Geriatric Pharmacotherapy

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Problems in geriatric drug therapy

• Taking more medications
• Major drug studies performed on individuals < 55 yrs
• Premarketing drug trials
• Effect of aging on drug metabolism
• Alteration of drug response among patients
Polypharmacy

• 5 or more drugs
• Greater risk of ADR
• Greater potential for drug interactions
• Independent risk factor for hip fracture
• Prescribing cascades
• Low adherence
Geriatric drug therapy

• General rules: ½ or 1/3 of the usual dose
• ADR rate: twice
• ADR symptoms: subtle: falling, altered cognition, sedation, confusion, constipation, decreased appetite, thrive
• Significant ADRs: narrow therapeutic index or saturable hepatic metabolism: e.g. phenytoin, warfarin, theophylline
• Increase risk of ADR in: multiple disease states, complicated drug therapy, poor compliance, age related changes
### Frequency of adverse drug events and preventable adverse drug events by drug class

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Total adverse drug events (n = 815) N (percent)</th>
<th>Preventable adverse drug events (n = 338) N (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>121 (15)</td>
<td>42 (12)</td>
</tr>
<tr>
<td>Atypical antipsychotics</td>
<td>92 (11)</td>
<td>42 (12)</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>69 (8)</td>
<td>33 (10)</td>
</tr>
<tr>
<td>Opioids</td>
<td>51 (6)</td>
<td>25 (8)</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>46 (6)</td>
<td>23 (7)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>45 (6)</td>
<td>27 (8)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>43 (5)</td>
<td>25 (7)</td>
</tr>
<tr>
<td>Laxatives</td>
<td>43 (5)</td>
<td>16 (5)</td>
</tr>
<tr>
<td>Benzodiazepines (intermediate acting)</td>
<td>39 (5)</td>
<td>30 (9)</td>
</tr>
<tr>
<td>Insulins</td>
<td>37 (5)</td>
<td>18 (5)</td>
</tr>
</tbody>
</table>

Only drug classes with the frequency of adverse drug events of 5 percent and more are presented. Some adverse drug events were associated with more than one drug class.

<table>
<thead>
<tr>
<th>Type</th>
<th>Total adverse drug events (n = 815)</th>
<th>Preventable adverse drug events (n = 338)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropsychiatric</td>
<td>199 (24)</td>
<td>97 (29)</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>159 (20)</td>
<td>53 (16)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>140 (17)</td>
<td>55 (16)</td>
</tr>
<tr>
<td>Renal/electrolytes</td>
<td>80 (10)</td>
<td>40 (12)</td>
</tr>
<tr>
<td>Metabolic/endocrine</td>
<td>64 (8)</td>
<td>35 (10)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>36 (4)</td>
<td>15 (4)</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>35 (4)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Extrapyramidal symptoms</td>
<td>30 (4)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Fall with injury</td>
<td>21 (3)</td>
<td>17 (5)</td>
</tr>
<tr>
<td>Fall without injury</td>
<td>21 (3)</td>
<td>11 (3)</td>
</tr>
<tr>
<td>Infection</td>
<td>19 (2)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Syncope/dizziness</td>
<td>16 (2)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>9 (1)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Ataxia/difficulty with gait</td>
<td>9 (1)</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Hematologic</td>
<td>8 (1)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>6 (1)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>3 (&lt;1)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Functional decline</td>
<td>3 (&lt;1)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Hepatic</td>
<td>1 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
</tbody>
</table>

Adverse drug events could manifest as more than one type. Neuropsychiatric events include oversedation, confusion, hallucinations, and delirium. Anticholinergic effects include dry mouth, dry eyes, urinary retention, and constipation.
Other Drug Therapy Problems

- **Affordability**
  Affects 30% of patients
  Higher non compliance rates
  Higher for patients with multiple co-morbidities

- **Dose availability**
  Required lower doses
  Splitting tablets
  Capsules
Drug-Drug Interactions

- Increased risk
- Warfarin
- Other most interactions with glyburide, digoxin, ACE-Inhs
Age related physiologic changes in relation with kinetics of drugs

