Pharmacology of geriatric

Recommendations for geriatric prescribing

Zulkarnain Rangkuty_Hasanul Arifin

Dep. Farmakologi & Terapeutik,
Fakultas Kedokteran
Universitas Sumatera Utara
Geriatric criteria based on WHO:

- Middle age: 45-59 Years
- Elderly: 60-74 Years
- Old: 75-90 Years
- Very old: > 90 Years
Problema penggunaan obat pada lansia

- makin bertambah usia
- penyakit penyerta
  - Kardiovaskular (CHD, CHF)
  - Degeneratif (OA)
  - Metabolik (DM), dll
- polifarmasi
  - ACE-inhibitor
  - OAINS
  - OAD, dll
- interaksi obat
- efek samping obat . . .
Medications in the Elderly

General
- 2/3 of elderly take Rx or OTC meds
- Avg of 5 Rx and 2 OTC/pt
- 30% of all RX written for pts > 65 yrs old
- Biochemistry of medications in the elderly
  - Longer duration of activity
  - More frequent adverse drug effects
  - Increase likelihood of drug toxicity
  - Lower doses needed to obtain therapeutic levels
Adverse Drug Events in older adults

• Common
• May present differently than in younger adults
• May precipitate or mimic common geriatric disorders

º Under-recognition
º Increased morbidity
º ?Additional prescriptions
Adverse Drug Events can mimic or precipitate geriatric syndromes

- Falls: psychotropics
- Urinary incontinence
  - Diuretics, caffeine, alcohol
  - Anticholinergic agents, including psychotropics
  - Sedative/hypnotics
  - Narcotic analgesics
  - Cardiovascular agents:
    - Alpha-adrenergic blockers and agonists
    - Beta-adrenergic agonists
    - Calcium channel blockers
Dementia due to medications

– Psychotropics
  • Benzodiazepines, Antidepressants, Neuroleptics
– Analgesics
  • Meperidine, Indomethacin
– Antihypertensives
  • Methyldopa, HCTZ, propranolol
– Others
  • $H_2$ Blockers, Amantadine, Insulin

Major Toxicity after Chronic Theophylline Intoxication

Why the elderly are at risk

**Patient-level factors**
- Age-associated changes in pharmacokinetics
- Age-associated changes in pharmacodynamics
- Comorbidity: drug-disease interactions
- Polypharmacy: drug-drug interactions
- Less physiologic reserve
- Frailty

**System level factors**
- Fragmentation of care (Poly-doctoring)
- Inadequate training in principles of geriatric practice
Why the elderly are at risk

- prescribing cascade,
- see several doctors, each of whom may prescribe different medications
- use over-the-counter medication regularly including “jamu” containing “steroid”
- get medications from more than one pharmacy, or from friends
Drug Use in the Elderly - Benefits

Examples

• Antihypertensives
  – Reduce risk of heart failure and stroke
• ß-blockers and aspirin
  – Reduce risk of mortality and recurrent heart attack after a myocardial infarction
• Angiotensin Converting Enzyme (ACE) Inhibitors
  – Reduce mortality and risk of hospitalization in heart failure
• Biphosphonates
  – Reduce risk of hip and vertebral fractures in osteoporosis
Drug Use in Community Dwelling Elderly*

Moxey, Health Care Financing Review 2003

*1996: N=27,285,988
Effective Therapies are Underutilized in Older Adults

• Thrombolysis for Acute MI
• Beta-blockers postinfarction
• Coumadin for Atrial Fibrillation
• Anything for osteoporosis
• Opioids for cancer pain
There is some evidence about increased drug sensitivity in elderly, which could be due to changes in:

1. Receptor number
2. Receptor affinity
3. Post receptor alterations and or
4. Homeostatic mechanisms impairment.
ADEs: Aging or Age-related?

Hutchinson et al J Chronic Dis 1986;39:533-42
What are the data for those >75 yo?

