

Pharmacotherapy in the Older Patient

Case

Mrs. Smith is an 88 year old woman with a history of coronary artery disease, atrial fibrillation, diabetes mellitus type 2, osteoporosis, and depression who is admitted after a fall at home. She was walking from her bedroom to the bathroom during the night when she lost her balance and fell. She developed sudden pain in her right hip and could not move after the fall. Unfortunately, she lives alone and was unable to get up until her part-time caregiver arrived at 8:00 am the next morning. She was brought to the emergency room for evaluation of her right hip pain and is found to have a hip fracture. She is admitted to the Geriatric service for further management of her fracture.

- *How many medications do you think she takes?*
- *What are some potential medication side effects that might have contributed to her fall?*
- *Is her creatinine clearance normal? Why or why not? (Think about her chronic conditions & acute event.)*

Background

- Adults over 65 years old comprise about 13% of the population and consume:
 - 25 - 30% of all prescription drugs
 - 40% of all non-prescription drugs
- The average number of medications for:
 - Community-based patients is 4.5
 - Nursing home patients is 9
- Approximately 30% of hospital admissions in elderly patients may be linked to drug-related problems or drug toxic effects.

Changes in Pharmacokinetics with Age (“What the body does to the drug”)

- Absorption – little to no change
- Distribution
 - Increased fat to lean ratio
 - water soluble drugs have a lower volume of distribution and less time is needed to reach steady state (e.g. lithium, digoxin)
 - lipid soluble drugs have a higher volume of distribution and more time is needed to reach steady state (e.g. benzodiazepines)
 - Decreased protein & albumin
 - Increased unbound, active levels of drugs that usually bind to albumin (e.g. warfarin, phenytoin, valproic acid, lorazepam, ceftriaxone)

- Metabolism
 - Phase I metabolism – oxidation (e.g. cytochrome P450), reduction & hydrolysis: declines with age; decrease is likely related to decreases in hepatic blood flow and liver mass
 - Phase II metabolism – conjugation: less affected by aging

- Elimination
 - Age-related decline in glomerular filtration and renal function due to decrease in renal mass, renal blood flow and number of functioning nephrons
 - Creatinine clearance decreases about 10% per decade after age 20

Polypharmacy

- General
 - Definition: taking multiple medications
 - Dilemma: Guidelines and medical conditions often require multiple medications
 - Rather than limit the number of medications, evaluate for appropriateness

- Potential Causes of Polypharmacy
 - Increased prevalence of multiple medical conditions
 - Multiple providers
 - Multiple pharmacies

- Consequences of Polypharmacy
 - Adverse drug events
 - Drug-drug interactions
 - Duplication of therapy
 - Decreased quality of life
 - Unnecessary financial costs

Adverse Drug Events

- Risk factors
 - 6 or more diagnoses
 - number of medications
 - < 5 drugs = 4% risk
 - 6-10 drugs = 10% risk
 - 10-15 drugs = 30% risk
 - > 15 drugs = 55% risk

