Geriatric Review: Medications In Older Adults

Objectives
- Identify the causes of polypharmacy in older adults and the adverse effects of polypharmacy.
- Identify changes in pharmacodynamics and pharmokinetics that occur with aging.

Prescriptions & Older Adults
- Older adults get 2-3 times as many prescriptions.
  - 44% of men & 57% of women take 5 or more medications.
  - 12% of both men & women take 10 or more medications.
  - Consume 40-50% of OTC medications which they do not disclose to PCP.
- Why?
  - More acute & chronic disease.
  - More doctors visits.
  - Fragmented with specialist care.
  - More trips to ED.
  - More side effects to medications.
    - Drugs often given to counteract a side effect of another drug.

Polypharmacy – “Many Drugs”
- Why does it happen?
  - In 2000, older adults made 200 million visits to healthcare providers.
  - 1/3 visits – no drug prescribed.
  - 1/3 visits – 1-2 drugs prescribed.
  - 1/3 visits – 3+ drugs prescribed.

Paradox of Medications – Not New
- “Medications are probably the single most important healthcare technology in preventing injury, disability, and death in the geriatric population.”
- “Any symptom in an elderly patient should be considered a drug side effect until proved otherwise.”

Adverse Drug Reactions/Interactions
- 2-3 times greater in older adults.
- Cause 10-35% of older adults hospital admissions.
- Happen because older adults:
  - Take more medications.
  - Have impaired drug metabolism due to liver & kidney changes.
  - Changes in volume distribution of drugs with fat-soluble – longer half-life & water soluble more concentrated.
Medication-Related Problem (MRP)

- Defined by Hepler & Strand
  - "an event or circumstance involving a patient’s drug treatment that actually, or potentially, interferes with optimal outcome."
  - Eight categories of MRP
    - Medical condition requires new or additional medication
    - Patient taking unnecessary drug given present condition
    - Wrong drug for patient’s medical condition
    - Correct drug, dose too low
    - Correct drug, dose too high
    - Adverse drug reaction
    - Drug interaction
    - Patient not taking drug correctly

Scope of Problem Risk Versus Benefit

- In US, estimates of as many as high as 200,000 people may die of medication-related problems or adverse drug reactions (ADR) each year.
- Risk of clinically serious ADR is 4 per 100 prescriptions, 1 in 1000 will die.
- Prescription drugs 80% of ADR, OTC 20% of ADR
- Estimates of 5-17% of hospital admissions are related to ADR
- "If adverse drug effects were classified as a distinct disease, it would rank as the fifth leading cause of death in the US."
- Medication-related problems/ADRs are estimated to cost the US $200 billion annually.

Medication-Related Problems/ADRs in Elderly - Costly Geriatric Problems

- Falls
- Cognitive Loss /delirium
- Dehydration
- Incontinence
- Depression
- End result can be
  - loss of functional capacity, quality of life and often nursing home placement is result

ADR - Preventable Problem

- Nearly one third of adverse drug events in ambulatory settings are preventable.
- Half of adverse drug events in nursing facilities are preventable.

Why A Greater Risk in Older Population

- Higher incidence of multiple chronic illness
  - CAD, Valvular disease
  - Hypertension, Stroke
  - Diabetes, Type II
  - Osteoarthritis
  - Dementia
  - Osteoporosis
  - Depression
  - Diminished hearing & vision
  - Chronic Pain

Healthcare Provider Factors that Contribute to Polypharmacy

- No med review with patient on regular basis
- Presumes that patient expects meds
- Prescribes without sufficiently investigating clinical situation
- Evidence that a particular drug is the “best” drug for a problem
  - Complicated by the existence of many problems and multiple providers
- Provides unclear, complex or incomplete instructions about how to take meds
- No effort to simplify medication regimen
- Ordering automatic refills
- Lack of knowledge of geriatric clinical pharmacology
- Fear of accusations of ageism or cultural bias
Patient Factors that contribute to Polypharmacy

- Seeing multiple providers and using multiple pharmacies
- Hoarding meds & insisting on taking meds that no longer maybe appropriate
- Do not accurately report meds taken or symptoms, can result in duplicate meds
- Assume that once medication started it should be continued
- Changes in activities, smoking, food and fluid intake can affect action of meds.

Why are older people more vulnerable?

