Bad Drugs:
It might not be dementia - It might be the medication!

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Lecture Objectives

1. Recognize why seniors are prone to toxicity
2. Know the bad drugs that kill memory and send seniors to the emergency room
3. Describe what to do to reduce drug poisoning in seniors
4. Know that complementary & alternative drugs can also cause toxicity in older adults
Medication Errors and Drug Toxicity

- Occur regularly in up to 59% of hospitalized patients
- Drug toxicity 4th leading cause of death: ahead of
  - Pulmonary disease
  - Diabetes Mellitus
  - AIDS
  - Pneumonia
  - Accidents & Motor Vehicle Injuries
- ~31% of all hospital admissions in the elderly a result of adverse drug events


Institute of Medicine, National Academy Press 2000.
A 77 year-old man with urinary tract infection

- Saw his primary care doctor on a Friday
- Has been on enalapril 20 mg once daily for 5 years to control his high blood pressure
- An antibiotic was started
A 77 year-old man with urinary tract infection

• On Monday, patient was rushed to the emergency room for irregular heart beat, dizziness, and high blood potassium (K=8)
• Admitted to the Intensive Care Unit
Which of the following antibiotics is responsible for the high potassium level-related hospitalization in this man?

(A) Nitrofurantoin
(B) Amoxicilin
(C) Bactrim
(D) Levafloxacin
(E) Keflex
Renal mechanism of trimethoprim-induced hyperkalemia

- Trimethoprim (in bactrim) is structurally and pharmacologically similar to the potassium-sparing diuretic amiloride
- It reduces urinary potassium excretion by approximately 40%
- Can cause high blood potassium level when used with other potassium sparing drugs

*Ann Intern Med.* 1993
Trimethoprim-sulfamethoxazole-induced hyperkalemia in patients receiving inhibitors of the renin-angiotensin system: a population-based study

- Bactrim (trimethoprim-sulfamethoxazole) use was associated with a 7-fold increased risk of hyperkalemia-associated hospitalization in older patients on ACEIs or ARBs
- No such risk was found with the use of comparator antibiotics

Hospital admission for drug toxicity

- **Hypoglycemia**: 6-fold increased risk if bactrim used in previous week in seniors already on glyburide
- **Digoxin toxicity**: 12-fold increased risk if macrolide used in previous week in those on chronic digoxin
- **Hyperkalemia**: 20-fold increased risk if potassium-sparing diuretics used within a week in patients on chronic ACE inhibitors

Why are seniors more prone to adverse effects of medications?

- Unable to eliminate drugs quickly
- On too many drugs
- On bad drugs or high risk drugs
Why are elders prone to drug toxicity

- Most drugs are eliminated by liver and/or kidneys
- Kidney and liver function decrease with aging
- So older adults are unable to eliminate drugs quickly
- Drugs at normal young adult doses can result in overdose in the elderly
Why are elders prone to drug toxicity

- Drugs need to be started at low dose in seniors
- Frequent evaluation of levels & effects of the top 3 drugs that cause a third of ER visits for drug toxicity
  - Digoxin
  - Coumadin
  - Insulin
Polypharmacy

• “Using too many drugs”
• Refers to patient being on > 3 drugs
• More drugs = higher risk of drug toxicity
• 6 drugs = 27% chance of drug toxicity
Polypharmacy

• **Two types**
  1. Harmful Polypharmacy – bad drugs
  2. Rational Polypharmacy – good drugs
Rational Polypharmacy: when seniors must be on several drugs

- Plus other drugs for
  - Hypertension
  - Diabetes
  - Hyperlipidemia
  - Atrial fibrillation
Rational Polypharmacy: when seniors must be on several drugs

- CHF
  - Beta blocker
  - ACE inhibitors
  - furosemide
  - digoxin
  - spironolactone
How do seniors end up being on bad drugs – bad polypharmacy?

- Prescribing cascade
- Failure to use non-drug methods
- Failure to stop a drug when initial condition no longer exists
- Seeing many MDs & pharmacists who don’t talk to one another
Prescribing cascade
Rochon & Gurwitz. BMJ 1997;315:1096-1099

• The clinician prescribes a 2\textsuperscript{nd} drug to treat the side effects of the 1\textsuperscript{st} drug whose indication is often unclear.
• Followed by a 3\textsuperscript{rd} drug to treat the side effects of the 2\textsuperscript{nd} drug.
• And so the cascade of incremental prescribing continues.
Prescribing Cascade: Mr. K Age = 76 Yr

