Drug Use in the Elderly

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I will prescribe regimens for the good of my patients according to my ability and my judgment and never do harm to anyone.

(Hippocrates, ~ 400 BC)
The percentage of population with prescriptions, and the number of medications per individual, increase with age.
Features of Polypharmacy

- Medication not indicated
- Duplicate medications
- Concurrent interacting medications
- Contraindicated medications
- Inappropriate dosage
- Drug treatment of adverse drug reaction
- Improvement following discontinuance
Pharmacological Principles

- Pharmacological agents work via **high affinity binding** to their cellular targets (receptors).
- **Agonist** binding to receptors initiates physiological functions.
- **Antagonist** binding to receptors blocks agonists from gaining access.
Pharmacokinetics

• Defined as: The handling of a drug within the body
  – Including:
    • Absorption
    • Distribution
    • Metabolism
    • Elimination
Pharmacokinetic Principles

- absorption
- plasma protein binding
- free drug in circulation
- tissue storage (fat, muscle, bone)
- biotransformation
- elimination
- target site availability
Pharmacokinetic Factors

drug solubility
  • determines absorption and distribution parameters
  • the partition coefficient of a drug is determined by a ratio of its fat solubility and its water solubility

therapeutic window
  • the concentration range at which a drug is effective without causing undesirable physiological effects

adverse drug reactions
  • undesirable side effects of drug therapy
  • may be dose-related or idiosyncratic
Predisposing factors to adverse drug effects in the elderly

• Physiologic changes due to aging
• Drug - disease interactions
• Drug- Drug interactions (polypharmacy)
• Compliance
  – cognition
  – functional status
  – personal beliefs
  – financial issues
Other Risk factors

- Female gender
- Low educational status
- Low socio-economic status
Age-related changes which affect pharmacokinetics

- decreased lean body mass
  - affects drug distribution
- decreased levels of serum albumin
  - affects drug distribution
- decreased liver function
  - affects drug metabolism/biotransformation
- decreased renal function
  affects drug elimination
Drug absorption changes in the elderly

gastrointestinal system (rarely significant clinically)
• acid production generally unchanged
• multiple prescriptions increase the probability of drug-drug interaction which may alter absorption
• splanchnic blood flow decreases (with little effect on drug absorption)
Pharmacokinetics: distribution

- affects the concentration of drug available at the target
- solubility: hydrophilic vs. lipophilic drugs
- protein binding
- \( C = \frac{D}{V_d} \)
  - \( C \), concentration
  - \( D \), dose
  - \( V_d \), volume of distribution

 absorption

 plasma protein binding

 biotransformation

 tissue storage (fat, muscle, bone)

 elimination

 target site availability
Drug distribution changes in the elderly

**fluid and tissue compartments**
- decrease in total body water
- increase in fat compartment
- decrease in muscle mass

**plasma drug-binding proteins (rarely significant clinically)**
- decrease in serum albumin levels
- no change in α-acid glycoprotein levels
Pharmacokinetics: biotransformation

**enzymatic reactions preparing drugs for elimination**

**Phase I reactions:**
- oxidation: catalyzed by cytochrome P$_{450}$ enzymes

**Phase II reactions:**
- conjugation: addition of small chemical groups which increase solubility to facilitate elimination
Drug metabolism changes in the elderly

liver

- decrease in hepatic blood flow often associated with decreased First Pass Effect
- Phase I metabolism decreased
- Phase II metabolism generally preserved
Pharmacokinetics: elimination

• removal of drug from the body by **excretion**

• **renal** elimination:
  - glomerular filtration
  - tubular secretion

• other minor pathways of elimination:
  - feces
  - breath
  - sweat
  - saliva
Drug elimination changes in the elderly

decrease in renal functions

- decreased blood flow to the kidneys
- decreased glomerular filtration
- decreased tubular secretion
- decline in creatinine clearance
- serum creatinine is NOT an accurate reflection of creatinine clearance in the elderly
Pharmacodynamics

• study of the **interaction** between a pharmacological agent and its target tissue
• Involves:
  – the mechanism,
  – intensity,
  – peak and
  – duration of a drug’s physiological actions
Physiological changes in elderly patients affecting pharmacodynamics

**target organ changes**
- decreased desirable effects of pharmacotherapy
- increased adverse effects

**homeostasis changes**
- decreased capacity to respond to physiological challenges and the adverse side effects of drug therapy (e.g. orthostatic hypotension)
Adverse Drug Reactions

The elderly are 2-3 times more at risk for adverse drug reactions due to:

- reduced stature
- reduced renal and hepatic functions
- cumulative insults to the body (e.g., disease, diet, drug abuse)
- higher number and potency of medications
- altered pharmacokinetics
- noncompliance
Common problems of drug administration in the elderly

- **reduced homeostasis**
  - decreased renal and hepatic functions
  - increased target organ sensitivity

- **polypharmacy**
  - increased chance of adverse drug reactions

- **lack of available data**
  - fewer clinical trials on elderly populations

- **non-compliance**
Geriatric Assessment

- Physical Assessment
- Cognitive Assessment
- Psychologic Assessment
- Social Assessment
- PHARMACOTHERAPY – key component!
Utility and clinical significance

• positive correlation between potentially inappropriate drug prescribing, as defined by the Beers criteria, and adverse drug reactions

• Geriatric evaluation and management reduces serious adverse drug reactions by 35%

• Reduces suboptimal prescribing, in frail elderly patients.