- Deterioration of physiologic systems with aging
  - Universal
  - Vary according to individual health
  - Decreased functional reserve makes "tipping over the edge" more likely.
  - Recovery is slower
  - Less Resilience
- With this deterioration pharmacodynamics & pharmacokinetics are altered

Physiologic changes of aging

- Variable according to genes, general health and environment
- Chronologic age not as important as biologic age.
- Decreased temperature regulation
- Poor judgment, diminished cognitive capacity
- Difficulty describing symptoms or adverse effects
- Increased fat to muscle ratio, decreased body water, decreased lean body mass
- Reduction in serum albumin
  - (less protein results in more free drug)

Musculoskeletal system

- Decreased muscle mass, strength and endurance
- Decreased water content of cartilage
- Decrease in bone density

Brain and nervous system

- Decreased numbers of neurons
- Decreased circulation (vessels narrow and stiffen)
- Decreased amounts of neurotransmitters
- Diminished balance and motor coordination
- Decreased ability to process and retain information

Cardiovascular System

- Diminished efficiency
- Less reserve
- Slowed response to B/P changes
- Vessels narrow and stiffen
Gastrointestinal System
- Swallowing difficulty is common
- Slowed transit
- Reduced gastric acid
- Reduced digestive enzymes
- Reduced size and flow of blood through the liver

Renal System
- Diminished ability:
  - To clear toxins
  - Concentrate urine
    - Urine more dilute, dehydration possible
  - Conserve electrolytes
    - Reduced sodium and potassium common
    - Acidify urine

Pharmacodynamics & Pharmacokinetics
- Drugs may cause outcomes that are entirely different than what is intended
- Absorption, distribution, metabolism and excretion can all be altered

Pharmacokinetic features
What the body does to the drug that affects absorption, distribution, metabolism & excretion
- Absorption affected by other diseases that may be present
- Distribution changed by whether drug is lipid or water soluble
- Less body water and intracellular water & increased body fat and less lean muscle mass
- Drugs that bind to proteins affected by lower albumin levels
- Permit more free drug to pass the blood-brain barrier
- Extension of half-life of drugs so drugs remain active in the body longer than expected

Pharmacokinetics
- Biotransformation occurs primarily in the liver
  - Phase I (oxidation/reduction) – less active metabolites are formed
    - Long-acting benzodiazepines & tricyclics more likely reduced hepatic clearance so longer affect (half life)
  - Phase II (conjugation/detoxification) – transformation to inactive metabolites remains stable (cytochrome P450 system)
    - So need no alteration in dosage such as acetaminophen and short-acting benzodiazepines such as lorazepam and oxazepam.

Pharmacokinetics
- Changes in kidney function beginning at age 35-40 can cause glomerular filtration rate to fall at 1% per year based on age alone
- Hypertension, diabetes and chronic illness and medication that are excreted renally further impact this rate
- This change causes very narrow therapeutic index (digoxin, antibiotics, etc)
- Creatinine clearance indirect measure of GFR
- GFR Calculation Cockcroft-Gault formula
  140 – age X (weight in Kg) 72 X serum creatinine (for men)
  Multiply the final result by 0.85 (for women)
Pharmacodynamic features

- Drug action at the tissue level due to physiological and pathological changes in target and non-target organs (beta receptor sensitivity reduction – diminished response to beta antagonists & agonists)
- Drugs can be enhanced by pharmacodynamics which can increase the adverse effects to the point of toxicity and delirium
- Must evaluate total anticholinergic or dopaminergic burden of the patient’s drug regimen
- In elders, cholinergic receptors more sensitive so exaggerate adverse effects
- Net effect is heightened sensitivity of the brain to adverse effects

Drugs that pharmacodynamically can cause delirium

- Sedatives & opioid analgesics
- Hypnotics & antidepressants
- Anticonvulsants & Histamine 2 blockers
- Central-acting antihypertensives
- Lidocaine & digoxin
- Corticosteroids & NSAIDs
- Isoniazid & theophylline & anticholinergic agents

Drug Reactions Look Like Growing Old

- Unsteadiness
- Dizziness
- Confusion
- Nervousness
- Fatigue
- Insomnia
- Drowsiness
- Falls
- Depression
- Incontinence
But is 5th leading cause of death in older adults

Common iatrogenic Drug Problems

- Confusion, dry mouth, constipation, blurred vision, urinary retention and orthostatic hypotension with anti-cholinergics & antiemetics
- Confusion and unsteady gait with tricyclics
- Digoxin toxicity with normal serum concentrations
- Confusion with H2 blockers
- CNS toxicity with long-acting benzodiazepines
- Confusion with narcotics and NSAIDs

Prevention of Polypharmacy

- Assess:
  - Living situation/social supports
  - Cognition
  - Funds to purchase meds
  - Functional capacity
  - Depression

Prevention of Polypharmacy

- Careful written medication instructions
- Counseling to take meds even though feeling well
- Discourage pill-sharing
- Assess other remedies patient maybe ingesting
- Encourage pill boxes, phone checks, pill counts or other med monitoring plans
- At least yearly have patient bring in all meds, Rx, OTC, vitamins, supplements, herbal preps, etc
Recognition of Drug-Induced Reactions

- Initial step:
  - Review the medications
  - Examine temporal relationships between new meds or increased/decreased dosage or discontinuation and onset of symptoms
  - Hyperactive state – suspect cholinergic toxicity, alcohol intoxication, stimulant intoxication, serotonin syndrome, alcohol or benzodiazepine withdrawal
  - Hypoactive state – suspect sedative or narcotic intoxication, alcohol or benzodiazepine intoxication

