



How to Teach About Drugs and Aging

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Challenges

- Prescription pad: Internist:: Scalpel: Surgeon
- Artificial split between theory and practice
- 60 minutes for key issues

Drugs and Aging-What you need to know

- What's different about old people that affects drug prescribing
- How to avoid getting into trouble with drugs in old people
- Specific examples for discussion

“It’s just because I’m OLD”

- FALSE
- You must understand the underlying pathophysiology of diseases, normal pharmacodynamic and pharmacokinetic changes with aging, and drug-drug and drug-disease interactions!!

Problems with data

- Variability between individuals
- Oldest-old often excluded from trials
- Data from “healthy” old

*What's different about old people
that affects drug prescribing*

What's different about old people that affects drug prescribing

- More diseases
- More drugs prescribed
- Pharmacokinetic changes
- Pharmacodynamic changes

Age-Related Pharmacokinetics

- Absorption
- Distribution
- Metabolism
- Elimination

Changes in Absorption

- Gastric acidity
- Splanchnic circulation
- First pass effect
- Surface area
- **Overall effect: Minimal**

Clinical Scenario

- Mr. J is a healthy 84 yo man who takes no medications and only occasionally drinks alcohol. During a routine visit, he mentions that when he was thirty, he was able to drink a six pack of beer without feeling any effect. Now, he notices that he feels intoxicated after two beers.
- Why?

Clinical Scenario part 2

- A few months later, Mr.. J's son suddenly dies. Both he and his healthy grandson are distressed and suffer insomnia. Both of them get prescriptions for diazepam 5 mg. While both note improvements in sleep, Mr.. J feels groggy well into the next day when he takes the diazepam.
- Why?

Changes in Distribution: Body Composition and Age

- Decrease in total body water and lean body mass
- Increase in body fat
- Reduction in loading dose for water soluble drugs (e.g., aminoglycosides, digoxin)
- Increased duration of effect of fat soluble drugs (e.g., benzodiazepines)

Clinical Scenario

- Mrs.. Q is a 78 yo woman with lung cancer requires 50 mcg of fentanyl for analgesia during her bronchoscopy. 6 months later, after her disease had progressed, this same dose caused apnea.
- Why?

Changes in Distribution: Protein Binding

- Altered concentrations of proteins with aging and disease
- Alterations in protein binding
- Interpret drug levels appropriately

Clinical Scenario

- Mr. G is a 78 yo man who is in the CCU after an episode of V. fib. He is in NSR on a Lidocaine drip. Twelve hours later, he suffers an MI and becomes slightly hypotensive. Over the next 24 hours, he becomes increasingly confused.
- Why?

Changes in Metabolism

- Reduced hepatic mass
- Reduced hepatic circulation
- Decreased phase I metabolism
- No change in phase II metabolism

Clinical Scenario

- Mrs.. P is a 98 yo woman who has CAD and DM. She has been on a stable regimen of insulin, atenolol, aspirin, and simvastatin for over 10 years. During this time, her resting pulse has declined from 64 to 48.
- Why?

Changes in Elimination

- Decline in glomerular filtration and tubular excretion
- Estimation of Creatinine Clearance:
 - Cr Cl = $\frac{[140 - \text{Age (y)}] \times \text{Weight (kg)}}{72 \times \text{Cr}}$
 - Multiply total by **.85** if pt is female

Age-Related Pharmacodynamics

- Autonomic nervous system
- Central nervous system
- Gastrointestinal system

Clinical Scenario

- Mrs. T is a 78 yo woman with essential htn who is given verapamil. At her follow-up visit, her blood pressure has responded well but she complains of lightheadedness when going from a supine to a standing position.
- What is the pathophysiology?

Age-Related Pharmacodynamics: *Autonomic nervous system*

- Decreased baroreceptor response
- Increased blood pressure sensitivity to vasodilatory agents

Age-Related Pharmacodynamics:

Central nervous system

- Increased effect at equal concentration
 - Benzodiazepines
 - Narcotics

Clinical Scenario

- Mrs. M is a 65 yo woman with hypertension, diabetic neuropathy, and mild Parkinson's. Her symptoms are well controlled with hydrochlorothiazide, carbidopa/levodopa, nortryptiline, enalapril, and insulin. She develops 4 dental caries over a period of a year.
- Why?

Age-Related Pharmacodynamics: *Gastrointestinal system*

- Xerostomia

*How to avoid getting into trouble
with drugs in old people*

How to avoid getting into trouble with drugs in old people

- Use proper prescribing etiquette
- Watch for drug-drug, drug-disease, and drug-food interactions
- Don't prescribe bad medications

Appropriate Drug Prescribing (proper etiquette)

- Review current prescription and non-prescription medications
- Ask about drug allergies, adverse reactions, use of alcohol
- Start low and go slow but treat adequately
- Maximize dose before switching to another drug
- Personal formulary

*Watch for drug-drug, drug-disease,
and drug-food interactions*

- Use ePocrates or similar program
- For drug-drug interactions, click on drug interactions
- For drug-disease interactions, click on contraindications/cautions
- www.drug-interactions.com

Clinical Scenario

- Mrs. N is a 74 yo woman with osteoporosis and new onset dysuria. She takes alendronate weekly and daily calcium and vitamin d supplements. She begins ciprofloxacin for a presumed UTI but calls 3 days later when her symptoms have not improved.
- Why is she not better?