• No RCTs
  – Fewer older adults with acute MI will meet criteria for thrombolysis
    • present without chest pain
    • present >3 hours after initial symptoms
  – Concern about intracranial hemorrhage

• Observational studies:
  – Prospective Cohort
  – Medicare databases
Prescribing for Older Adults

Benefits

Risks

Burdens
## Proses Penuaan Yang Mempengaruhi Farmakokinetik Obat

<table>
<thead>
<tr>
<th>Variable Body</th>
<th>Young Adults (20–30 years)</th>
<th>Geriatrics Adults (60–80 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Water (% of body water)</td>
<td>61</td>
<td>53</td>
</tr>
<tr>
<td>Lean Body Mass (% of body weight)</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>Body Fat (% of bodyweight)</td>
<td>26-33 (woman) 18-20 (man)</td>
<td>38-45 (woman) 36-38 (man)</td>
</tr>
<tr>
<td>Serum Albumin (g/dl)</td>
<td>4,7</td>
<td>3,8</td>
</tr>
<tr>
<td>Kidney Weight (% of young adult)</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>Hepatitic Blood Flow (% of young adult)</td>
<td>100</td>
<td>55-60</td>
</tr>
</tbody>
</table>
Effects of Aging on Rx use
(Absorption)

- Reduced gastric acid production
  - Raises gastric pH
  - May alter solubility of some drugs (ASA etc)
- Longer gastric emptying
  - Delay or reduce absorption
- Decreased esophageal motility
  - Capsules more difficult to swallow
- Loss of subcutaneous fat
  - Increased rate of absorption of topical medications
- Increased fragility of veins
  - IV administration more difficult
Effects of Aging on Rx use (Distribution)

- Distribution
  - ↑ fat (18=>36% in men, 33=>45% women)
    - ↑ in VOD for lipid soluble drugs
    - ↑ concentration in body, longer $T_{1/2}$
  - ↓ lean body mass
  - ↓ total body water – 10-15%
    - ↑ Na+ space, ↑ serum/tissue levels of hydrophilic drugs
  - Albumin ↓, therefore ↓ binding and drug’s free (unbound) form is more active
Effects of Aging on Rx use
(Metabolism)

• Difficult to predict, depends on
  – General health & nutritional status
  – Use of alcohol, medications
  – Long term exposure to environmental toxins/pollutants

• Aging causes decreased liver mass/ hepatic blood flow
  – Delayed/reduced metabolism of drugs
  – Higher plasma levels

• Lower serum protein levels
  – Loss of protein binding

• Idiosyncratic reactions
Liver metabolism decreases with age

- ↓ in # of hepatocytes and enzymatic activity
- ↓ hepatic blood flow
- First-pass ↓ metabolism of some, not all drugs
- Phase I metabolism = CYP-450 system - produces active metabolites \( \rightarrow \) this slows with age (30-40%)
- Phase II metabolism = Acetylation \( \Rightarrow \) inactive metabolites
  - this does NOT CHANGE with elderly
- Not possible to predict ability to metabolize a specific drug – commonly need to reduce doses by 30-40%
Effects of Aging on Rx use
(Excretion)

• Renal elimination
  – ↓ plasma blood flow
  – ↓ GFR (up to 30%)
  – Serum Cr is NOT a good measure of renal function -- a function of muscle breakdown (Elderly person with ↓ muscle → low cr)
  – Longer half-life of medications
  – Increased side effects
  – Increased potential for toxicity

• Est. Creatinine clearance: Males
  – \[ \frac{[(140 - \text{age}) \times \text{wt (kg)}]}{[72 \times \text{Cr (mg/dl)}]} \]
  – Females = males X 0.85
Kinetic profile of drug in young and elderly subjects

t-1/2 associated to drug accumulation

give once daily of short half-life agent
PK changes: So What?

• Decreased clearance
  – \( Cl_{\text{organ}} = \text{Organ Blood Flow} \times \text{Extraction Ratio} \)
  – Drug clearance is additive
  – Total clearance = \( Cl_{\text{renal}} + Cl_{\text{hepatic}} + Cl_{\text{other}} \)

• Increased steady-state concentration
  
• Need to decrease dose

• Prolonged half life (\( t_{1/2} \)) is common
  
  \[
  t_{1/2} = \frac{0.693 \times V_d}{Cl}
  \]
  
  è Longer dosing interval
  è Longer
    – to steady state
    – until body is drug-free
DOSIS OBAT UNTUK GERIATRIK

• 65-74 TAHUN : DOSIS LAZIM – 10%
• 75-84 TAHUN : DOSIS LAZIM – 20%
• > 85 tahun : DOSIS LAZIM – 30%
Pharmacological problems in the elderly

- Dementia
- Blindness
- Anorexia
- Hearing loss
- Heart disease
- Dyspnoe
- Liver impairment
- Renal impairment
- Cancer
- Arthralgia
- Constipation
- Weakness
I have got them, but I forgot how to consume the drugs.

Have I eaten them before?

Where are my medicines?

3 x 1 ≠ 1 x 3

Efek terapeutik ≠ Efek samping obat

Hindari pemakaian obat yang berbahaya . .