Chang C.M. *Pharmacotherapy* 2005; 25: 831-8
Clinical Significance

• Inappropriate medication use increased the likelihood of experiencing at least one adverse health outcome (hospitalizations, emergency department visits, or deaths) more than twofold.

Perri M. *Ann Pharmacother* 2005; 39: 405-11
Good news

• significant decline in the use of potentially inappropriate drugs by elderly patients,
• particularly those drugs linked to the most severe outcomes. (25% - 21%)

Bad news

• Approximately 7 million elderly patients still received potentially inappropriate drugs in 1999

• Underscoring the continued need for effective interventions to improve prescribing for this vulnerable population.

Rules of prescribing in older adults

• Start low, go slow
• Try to limit number of medications and avoid prescribing “a pill for every ill”
• Try not to start two drugs at the same time
• Make sure it is the right dose
• Avoid “inappropriate medications” - Beers criteria
• Watch out for potential drug-drug, drug-disease interactions
• Make sure patient and caregiver understand what the medication is for, how and when to take it, possible side effects
• Avoid expensive new medications that have not been shown to be superior to less expensive generic alternatives
Rules of prescribing

- Ask patient about all medications (including OTC, herbal prep)
- Ask patient how each medication is being taken
- Look for medications with duplicate therapeutic or pharmacologic profiles
- Eliminate unnecessary medications
- Simplify the medication regimen – fewest possible number of medications and doses per day
- Always review any changes in writing with the patient and caregiver
- If possible, use technology to monitor parameters of efficacy and eliminate duplicative therapy, and also to detect potential drug–drug interactions and drug disease interactions
Considerations for pharmacotherapy in the elderly

- Is drug therapy required?
- Choice of appropriate drug and preparation
- Dosage regimen to accommodate changes in physiology
- Detailed monitoring and periodic re-evaluation of drug therapy
- Clear and simple instructions

*Figure 1. Effects of medication reduction on hospitalization and death rates.*
Summary

- changes in the physiology of the elderly alter responses to drug therapy
- pharmacokinetic changes affect the effective concentration of drug in the body
- pharmacodynamic changes alter the body’s response to the drug therapy
- adverse drug reactions are more common in the elderly and can be avoided with better primary care
Quality of medication prescribing in Belgian nursing homes
Results and conclusions are based on analyses of the databank of the field study Prescribing in Homes for Elderly in Belgium (PHEBE) performed in order of the Belgian Health Care Knowledge Centre

On behalf of the research consortium:
PHEBE

• A cross-sectional descriptive study
• Nursing homes (> 30 beds, including long term care beds) in the provinces of Antwerp, East Flanders and Hainaut (public and private homes)
• 2510 residents in 112 nursing homes were randomly selected
Chronic medication

- 1.1% of the residents had no medication
- 22.7% of the residents had 1-4 chronic medications
- 53.1% of the residents had 5-9 chronic medications
- 20.8% of the residents had 10-14 chronic medications
- 2.1% of the residents had more than 14 chronic medications
Prevalence of medication usage per therapeutic group in Belgian Nursing homes

[Bar chart showing medication usage per group]
Quality of medication prescribing

Three existing sets of prescribing quality indicators, adapted to the setting of the elderly, were applied

- ACOVE Criteria (Assessing Care of Vulnerable Elders) for underprescribing
- Beers Criteria for inappropriate prescribing
- Bednurse Criteria (Bergen District Nursing Home Study) for nursing home residents
Results

Underutilisation according to 7 ACOVE criteria was observed with regard to cardiovascular risk in heart failure (HF), diabetes and osteoporosis respectively

- **23 %** of residents with HF did not receive **beta blockers**
- **20 %** of residents with HF did not receive **ACE-I**
- **18 %** of residents with **myocardial infarction** in their medical history did not receive **beta blockers**
- **15 %** of residents with osteoporosis did not receive **bisfosfonates/VitD/Calcium**
- **11 %** of residents with **myocardial infarction** in their medical history did not receive **aspirin**
- **9 %** of residents with **diabetes** did not receive **aspirin**
- **8 %** of residents with **osteoporosis** who received bisphosphonate or Vit D did not receive **calcium supplements**
Beers Criteria: % of residents scoring on individual items (N=1,730)

- **clorazepate potassium**
- **fluoxetine**
- **dipyridamole**
- **amitriptyline**
- **diazepam**
- **ergoloid mesylates**
- **nifedipine**
- **amiodarone**
- **oxybutynin**
- **digoxin**
• 12 % of the residents used antipsychotics
• 25 % of the residents used a combination of antidepressants and antipsychotics or benzodiazepines
• 4 % of the residents used multiple antidepressants
• 2 % of the residents used long-acting benzodiazepine
• 4 % of the residents used chronic NSAID
• 11 % of the residents used combination of medicines with a risk of hyperkalemia
Conclusions

- Beta blockers and ACE-I are not often enough prescribed in residents with heart failure as well as post-myocardial infarction
- A limited group of inappropriate use of digoxine, oxybutinine and amiodarone was identified by Beers Criteria
- A high prevalence of chronic use and combination of psychotropic medication