Drug interactions: absorption

- Cations may chelate antibiotics (quinolones, tetracycline)
- Binding resins, psyllium, sucralfate
- Antacids may prevent absorption (ketoconazole)

Clinical Scenario

- Mr... G is a 78 yo man who is hospitalized for treatment of nursing home acquired pneumonia and hypernatremia. He experiences seizures which do not respond to the phenytoin which was added to his iv solution of D5W
- Why does he continue to have seizures?

Drug interactions: absorption

- Interactions can occur outside the body
- Phenytoin precipitates in dextrose solution
- Amphotericin precipitates in saline (can erode bladder wall if used for washing)

Clinical Scenario

- Mr. Z is a 84 yo man with a fib and BPH. He takes tamsulosin, warfarin, and atenolol. He develops new dysuria and is given TMP/SMX empirically for a UTI. In 3 days, he calls because he has developed hematuria.
- Why?

Drug interactions: distribution

- Protein “bumping” not a significant source of interactions

Drug interactions: metabolism

- Phase I metabolism—cytochrome P450
- Metabolism can activate or inactivate drug
 - 2C9 inhibited by sulfamethoxazole
 - 2C9 responsible for metabolizing S-enantiomer of warfarin

Cytochrome p450 nomenclature

- Name does NOT imply function!
- CYP □ □ □
 - Genetic Family
 - Subfamily
 - Specific Gene

Clinical Scenario

- Mrs. A is a 67 yo woman with depression well treated by fluoxetine. She falls and suffers a compression fracture of L4. She is given acetaminophen with codeine for analgesia. After 4 days, she calls concerned that her pain has not improved.
- Why?

Drug interactions: metabolism

- Codeine is prodrug—requires 2D6 for activation
- Fluoxetine inhibits 2D6
- Genetic variability

Clinical Scenario

- Mr.. R is a 75 yo man whose HTN is well controlled with felodpine. While attending a citrus convention in Orlando, he begins to feel lightheaded and fatigued. His blood pressure is noted to be 80/40.
- Why?

Drug interactions: metabolism

- 3A in enterocytes in small intestine
- 250 mL grapefruit juice may inhibit enzyme for 24-38 hours
- Dramatic increase in bioavailability
- Atorvastatin, clarithromycin, felodipine affected

Clinical Scenario

- Ms U is a 75 yo woman with a fib (rate controlled with digoxin) who twists her ankle at yoga class. She takes ibuprofen and achieves adequate analgesia. 5 days later, she becomes confused.
- Why?

Drug interactions: elimination

- Increased half life
- Increased serum concentration
- Problem for drugs with narrow therapeutic index

Drug-disease interactions

- Delirium: benzos, narcotics, anticholinergics
- Exacerbation of CHF: NSAIDs
- Worsening of urinary incontinence: diuretics, alpha blockers

Drug-disease interactions (cont)

- Urinary retention: anticholinergics, tricyclics
- Constipation: anticholinergics, narcotics, calcium channel blockers, tricyclics
- Falls: benzos
- Postural hypotension: tricyclics, diuretics, antihypertensives.

Don't prescribe bad medications

- long-acting benzodiazepines [e.g., diazepam (Valium), flurazepam (Dalmane)]
- propoxyphene (Darvon)
- meperidine (Demerol)
- anticholinergics [e.g., antihistamines (Benadryl), antispasmodics (Levsin)]
- amitriptyline (Elavil)
- indomethacin (Indocin)
- muscle relaxants (e.g., Soma, Flexeril)

Drugs with Dosage Limitations

- HCTZ 25 mg/day
- Digoxin 0.125 mg/day
- Ativan 3 mg/day (0.5-1 mg/dose)
- Ambien 5 mg/day
- Haldol 2 mg/day (0.5-1mg/dose)
- FeSO₄ 324 mg/day

Adherence

Increase

- Belief that med will treat condition
- Careful explanation by MD

Decrease

- Number of drugs
- Belief that med is toxic
- Long duration of therapy
- Complex scheduling
- Safety bottles

Conclusions: Drugs and Aging

- Try to gather complete information on medication usage
- Remember risk factors for trouble
 - comorbidity, frailty
 - polypharmacy
 - use of agents with low therapeutic index
 - age-related changes in drug distribution, hepatic metabolism and renal excretion

Conclusions: Drugs and Aging (cont)

- When adding new medications, check for drug-drug and drug-disease interactions
- Know which medications to avoid
- Become familiar with good drug management of common clinical scenarios

Special Thanks

- Joshua Chodosh, MD
- David Reuben, MD



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