..................... pilihlah obat yang aman

.. dengan regimen obat yang sederhana
Lingkaran setan ...

- Lansia
- Bermacam-macam problem klinis
- efek samping ↑
- Poli-farmasi
- tanda/ simptom baru ?
- terapi lanjutan
Kurata et al., (1999)

NSAID loxoprofen prescribed by an orthopedic to treat a patient with lumbago

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Elderly (80 years)</td>
</tr>
<tr>
<td>Gender</td>
<td>Woman</td>
</tr>
<tr>
<td>Concomitant disease</td>
<td>hypertension</td>
</tr>
<tr>
<td>(CVS, kidney &amp; liver)</td>
<td></td>
</tr>
<tr>
<td>Concomitant drugs used</td>
<td>ACE-Inhibitor imidapril</td>
</tr>
</tbody>
</table>

The grandmother was syncope due to hyperkalemia, bradycardia

What next?
Drug-Disease Interactions

↑ CHF: *NSAIDs*

↑ Claudication: *Beta blockers*

↑ Stress incontinence: *Alpha<sub>1</sub> blockers*

↑ Constipation
  
  — *CCB, anticholinergics, Betablockers, narcotics*

↑ BPH:
  
  — *Decongestants, anticholinergics, calcium channel blockers*

• Parkinsons or Dementia: *Anticholinergic delirium*
Drug-Nutrient Interactions

\ Protein-bound B$_{12}$: omeprazole
\ Folate and Vit D: diphenylhydantoin
\ Thiamine: furosemide
\ Coumadin effect: Vitamin K
\ Calcium channel blocker bioavailability: grapefruit juice
Drugs to Avoid in Older Adults

• Analgesics
  – Narcotics: Propoxyphene (Darvon\textsuperscript{TM}), Meperidine (Demerol\textsuperscript{TM}), pentazocine (Talwin\textsuperscript{TM}),
  – NSAIDs: Indomethacin, Phenylbutazone

• Muscle Relaxants
  – Robaxin\textsuperscript{TM}, Soma\textsuperscript{TM}, Ditropan\textsuperscript{TM}, Paraflex\textsuperscript{TM}, Skelaxin\textsuperscript{TM}, Flexeril\textsuperscript{TM}

• GI Antispasmodics
  – Bentyl\textsuperscript{TM}, Levsin\textsuperscript{TM}, Pro-Banthine\textsuperscript{TM}, Donnatol\textsuperscript{TM}, Librax\textsuperscript{TM}

Beers M Arch Intern Med 1997;157:1531-1536
Drugs to Avoid in Older Adults

- Cardio- or Cerebrovascular Drugs
  - Disopyramide (Norpace™)
  - Dipyridamole (Persantine™)
  - Methyldopa, Reserpine
  - Ticlopidine (??)
  - Hydergine, cyclospasmol
- Chlorpropamide (Diabenase™)
- Psychotropics
  - Antidepressants: Amitriptyline, doxepin
  - Sedatives: Meprobamate, chlordiazepoxide, diazepam, flurazepam, barbiturates
- $H_1$ Blockers (lipid soluble)
  - Chlorpheniramine, hydroxyzine, cyproheptadine, promethazine, dexchlorpheniramine, tripelennamine

Beers M Arch Intern Med 1997;157:1531-1536
BUT Remember . . . .

Prescribing is dynamic, not static.

Patients are dynamic, not static.
Individualize Therapy

What is the patient’s potential for:

• An adverse drug event?
• An altered dose response?
• A “drug interaction”?  
  – drug-drug  
  – drug-disease  
  – drug-nutrient  
• Treatment non-adherence?

• All elders are not alike  
  – Significant heterogeneity  
  • greater among older individuals than younger
• ADEs are common among older patients
• ADEs can be minimized with strict attention to  
  ✓ risk factors  
  ✓ drug-drug interactions  
  ✓ drug-disease interactions
• Start low, go slow
Recommendations for geriatric prescribing

- Know your patient’s medications and medication history.
- Individualize therapy.
- Reevaluate indications for continued drug use.
- Minimize dose and total number of drugs.
- Start low, go slow. Use blood levels judiciously.
- Treat adequately. Do not withhold therapy for treatable diseases.
- Consider the possibility that any new symptom is an ADE.
- Know the drugs you and your patients use.
- Use new agents with caution.
- Encourage treatment adherence.
An Apa Tani woman from northeast India with wooden disks in nose and earlobes.

Start an active agent regiment with low dose and then slowly increase the dose of a short half-life agent.