infection
  - Cellulitis
  - Osteomyelitis
  - Systemic infections
- Surgery
- Psychosocial

Risk Factors

- Over 100 risk factors have been identified, but not well validated

- Most important factors
  - Immobility
  - Malnutrition
  - Reduced perfusion
    - Volume depletion, hypotension, vasoconstriction, heart failure, medication, or PAD
  - Sensory loss
    - Dementia, delirium, spinal cord injury, or neuropathy

Prevention

- The Key to improve patient outcome!
  - Risk assessments
  - Pressure redistribution
  - Supportive interventions
  - Education/quality initiatives
Risk Assessment

- Identify at-risk patients is central to prevention
- Comprehensive history and physical exam
  - Identify factors that are correctable
- National Institute for Health and Care Excellence (NICE), as well as NPUAP and EPUAP recommend the use of a risk assessment tool
  - Norton Scale
  - Braden Scale

Norton Scale

<table>
<thead>
<tr>
<th>Physical Condition</th>
<th>Mental Condition</th>
<th>Activity</th>
<th>Mobility</th>
<th>Incontinent</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 = Good</td>
<td>4 = Alert</td>
<td>4 = Ambulant</td>
<td>4 = Full</td>
<td>4 = Not</td>
</tr>
<tr>
<td>3 = Fair</td>
<td>3 = Apathetic</td>
<td>3 = Walk(help)</td>
<td>3 = Slightly limited</td>
<td>3 = Occasional</td>
</tr>
<tr>
<td>2 = Poor</td>
<td>2 = Confused</td>
<td>2 = Chair/bedbound</td>
<td>2 = Very Limited</td>
<td>2 = Usually/urine</td>
</tr>
<tr>
<td>1 = Very Bad</td>
<td>1 = Shakier</td>
<td>1 = Bed</td>
<td>1 = Incontinent</td>
<td>1 = Doubly</td>
</tr>
</tbody>
</table>

Score:_____ Score:_____ Score:_____ Score:_____ Score:_____ A score of <14 is indicative of a high risk

Braden Scale

<table>
<thead>
<tr>
<th>Sensory Perception</th>
<th>Moisture</th>
<th>Activity</th>
<th>Mobility</th>
<th>Nutrition</th>
<th>Friction &amp; Shear</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 = Completely limited</td>
<td>1 = Constantly moist</td>
<td>1 = Bed-bound</td>
<td>1 = Completely immobile</td>
<td>1 = &quot;very poor&quot;</td>
<td>1 = Problem</td>
</tr>
<tr>
<td>4 = Very limited</td>
<td>3 = Occasional moist</td>
<td>2 = Chair bound</td>
<td>2 = &quot;very limited&quot;</td>
<td>2 = &quot;probably adequate&quot;</td>
<td>2 = Potential problem</td>
</tr>
<tr>
<td>3 = Slightly limited</td>
<td>3 = Walks occasionally</td>
<td>3 = Slightly limited</td>
<td>3 = Adequate</td>
<td>3 = &quot;no apparent problem&quot;</td>
<td></td>
</tr>
<tr>
<td>2 = Poor</td>
<td>4 = Walks frequently</td>
<td>4 = No limitation</td>
<td>4 = Excellent</td>
<td>4 = &quot;does not need applied load&quot;</td>
<td></td>
</tr>
<tr>
<td>1 = Very Bad</td>
<td>4 = No impairment</td>
<td>4 = Full</td>
<td>4 = Not restricted</td>
<td>4 = &quot;needs applied load&quot;</td>
<td></td>
</tr>
</tbody>
</table>

Score:_____ Score:_____ Score:_____ Score:_____ Score:_____ Maximum score is 23, a score < 18 is indicative for high risk

Pressure Redistribution

- The most effective way to prevent pressure ulcer
  - Pressure reducing devices or surface
  - Proper repositioning

Support Device or Surface

- Classified by the National Pressure Ulcer Advisory Panel Support Surface Standards Initiative
  - Reactive support surface
  - Active support surface
  - Integrated bed system
  - Non-powered support surface
  - Overlay
  - Mattress
  - Reactive VS Active Support Surface
  - Needs applied load
  - Not necessary needs power
  - Able to change load distribution
  - Does not need applied load
  - Requires power
Positioning

- Position the patient with particular attention to vulnerable areas
  - Pillows or foam wedges should be placed between ankles and knees
  - Slightly elevated the heel
  - The head of the bed should NOT be elevated >30 degree

- Repositioning
  - Back -> one side -> the other side
  - Every 2 hours, recommend 1 hour for chair-bound patients

Rotational Bed Therapy

- Mechanical bed that continuously rotates around its longitudinal axis
  - Pressure reduction/redistribution
  - Continuous shearing force

Supportive Interventions

- Indicated on the basis of patient specific factors
  - Improve mobility
  - Improve skin perfusion
  - Provide skin care
  - Minimize excess moisture
  - Correct malnutrition

Education and Quality Initiatives

- Pressure ulcer prevention requires multidisciplinary effort
  - Sufficient knowledge
  - Communication
  - Policy development
  - Equipment upgrade
  - Audit and feedback

Management

- Reduce or eliminate underlying cause
- Document and monitor ulcer progression
- Provide wound care
- Pain control
- Optimize nutrition
- Treat infection

Documentation

- Ulcers surface area and depth
- Categorize the ulcer
- Track the progression
- Monitor the status of the dressing
Wound Care

- Wound dressing
  - Protect the wound from contamination and absorb exudate
- Topical Ointments
  - Zinc oxide or silver containing products
  - Recommended only for early stages (1-2)
  - Efficacy not well established
- Debridement
  - Remove the necrotic tissue and promote healing
  - Mechanical, surgical, or enzymatic

Topical Ointments
- Zinc oxide or silver containing products
- Recommended only for early stages (1-2)
- Efficacy not well established

Debridement
- Remove the necrotic tissue and promote healing
- Mechanical, surgical, or enzymatic

Pain, Infection, and Nutrition

- Pain
  - Initial and ongoing pain assessment with pain scale
  - Topical vs. Non-opioid vs. opioid analgesics
- Infection
  - Would culture vs. clinical evidence
  - Deep ulcer-> osteomyelitis
- Nutrition
  - Optimize protein (1.5g/kg) and total caloric intake (30kcal/kg)
  - Oral intake-> TPN
  - Role of prealbumin in this patient population is unclear

Adjunctive Therapy

- Negative pressure wound therapy
  - Portable pump $500

Summary and Roles of Pharmacists

- Avoidable harm!
- Prevention is the key
  - Identify patients with high-risk medications
  - Management hypotension/hyperfusion
  - Correct malnutrition
- Education
- Management-supportive
  - Optimize pain control
  - Antibiotic stewardship

References


T/F Questions

- Severe pain is generally not associated with decubitus ulcer; therefore, a topical analgesic such as lidocaine is the most commonly used agent for pain control
- Decubitus ulcer may lead to severe infections such as septicemia
- Correcting a patient’s malnutrition status is one of the most important strategies when comes to decubitus ulcer prevention