- Seen in clinic by his PCP; BP = 140/85
- Receives amlodipine 5 mg once daily
- Develops feet swelling
- Receives furosemide & potassium

Prescribing Cascade: Mr. K Age = 76 Yr

- Potassium pills aggravates his heartburn
- Receives omeprazole, develops diarrhea
- Receives lomotil (atropine/diphenoxylate)
- Dizzy, delirious, fell & sustained hip fracture

Examples of prescribing cascade

- Dizziness from anti-hypertensive treated with meclizine
- Feet swelling from a calcium-channel blocker treated with furosemide and KCL
- Parkinson tremors from metoclopramide treated with drugs for Parkinson’s disease
- Hypertension from NSAID’s (e.g. ibuprofen or naproxen) treated with antihypertensives
“Any symptom in an elderly may be a drug side effect until proven otherwise”

(Gurwitz)
Poor communication contributes to the high rates of drug poisoning in seniors

- **Doctors’ failure** to recognize and respond to drug toxicity symptoms reported by patients

- **Patients’ failure** to recognize and report drug toxicity symptoms to doctors

# Common symptoms of drug toxicity in the elderly

<table>
<thead>
<tr>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deconditioning</td>
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<tr>
<td>Dizziness,</td>
</tr>
<tr>
<td>Dysmobility</td>
</tr>
<tr>
<td>Drowsiness</td>
</tr>
<tr>
<td>Delirium</td>
</tr>
<tr>
<td>Dehydration</td>
</tr>
<tr>
<td>Depression</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
<td>Weight loss</td>
</tr>
<tr>
<td>Memory loss</td>
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<tr>
<td>Insomnia</td>
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<tr>
<td>Incontinence</td>
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<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Nausea &amp; Vertigo</td>
</tr>
<tr>
<td>Sedation</td>
</tr>
<tr>
<td>Falls and poor balance</td>
</tr>
</tbody>
</table>
Electronic prescribing systems improves patient safety by offering drug allergy and drug interaction alerts

• Computerized clinician order entry reduces medication errors among inpatients & outpatients if the warnings are heeded

Reducing Polypharmacy

Use one drug to treat multiple symptoms:

• Mirtazapine (remeron): depression, weight loss*, insomnia, anxiety, nausea*, emesis*, tremors*, diarrhea* & pruritus*

• Duloxetine (cymbalta): diabetic neuropathic pain, depression, anxiety & incontinence*

Raji M. *Chest* 2006.

* Off label use
Improving patient understanding of prescription drug label instructions

Seniors with Low Health Literacy on Glipizide, 5 mg

<table>
<thead>
<tr>
<th>Type of Instruction</th>
<th>Example Instructions</th>
<th>Follow Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Times per day</td>
<td>Take 2 pills by mouth 2 times daily</td>
<td>33%</td>
</tr>
<tr>
<td>Time periods</td>
<td>Take 2 pills in the morning and 2 pills in the evening</td>
<td>76%</td>
</tr>
<tr>
<td>Specific times</td>
<td>Take 2 pills by mouth at 8 a.m. and 2 pills at 6 p.m.</td>
<td>70%</td>
</tr>
</tbody>
</table>

Use *explicit times periods* (i.e., morning) or *precise times of day* versus instructions with times per day (i.e., twice) or hourly intervals

Medications associated with adverse symptoms when stopped suddenly

- Chronic Anti-Epileptic Drugs
- Chronic Corticosteroids
- Chronic Clonidine
- Chronic Beta Blockers, e.g., toprol
- Chronic Benzodiazepine, e.g. ativan

Avoid drugs on the Beers’ list of bad drugs “inappropriate drugs in the elderly”

- These have higher potential for bad outcomes than benefits in elders

Avoid drugs on the Beers’ list of bad drugs “inappropriate drugs in the elderly”

- Most are ineffective or have very high toxicity, e.g., muscle relaxants e.g., carisoprodol

Bad medications that seniors should avoid – See your doctor

- Barbiturates
- Meprobamate
- Belladona alkaloids
- Dicyclomine
- Hyoscyamine
- Carisoprodol
- Chlorzoxazone
- Cyclobenzaprine
- Metaxalone
- Methocarbamol
- Atropine (in lomotil)

Medications that can kill your memory

- Long-acting benzodiazepine: diazepam (valium), chlordiazepoxide (librium)
- Narcotics: meperidine & propoxyphine


Medications that can kill your memory

- Anticholinergics: high dose amitryptiline for depression, chronic use of diphenhydramine for insomnia (many brands)