Beers Criteria
Developed in 1991-92 and revised 1997 & 2012

- Provided explicit criteria for determining which medications were inappropriate for elderly patients
- This list of drugs with evidence based research that has lead to the recommendations not to use the medications.
  - https://www.dcri.org/trial-participation/the-beers-list/

Potentially inappropriate medications

- Psychotropics
  - Sedative/hypnotics
    - Shorter acting are preferred
      - Ativan, Ambien, Serax
    - Long acting can be dangerous
      - Restoril, Halcion, Barbiturates (avoid completely)
      - Benzodiazepines
        - Librium, Valium, Tranxene, Klonopine
        - Long half life, accumulating to toxic levels quickly if taken every day
        - Cause sedation and dizziness, profound confusion
        - Ataxia and falls

Antipsychotics (con’t)
- Used only as last resort, efficacy unclear
- Side effects:
  - Sedation
  - Anticholinergic effects: Dry mouth, urinary retention, constipation, confusion
  - Orthostatic hypotension
  - Extrapyramidal symptoms: Dystonia, pseudoparkinsonism, akathisia (a form of agitation)
  - Tardive dyskinesia (TD): Rhythmic involuntary movements of tongue, lips, jaw.

Antipsychotics (con’t)
- Newer (atypical) less likely to cause side effects:
  - Clozaril, Zyprexa, Seroquel, Risperdal, Abilify
  - Used in low doses
  - Requires ongoing evaluation of effectiveness and trials of dose reduction
  - More expensive
- Older (typical) rarely used anymore except Haldol
  - Higher incidence of extrapyramidal signs and TD
    - Thorazine, Stelazine, Prolixin, Mellaril, Haldol

Neuroleptics
- Dilantin, Tegretol, Lamictal
- Neurontin, Lyrica
- Sedation
- Ataxia
- Dizziness
Potentially inappropriate...

- **Psychotropics**
  - Antidepressants:
    - Tricyclics (Elavil, Nortriptyline)
      - Highly effective but sedating, anticholinergic, hypotension
      - Probably should be avoided even in small doses
    - SSRI's
      - Very effective but interact with other medications
      - Coumadin, benzodiazepines, statins
      - Half life should be considered
      - Celexa and Lexapro may be better

Potentially inappropriate...

- **Analgesics**
  - Opioids
    - Morphine, Vicodin, Percocet, Codeine
      - OK in small doses, constipating, sedating, confusion
    - Demerol, Darvocet, Talwin should not be used
      - Strongly anticholinergic, confusion, hallucinations
      - Not particularly effective
    - Non-opioid
      - Tylenol, Ultram usually OK
      - NSAID's: Indocin – CNS symptoms
      - All can cause silent bleeding – anemia – dizziness - falls

Potentially inappropriate...

- **Antiarrhythmics**
  - Digoxin
    - Bradycardia, dizziness and weakness
  - Amiodarone
    - May cause irregular heartbeat and dizziness
  - Beta blockers: metoprolol, atenolol,
    - May precipitate syncope (faint)
    - Can cause sedation
    - Bradycardia and weakness

Potentially inappropriate...

- **Antihypertensives**
  - Beta blockers
  - Alpha Blockers, minipres, catapress, cardura
    - Sudden drop in B/P
  - Calcium channel blockers (diltiazem, Nifidepine)
    - Short acting can cause sudden drops in B/P

Potentially inappropriate...

- **Diuretics**
  - HCTZ, Diazide, Lasix, Bumex
    - Lower B/P
    - Alter electrolytes and fluid balances
    - Cause frequent (often hurried) trip to the bathroom

Potentially problematic

- **Even antibiotics**
  - Macrolides & Fluoroquinones associated with delirium
Potentially inappropriate...

- Combinations of drugs that can lead to falls
  - SSRI + trycyclics
  - SSRI + St John’s wort (serotonin syndrome)
  - SSRI+Ultram (serotonin syndrome)
  - Coumadin and almost everything
  - Viagra and nitrates (sudden drops in B/P)
  - Benzodiazepines and antipsychotics

Potentially Inappropriate...

- Don’t forget alcohol
  - Interacts negatively with almost everything
  - An independent delirium & fall risk hazard
  - Not uncommon for elderly to drink
  - Reduced tolerance even small amounts

In Summary

Polypharmacy can lead to:

- Adverse drug reactions (ADR) – 10-20% of those admitted to medical services due to OTC meds
  - # of drugs is single greatest risk for ADR
- Drug-drug reactions
- Decreased medication compliance
- Poor quality of life
- Unnecessary drug expense

Geriatric Considerations

- Believe any new symptom is a side effect of current medications even if no new medications until proven otherwise.
- Medications prescribed more than twice daily will not be taken properly.
- Older adults will have difficulty remembering the medications they are taking reliably so lists or “brown bag” analysis is important.