- Elevated GI pH
- Delayed gastric emptying
- Decreased GI mobility/ intestinal blood flow/ absorptive surface area
- Reduced gastric secretion
Consequences of Delayed Gastric Emptying

- More contact time for potentially ulcerogenic drugs (e.g. NSAIDs, bisphosphonates)
- Antacid drug interaction (increased time for binding)
- Increased absorption of poorly soluble drugs
- Higher incidence of diarrhea and a delay in onset action of basic drugs
<table>
<thead>
<tr>
<th>Process</th>
<th>Physiologic Effect</th>
</tr>
</thead>
</table>
| Absorption       | Reduced gastric acid production  
Reduced gastric-emptying rate  
Reduced GI motility  
Reduced GI blood flow  
Reduced absorptive surface |
| Distribution     | Decreased total body mass  
Increased percentage of body fat  
Decreased percentage of body water  
Decreased plasma albumin  
Disease-related increase in alpha-1-acid glycoprotein  
Altered relative tissue perfusion  
Altered protein binding |
| Metabolism       | Reduced liver mass  
Reduced liver blood flow  
Reduced hepatic metabolic capacity  
Reduced enzyme activity  
Reduced enzyme induction |
| Excretion        | Reduced renal blood flow  
Reduced glomerular filtration  
Reduced renal tubular secretory function |
| Tissue sensitivity| Alterations in receptor number  
Alterations in receptor affinity  
Alterations in second messenger function  
Alterations in cellular response  
Alterations in cellular nuclear response |
Age related pharmacokinetic changes

- Delayed absorption of transdermal patches: opioid patches
- Decreased IM absorption
- Using controlled released drugs
- Effect of clinical factors (e.g. CHF,...)
Protein Binding

- Albumin decreases to 3.5 g/dL after 80
- Residents of nursing homes: 3 g/dL or less
- AAG decreases
- Protein binding = major determinant of drug activity

Decrease of pr binding : increase of unbound (active) drug
Increased free fraction

NSAIDs in general
(naproxen) and salicylates:
higher gastric bleeding

• Phenytoin: seizure control with lower doses
Select drugs with no or minimum change in protein binding
Lean Body Weight

- Total body water ↓
- Total body fat ↑
- Influence on the onset and duration of drugs
  - Digoxin
  - Alcohol, Morphine, Li
Volume of Distribution

- Vd of lipophilic drugs increases
- Delayed onset of action
- Accumulation in tissues: longer duration of action: toxicity
- TCAs, barbiturates, BDZs, CCBs, phenothiazines
elimination

- Hepatic metabolism
- Renal excretion
Hepatic metabolism
Beta blockers, lidocaine, narcotics

Decrease of hepatic blood flow → Elevation of drug concentration in blood → Toxicity
Renal Clearance

- Most age related declines in drug clearance is due to reductions in renal function
- Decrease of GFR to as much as 50%
  - Serum Cr
  - BUN
  - Cl Cr
  - Dose adjustment
Age related pharmacodynamic changes

- Decreased tolerance to the drug
- Decreased Ach, DA, 5HT
- Decreased enzymatic degradation of MAO
- Impaired baroreceptor response to BP changes
- Decreased responsiveness of beta-adrenergic receptors
- Increased pain tolerance
- Decreased Ab response to vaccination
- Decreased insulin sensitivity
- Decreased cortisol suppression
Pharmacodynamic changes

- Exaggerated pharmacologic response: barbiturates, BDZs, halothane, hydroxyzine, metoclopramide, warfarin
- Diminished pharmacologic response: beta blockers, beta agonists, CCBs
- Irreversible TD
- Difficulties of dose adjustment
Practical recommendations to reduce medical errors

1. Maintain an accurate list of all medications (drug name (generic and brand), dosage, frequency, route, and indication).

2. Advise periodic "brown bag check-ups." Instruct patients to bring all pill bottles to each medical visit; bottles should be checked against the medication list.

3. Patients should be made aware of potential drug confusions: sound-alike names, look-alike pills, and combination medications.

4. Patients should be informed of both generic and brand names

5. Community pharmacists
References

- UpToDate 19.3, 2012
- Geriatric Pharmacotherapy 2007
- Clinical Pharmacokinetics 2008