Never prescribe diphenhydramine for insomnia in the elderly

- Benadryl®
- Benadryl® Allergy
- Benadryl® Allergy Ultratab®
- Benadryl® Dye-Free Allergy Children's
- Diphenhist®
- Diphenhydramine Hydrochloride Caplets®
- Nytol® QuickCaps® Caplets®
- Excedrin P.M.® Tablets
- Bayer® PM
- Tylenol® PM
- Goody's® PM Powder
- Simply Sleep® Nighttime Sleep Aid
- Sleepinal® Night-time Sleep Aid Softgels®
- Unisom® SleepGels® Maximum
- Diphen® AF Elixir
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<thead>
<tr>
<th>Impact</th>
<th>Drug Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Learning, memory, and attention</td>
<td>Tricyclic antidepressants</td>
<td>Amitriptyline, doxepin</td>
</tr>
<tr>
<td></td>
<td>Antispasmodics, gastrointestinal</td>
<td>Belladonna alkaloids, dicyclomine</td>
</tr>
<tr>
<td></td>
<td>Antispasmodics, genitourinary</td>
<td>Short-acting oxybutynin chloride</td>
</tr>
<tr>
<td></td>
<td>Muscle relaxants</td>
<td>Cyclobenzaprine, methocarbamol</td>
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<tr>
<td></td>
<td>Antihistamines</td>
<td>Diphenhydramine</td>
</tr>
<tr>
<td>Wakefulness and alertness</td>
<td>Benzodiazepines</td>
<td>Chlordiazepoxide, diazepam</td>
</tr>
<tr>
<td></td>
<td>Antiepileptics</td>
<td>Long-acting barbiturates</td>
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<tr>
<td></td>
<td>Antipsychotics</td>
<td>Thioridazine, mesoridazine, chlorpromazine</td>
</tr>
<tr>
<td>Orientation and reality awareness</td>
<td>Narcotics</td>
<td>Propoxyphene, meperidine</td>
</tr>
<tr>
<td></td>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td>Indomethacin, piroxicam</td>
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<tr>
<td></td>
<td>Corticosteroids</td>
<td>Prednisolone</td>
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<tr>
<td></td>
<td>Antidiarrheals</td>
<td>Diphenoxylate and atropine</td>
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<tr>
<td></td>
<td>Histamine-2 receptor antagonists</td>
<td>Cimetidine</td>
</tr>
<tr>
<td></td>
<td>Antihypertensive agents</td>
<td>Clonidine</td>
</tr>
</tbody>
</table>

Contains information from references 10, 13, 16-21.
Complementary Meds & Toxicity

• Alternative and Complementary Medications can also harm or kill
• Never use Kava Kava – causes liver failure, sometimes requiring liver transplantation
• Never use grapefruit juice to take your pills – it raises levels of drugs
  » Statins
  » Verapamil
  » Viagra
  » felodipine
Seniors on any prescription medications should avoid using St. John’s Wort

- Used for mild depression
- St John's Wort induces the activity of liver enzymes
- Leads to reduced effectiveness of 50% of all marketed drugs

*JAMA. 2003;290:1500-4*
Seniors on any blood thinner must avoid *Ginkgo biloba*

- *Ginkgo biloba* extract (EGb 761) used for memory loss
- Gingko increases the risk of bleeding in patients on
  - Plavix
  - coumadin or any blood thinner
Summary:
How to avoid drug poisoning in older adults
Preventing drug poisoning in seniors

**Just Say No**

- No meperidine as analgesic, *ever!*
- No Kava Kava, *ever!*
- No grapefruit juice with your pills, *ever!*
- No bactrim with chronic ACEI or ARBs
- No bactrim with glyburide
- No Gingko with blood thinners
- No St Johns Wort with prescription drugs
Preventing drug poisoning in seniors

- Review all medications including non-prescription and herbal preparations
- Check for interactions (drug, dx & food)
- Start seniors on low drug dose, then go slow with dose increase based on response & safety
Preventing drug poisoning in seniors

- Simplify therapeutic regimen
- Use instructions with explicit times periods (i.e., morning) or precise times of day
- All drugs may cause illness
“Any symptom in an elderly may be a drug side effect until proven otherwise”

(Gurwitz)
“All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy”

Paracelsus (1493-1541)
Thank you

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References


References


Raji MA. On depression, antidepressant medications and resuscitation preferences in COPD patients. Chest 2006;129:211.

Budnitz et al. Medication use Leading to emergency department visits for adverse drug events in older adults. Ann Intern Med 2007;147:755-765. [Table 2 contains names (derived number article #2) of bad drugs]


http://virtualmentor.ama-assn.org/2008/06/medu1-0806.html