- prior history an adverse drug event
 - low body weight
 - >85 years old
 - creatinine clearance <50 ml/min
- “Updating the Beer’s Criteria for Potentially Inappropriate Medication Use in Older Adults” (*Arch Intern Med.* 2003; 163:2716-2724) – Discuss Table 1 and Table 2
 - “Drugs that May Cause Psychiatric Symptoms” (*The Medical Letter.* 2002; 1134:59-62) – Review Tables
 - Potential Side Effects of Common Medications
 - Tertiary amines (amitriptyline, imipramine): anticholinergic side effects including sedation; orthostatic hypotension due to alpha-adrenergic blockade
 - SSRI (fluoxetine, paroxetine, sertraline): fluoxetine has a longer half life and has been associated with anorexia, nausea, and agitation; all may cause hyponatremia
 - bupropion (Wellbutrin): immediate release is associated with dose dependent seizure activity, therefore, sustained release preferred
 - benzodiazepines: can cause daytime drowsiness, impair cognition, increase body sway; short-acting agents are preferred over long-acting
 - risperidone, olanzepine: orthostatic hypotension due to alpha-adrenergic blockade; parkinsonism; extrapyramidal effects; and potential for onset of diabetes
 - digoxin: accumulation can cause anorexia, delirium, & cardiac toxicity; adjust dose for renal function
 - NSAIDs: gastrointestinal hemorrhage; CNS effects such as drowsiness or confusion; worsening renal function (decreased renal prostaglandins); hyperkalemia (NSAID-induced hypoaldosterone, hyporenin state); edema and/or hypertension due to retention of salt and waters (decreased renal blood flow and increased sensitivity of renal tubular cells to ADH)
 - antihistamines (diphenhydramine, hydroxyzine): anticholinergic and CNS effects; diphenhydramine is commonly found in OTC allergy, cold and sleep medications
 - opioids: constipation; CNS effects such as drowsiness or confusion; avoid meperidine (active metabolite increases risk for seizure) and propoxyphene (similar analgesia to acetaminophen with opioid side effects)]

Most Frequently Omitted Medications (...left off admission or discharge orders when indicated)

- calcium & vitamin D
- iron supplementation for post-operative patients with concomitant bowel prophylaxis
- cholesterol-lowering agents
- oral hypoglycemic agents
- bronchodilators
- pain medications
- potassium supplementation
- stool softener

Pearls for Prescribing and Managing Medications in Older Patients

- Regular review of patient medications including non-prescription drugs and herbal medications
- Start low and go slow
- Provide clear dosing instructions
- Longer intervals between doses (e.g. every 8 hours rather than every 6 hours)
- Longer periods between changes in doses
- Encourage the use of pillboxes
- Consider cost to the patient and opportunities for pharmaceutical company-subsidized prescription programs
- Keep in mind the following questions when reviewing medication lists:
 - Is each medication still indicated?
 - Could any of the patient's complaints be from the medication?
 - Are there any drug-drug or drug-disease interactions present?
 - Is the benefit-to-risk ratio still the same as when the medication was started?
 - Is non-drug therapy an option?
 - Does the patient need additional education on the medication?

Tutor Guide

How many medications do you think she takes?

This is an exercise just to get the residents thinking about how different disease processes can often require multiple medications, and how this can lead to a long medication list. Encourage the residents to think about the potential number of medications and how disease processes often require multiple drugs with multiple side effects. Have them try to generate a potential list.

For example,

CAD – ASA, statin, ACEI, beta blocker, fish oil

Atrial fibrillation – beta blocker and/or digoxin, ?coumadin

DM – hypoglycemic agent, glucophage, insulin

Osteoporosis – bisphosphonate, calcium with Vitamin D

Depression – SSRI, ?add'l agent for sleep or anxiety

What medication side effects might have contributed to her fall?

Ask the residents to look over the medication list that they generated and suggest potential side effects that could have contributed to her fall.

For example,

Hypotension from ACEI, BB

Bradycardia from BB, digoxin

Hypoglycemia from sulfonylurea agent or insulin

Hyponatremia from SSRI

Is her creatinine clearance normal? Why or why not? (Think about her chronic conditions & acute event.)

No. The residents will probably know that her creatinine clearance is not normal. The physiologic changes of aging with are described briefly in the handout. Discuss with them potential chronic and acute causes of decreased creatinine clearance in this patient. Emphasize the importance of renal function when selecting and dosing medications.

For example,

Potential chronic factors for her decline in creatinine clearance include: the expected decrease associated with aging; diabetes and associated nephropathy; history of atherosclerotic disease; potential for effects of medications such as ACEI, digoxin.

Potential acute factors that might contribute to a worsened creatinine clearance: elevated CK/rhabdomyolysis from her fall and being down for hours; dehydration.

After spending 5 – 10 minutes on the case, review the rest of the handout with the residents. Spend some time looking over the Beer's list of inappropriate medications and the Medical Letter list of drugs with psychiatric side effects.