Polypharmacy in the Elderly: Concerns and Challenges

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OBJECTIVES

• Discuss important considerations regarding polypharmacy in the elderly

RESPONSE TO A MEDICATION

Pharmacodynamics

Pharmacokinetics

CHANGES WITH AGING:

• Body composition
• Decline in renal function
• Reduced hepatic clearance / metabolism
• Increased sensitivity to some drugs

Drug Effect

AGE-RELATED CHANGES IN THE LIVER

• Reduced hepatic blood flow
  • When hepatic clearance of drug = hepatic blood flow…
  • Hepatic clearance of drug is reduced
  • Examples: fentanyl, labetolol, lidocaine, metoprolol, morphine, propofol
  • When hepatic clearance of drug < hepatic blood flow…
  • Hepatic clearance of drug is reduced if highly bound to albumin (higher unbound drug fraction when albumin concentration declines)
  • Examples: naproxen, ibuprofen, warfarin
• Reduced drug metabolism
  • Cytochrome P450 Æ ~ 30% reduction after age 70
  • Glucuronidation
• Possible increased bioavailability of oral drugs with a first pass effect
  • Examples: beta-blockers, nitrates, antidepressant

DRUGS TRIALS & THE ELDERLY

• Premarketing (Phase I to III) FDA trials don’t reflect “real-world” patients or predict postmarketing drug response
• Postmarketing (Phase IV) trials are necessary to evaluate safety or efficacy in “real-world” setting. Examples:
  • Older patients with comorbidities and concurrent medications
  • Increased risk of mortality with antipsychotics in elderly patients
  • Detected through data analysis by regulatory bodies
  • Confirmed by meta-analysis of RCTs and observational studies
• Postmarketing data, however, generally relies on voluntary reporting
  • Adverse effects are often nonspecific and multifactorial

"51% of drugs have label changes due to major safety issues discovered after marketing."

"Four percent of approved drugs are ultimately withdrawn from the market for safety reasons."

REAL-LIFE CONDITIONS IN THE ELDERLY

• Noncompliance
  • Visual / hearing impairment, poor hand function, difficulty swallowing, cognitive impairment
• Multiple medical conditions
• Frailty
  • No consensus definition
  • One definition* is the presence of three or more of the following:
    • Exhaustion
    • Shrinking
    • Weakness
    • Slowness
    • Low activity

* Mechanisms Ageing Dev 2002;123:1457
J Gerontology 2012;67A:152
J Gerontology 2012;67A:181


J Gerontology 2012;67A:181
**POLYPHARMACY**

BEST DEFINED AS THE TAKING OF A MEDICATION THAT IS NOT CLINICALLY WARRANTED

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**BEERS CRITERIA**

"Originally conceived of in 1991 by the late Mark Beers, MD, a geriatrician, the Beers Criteria catalogues medications that cause adverse drug events in older adults due to their pharmacologic properties and the physiologic changes of aging. In 2011, the AGS undertook an update of the criteria, assembling a team of experts and funding the development of the AGS 2012 Beers Criteria using an enhanced, evidence-based methodology. Each criterion is rated (quality of evidence and strength of evidence) using the American College of Physicians' Guideline Grading System, which is based on the GRADE scheme developed by Guyatt et al."

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**THREE CATEGORIES**

1) Potentially inappropriate medications and classes to avoid in older adults

2) Potentially inappropriate medications and classes to avoid in older adults with certain diseases and syndromes that the listed drugs can exacerbate

