Drug Interactions and Polypharmacy

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Objectives

- Discuss etiology of various adverse drug reactions
- Define polypharmacy
- Discuss risks of polypharmacy in the elderly
- Identify risks for polypharmacy
- Review the principles of the BEERS list
- Identify ways to prevent and manage polypharmacy
Definition of drug interaction

- Chemical or physiological reaction that can occur when two different drugs are taken together
  - Drug-drug
  - Drug-diet
  - Drug-endogenous chemical
  - Drug-test
Epidemiology

• Adverse drug reactions secondary to drug interactions are estimated to be 6-22%

• Patient populations at highest risk
  – Geriatric
  – Critical Care
  – Complicated surgical patients
Outcomes of drug interactions

- Disease progression
- Increased monitoring
- Increased length of stay and healthcare cost
- Decreased productivity and lost wages
- Decreased patient and family satisfaction
- Injury
- Death
Patient Risk Factors

- **Multiple disease states**
  - Cardiac disorders
  - Diabetes
  - Psychiatric disorders
- **Renal or hepatic diseases**
- **Multiple prescribers**
- **Multiple pharmacies**
- **Polypharmacy**
Patient Risk Factors

• Drugs associated with interactions
  – Anticoagulants
  – Antiepileptic
  – Antipsychotics
  – Antibiotics
  – Endocrine agents
  – Antiarrythmics
Pharmacodynamic drug interactions

- What the drug does to the body
- Alterations in the end-organ response to a drug
  - Change in receptor binding
  - Decrease in receptor number
  - Altered response to a receptor
- Synergism
  - Effect more than sum of two drugs alone
- Antagonism
  - Effect less than sum of the two drugs
    - Competitive
    - Noncompetitive
Pharmacokinetic drug interactions

• Increase in receptor response in elderly
  – Benzodiazepines
  – Warfarin
  – Opiates

• Some organs have increased response to drug
  – CNS
  – Bowel
  – Bladder
  – Heart
Pharmacokinetic Drug Interactions

• What the body does to the drug
  – Absorption
  – Distribution
  – Metabolism
  – Excretion

• Mediators
  – Stomach and small intestine absorption
  – Protein binding
  – Liver metabolism
  – Renal function
Pharmacokinetic drug interactions

• Absorption
  – Changes in GI motility
    » Increased: reduced absorption
    » Decreased: increased degradation
  – Changes in pH
    » Some drug require a specific pH to be activated or absorbed appropriately
  – Chelation
    » Irreversible binding of the drug
    » Separate administration of drugs by at least 2 hours
Pharmacokinetic drug interactions

- Antacids can decrease absorption:
  - Phenytoin
  - Quinolones
  - Ketoconazole
  - Iron

- Drugs that alter GI motility
  - Anticholinergics
  - Ant diarrheal medications
  - Laxatives
Pharmacokinetic Drug Interactions

- **Distribution**
  - Effects transport of a drug to desired destination
    - Volume of distribution
    - Protein binding
    - Drug solubility
  - All these factors can be altered with age
    - Decrease in body water composition
    - Decrease in plasma protein concentration
    - Increase in adipose tissue
Pharmacokinetic drug interactions

- Decrease in plasma protein concentration
  - Increased amount of free (active) drug in body
    » Highly protein bound drugs (warfarin, phenytoin)

- Decrease in total body water → decreased Vd of water soluble drugs
  - Increased serum concentration

- Increase in adipose tissue → larger Vd for lipid soluble drugs
  - Prolongs the half-life of drug
  - Important for drugs that affect the CNS
    » Barbiturates and benzodiazepines
Pharmacokinetic Drug Interactions

- Metabolism
  - 2 major ways of metabolism
    » Phase 1
      - P-450 enzyme system
        » Major source of drug interactions
        » Declines with age
        - Can result in active metabolites
    » Phase 2
      - Conjugation
        » Acetylation
        » Glucuronidation
        » Sulfation
Pharmacokinetic Drug Interactions

• Excretion
  – Determined by renal function
    » Renal function decreases with age
    » Use creatinine clearance to determine renal function
      – Adjust dosing based on clearance
  – Creatinine Clearance (Cockcroft-Gault Equation)
    » \( (140 - \text{Age}) \times \text{Wt (kg)} \times 0.85 \) (for females)
    » \( (72 \times \text{Scr}) \)
    » Be careful of falsely elevated clearance!
Drug interactions

• Pharmacodynamics and pharmacokinetics change as a person ages
  – Longer duration of activity of a drug
  – A greater or lesser drug effect
  – An increase in adverse drug reactions
Polypharmacy

- Many definitions
  - Greater than or equal to 5 drugs
  - Use of multiple medications
  - Use of at least one potentially inappropriate drug
  - Underutilization of drugs
Polypharmacy

- Risks for polypharmacy include:
  - Increasing age
  - Chronic disease states
    - CAD, Stroke, CHF, DM, COPD
  - Multiple prescribers
  - Multiple office visits
  - Long-term care resident
Polypharmacy prevalence

- **Direct correlation between age of patient and number of medications taken daily**
  - > 90% of older adults take at least one prescription daily
  - Most take two or more prescriptions daily
- **Long term care residents**
  - Three or more medications are taken daily by 2/3 of the residents
  - Seven different medications per patient per day on average
  - 2/3 of nursing home residents will experience an ADR over 4 years
    - 1:7 results in hospitalization
- **Hospitalized older adults**
  - 10-17% of hospital admissions in the older adult are related to an ADE
  - Patients receive 8 different medications per hospitalization on average
  - 19% of major complications in the hospital are related to medications
Polypharmacy

- Risks of polypharmacy include:
  - Medication interactions
  - Medication non-adherence
  - Cognitive impairment
  - Falls
  - Sedation
  - Hospitalizations
  - Adverse drug events
  - Death
Managing polypharmacy

- Have a clear indication to prescribe new drugs
- Carefully weigh the risks vs. benefit
- Start low, go slow
- Make only one change at a time if possible
- Inquire about the use of OTC and alternative medications
- Review the patient’s list of medications
- Monitor renal function
- Simplify medication schedules
  - Combination medication
  - Once daily dosing
  - One drug with multiple indications
  - Look for drugs that are being used to prevent adverse effects of other drug
Beers Criteria

- Developed in 1991 for SNFs
- Expanded to all settings in 1997
  - Updated in 2003 and 2012
- 11-member expert panel:
  - Geriatricians
  - Nurses
  - Pharmacists
  - Research and quality measure experts
- Medications categorized by:
  - Organ system or therapeutic category
  - Disease or syndrome
Summary

- Polypharmacy will continue to be a concern as our population ages.
- Polypharmacy increases the risks of adverse drug reactions.
- Polypharmacy can be part of the optimal treatment of medical conditions:
  - Monitor
  - Alter regimens as needed
  - Treat the patient, not the value!
References

Questions?