3) Medications that should be used with caution in older adults

53 Medications or Medication Classes

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**Therapeutic Category** | **Medications to Avoid (select example)**
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Anticholinergics | First generation antihistamines (promethazine, diphenhydramine except for acute allergic reaction), benztropine, belladona, scopoderm, scopolamine, dicyclomine (confusion, constipation, dry mouth, etc.)
Antithrombotics | Ticlopidine
Antiinfectives | Nitrofurantoin (pulmonary toxicity)
Cardiovascular | Doxazosin, prazosin, terazosin (orthostatic hypotension)
Antiarrythmic drugs | Amiodarone, dofetilide, etc. (prefer rate, not rhythm, control for atrial fibrillation for most adults)
Endocrine | Androgens, desiccated thyroid, estrogens (vaginal cr OK), growth hormone, megestrol, sliding scale insulin, glyburide and chlorpropamide (risk of prolonged hypoglycemia)
Gastrointestinal | Metoclopramide, mineral oil, trimethobenzamide
Pain Medications | Meperidine, non-selective NSAIDs (chronic use unless other agents not effective & can take gastrosprotective agent), indomethacin, muscle relaxants (cyclobenzaprine)
Therapeutic Category | Disease or Syndrome | Medications to Avoid due to Drug-Disease or Drug-Syndrome Interactions that May Exacerbate Disease or Syndrome (select examples)
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Cardiovascular | Heart Failure | NSAIDs, COX-2 inhibitors, diltiazem, verapamil, pioglitazone, pioglitazone, cilostazol, drotaverine → fluid retention, exac HF
| Syncope | AChEIs, doxazosin, prazosin, olanzapine → orthostatic hypoten
CNS | Seizures, epilepsy | Buproprion, olanzapine, tramadol → lowers seizure threshold
| Dementia | TCAs, anticholinergics, benzos, steroids, H2 blockers, meperidine, sedative hypnotics → inducing or worsening delirium
| Ataxia, syncope, impaired psychomotor function | Anticonvulsants, antipsychotics, benzos, nonbenzo hypnotics, TCAs, SSRIs → ataxia, syncope, impaired psychomotor function
| Fracture | Antipsychotics, metoclopramide, prochlorperazine, promethazine → worsening of Parkinson’s disease
Gastrointestinal | Chronic constipation | Oral antimuscarinics for urinary incontinence, diltiazem, verapamil, first generation antihistamines (diphenhydramine), anticholinergics/antispasmodics, TCAs → worsen constipation
| NSAIDs, triamterene → increase kidney injury
| Estrogens (not vaginal cr) → aggravates incontinence in women
| Strong anticholinergics → reduce urinary flow; urinary retention
| Doxazosin, prazosin, terazosin → avoid in women; aggravate incontinence
Kidney / Urinary Tract | Chronic Kidney Disease (Stage IV & V), Urinary Incontinence | NSAIDs, triamterene → increase kidney injury
| Estrogens (not vaginal cr) → aggravates incontinence in women
| Strong anticholinergics → reduce urinary flow; urinary retention

BEERS CRITERIA CAVEATS
- Criteria measure "pharmacological appropriateness" and are not intended to replace clinical decision-making
- Most criteria aimed at general population age 65 and older
  - Age 70 + and older
  - Frailty
  - Drug-drug interactions
  - Drug class duplication
- Some medications are not mentioned
  - Example: hydrochlorothiazide with hx of gout → may exacerbate gout
- Doesn’t allow for exceptions (e.g. palliative care)
- Doesn’t alert prescriber to omission error

STOPP / START RISK ASSESSMENT TOOLS
STOPP = Screening Tool of Older Person’s Prescriptions
START = Screening Tool to Alert doctors to Right Treatment

Differ from Beers’ criteria in that they:
- Are organized by physiological systems
- Pay attention to drugs affecting fall risk
- Pay attention to opioid use in elderly
- Include duplicate drug classes
- Include potentially serious errors of prescribing omissions

EXAMPLE: STOPP

STOPP VS. BEERS’ CRITERIA #1
- 715 older patients (65+) admitted with an acute illness
- Both criteria applied to determine connection or contribution to primary reason for admission
- Results
  - STOPP identified 336 potentially inappropriate medications affecting 247 patients (35%)
  - Of these 247 patients, 82 (33%) presented with an associated ADE
  - Beers’ criteria identified 226 potentially inappropriate medications affecting 177 patients (25%)
  - Of these 177 patients, 43 (24%) presented with an associated ADE
- Conclusion
  - STOPP-related potentially inappropriate medications contributed to 11.5% of all admissions
  - Beers’ criteria-related potentially inappropriate medications contributed to 6% of all admissions
STOPP VS. BEERS’ CRITERIA #2
- 600 older patients (65+) admitted with an acute illness
- Potentially inappropriate medications defined by both criteria
  - Adverse drug events identified and assessed
    - Causal or contributory to current admission
    - Avoidable or potentially avoidable
- Results
  - 329 ADEs detected in 158 patients (26% of patients)
  - 219 ADEs (67%) considered causal or contributory to admission
  - 151 ADEs (69%) considered avoidable or potentially avoidable
  - After adjusting for cofounders (age, sex, comorbidity, etc.),
    - Likelihood of a serious avoidable ADE increased significantly when STOPP criteria was used (odds ratio, 1.847, P<0.001)
  - Use of Beers’ criteria did not prevent serious avoidable ADEs

GENERAL APPROACH
- Detailed and current medication list
  - OTC meds, herbs, dietary supplements
  - Prescribing physician, pharmacy that filled medication
  - Another person’s medication?
- Diagnosis and assessment
  - Is each medication necessary?
  - Is drug contraindicated in the elderly?
  - Are there duplicate medications?
  - Is the dose the lowest effective dose?
  - Can regimen be simplified?
- Compliance
  - Concerns / difficulties with medication regimen
- STOPP, START and ARMOR tools

CONCLUSION

Less is More

QUESTIONS?

Thank you!