Chapter 61

Special Aspects of Geriatric Pharmacology
Focus

- Pharmacologic changes associated with aging
- Behavioral & lifestyle changes
- Major drug groups
- Adverse drug reactions in the elderly
- Practical aspects of geriatric pharmacology
Pharmacologic changes associated with aging

Effect of age on some physiologic functions

Geriatric pharmacology
Some changes related to aging that affect pharmacokinetics of drugs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Young Adults (20–30 years)</th>
<th>Older Adults (60–80 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body water (% of body weight)</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 body weight)</td>
<td>26–33 (women)</td>
<td>38–45</td>
</tr>
<tr>
<td></td>
<td>18–20 (men)</td>
<td>36–38</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>Hepatic blood flow (% of young adult)</td>
<td>(100)</td>
<td>55–60</td>
</tr>
</tbody>
</table>
Pharmacokinetic changes

- Absorption
- Distribution
- Metabolism
- Elimination

Geriatric pharmacology
Absorption

- Altered nutritional habits
- More consumption of nonprescription drugs (antacids, laxatives)
- Gastric emptying---slower
Distribution

- Decrease in serum albumin
- Increase in serum orosomucoid
No consistent decline with age

Phase I (oxidation, deoxidize, hydrolization) has much more changes than phase II (combination)

Decrease of liver blood flow is important factor

Heart failure and malnutrition are more common etiopathogenesis of hepatic impairment
Some changes related to aging that affect pharmacokinetics of drugs

<table>
<thead>
<tr>
<th>Age-Related Decrease in Hepatic Clearance Found</th>
<th>No Age-Related Difference Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Isoniazid</td>
</tr>
<tr>
<td>Carbenoxolone</td>
<td>Lidocaine</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>Lorazepam</td>
</tr>
<tr>
<td>Chlormethiazole</td>
<td>Nitrazepam</td>
</tr>
<tr>
<td>Clobazam</td>
<td>Oxazepam</td>
</tr>
<tr>
<td>Desmethyldiazepam</td>
<td>Prazosin</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Salicylate</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Warfarin</td>
</tr>
<tr>
<td>Imipramine</td>
<td></td>
</tr>
<tr>
<td>Meperidine</td>
<td></td>
</tr>
<tr>
<td>Nortriptyline</td>
<td></td>
</tr>
<tr>
<td>Phenylbutazone</td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td></td>
</tr>
<tr>
<td>Quinidine, quinine</td>
<td></td>
</tr>
<tr>
<td>Theophylline</td>
<td></td>
</tr>
<tr>
<td>Tolbutamide</td>
<td></td>
</tr>
</tbody>
</table>

Geriatric pharmacology
Elimination

- Creatinine clearance reduced in two thirds of population.
- It’s not reflected in an equivalent rise in serum creatinine because the production of creatinine is also reduced.
- The half-life of drugs is marked prolonged.
Allowance for reduced renal clearance

Cockcroft-Gault formula:

\[
\text{Creatinine Clearance} = \frac{(140-\text{Age}) \times (\text{Weight in kg})}{72 \times \text{Serum creatinine in mg/dL}}
\]

For women, the result should be multiplied by 0.85
As a result of reduced respiratory capacity, the use of parenteral is more common than inhalation anesthesia in the elderly.
Pharmacodynamic changes

- Most of more “sensitive” to the action of drugs result from altered pharmacokinetics or diminished homeostatic responses.
More sensitive to some sedative-hypnotics and analgesics
Decrease in responsiveness to β-receptor
Orthostatic hypotension
Average 2-hour postprandial blood glucose level increases by about 1mg/dL for each year of age above 50
Poorly tolerated to hypothermia
Behavioral & lifestyle changes

- Cognitive impairment
- Economic stresses
- The loss of a spouse
Major drug groups

1. Central nervous system drugs
2. Cardiovascular drugs
3. Antimicrobial drugs
4. Anti-inflammatory drugs
Sedative-hypnotics

The half-lives of many benzodiazepines and barbiturates increase by 50-150% between age 30 and age 70 because decline in renal function and liver disease, and increased volume of distribution.

Lorazepam and oxazepam may be less affected.
Analgesics

- The opioid analgesics show variable changes in pharmacokinetics with age.
- Markedly more sensitive to the respiratory function
- Are consistently underutilized in patients
Antipsychotic & antidepressant drugs

- Useful in the management of schizophrenia
- Also in treatment of some symptoms associated with delirium, dementia, agitation, combativeness, and a paranoid syndrome
- When a sedative antipsychotic is desired, thioridazine is appropriate. Otherwise haloperidol is more appropriate. The latter drug has increased extrapyramidal toxicity.
- Chlorpromazine often induce orthostatic hypotension because of their a-receptor blocking effects.
Thioridazine’s half-life is more than doubled
Plasma protein binding of fluphenazine is reduced
Lithium is often used in the treatment of mania in the aged.
Concurrent use of thiazide diuretics reduces the clearance of lithium.
The elderly are as responsive to antidepressants as younger patients but are more likely to experience toxic effects.
Drugs used in AD

- Progressive impairment of memory and cognitive functions and may lead to a completely vegetative state and early death
- Marked decrease in choline acetyltransferase and other markers of cholinergic neuron activity
- Abnormal neuronal lipoprotein processing—apolipoprotein E4

Geriatric pharmacology
Geriatric pharmacology

- Cholinomimetic drugs
- Monoamine oxidase (MAO) type b inhibitor
- Nerve growth factor
- Lipid-lowering statin
Tacrine
the first beneficial drug in AD, long-acting cholinesterase inhibitor

Donepezil, Rivastigmine, Galantamine
newer cholinesterase inhibitor, adequate penetration into CNS, more selective, less adverse reaction
Antihypertensive drugs

The basic principles of therapy are not different in geriatric age group patient

**Thiazides** are a reasonable first step in drug therapy

**CCB** are effective and safe

**β-blockers** are less useful than CCB, so as ACEI
Positive inotropic agents

- Heart failure is a common and particularly lethal disease in the elderly. Fear of this condition may be one reason why physicians overuse cardiac glycosides.
- The toxic effects are dangerous in elderly, especially arrhythmia.
- Renal function is also focused.
- Hypokalemia, hypomagnesemia, hypoxemia are concurrent reasons of toxic effects.
Antiarrhythmic agents

- Disopyramide should be avoided because its major toxicities—antimuscarinic action
- Atrial fibrillation
  - simple control ventricular rate do as well as conversion to normal sinus rhythm
The basic principles have no different with younger patients.
Anti-inflammatory drugs

- **Aspirin** can cause gastrointestinal irritation and bleeding.
- **Newer NSAIDs** cause irreversible renal damage.
- **Corticosteroids** are extremely useful in elderly patients who cannot tolerate full doses of NSAIDs. But they can cause an increase in osteoporosis.
Adverse drug reactions in the elderly

- More drugs, more adverse reactions.
- The overall incidence of drug reactions in geriatric patients is estimated to be at least twice that in the younger population
Reasons include errors of part of the practitioner and errors in drug usage by the patient.

For the practitioner, does not appreciate the importance of changes in pharmacokinetics with age and age-related disease, or unaware of incompatible drugs prescribed by other practitioners for the same patient.

Patient errors may result from noncompliance for prescription.
Practical aspects of geriatric pharmacology

- The quality of life in elderly patients can be greatly improved and life span can be prolonged by the intelligent use of drugs.
- The prescriber must be aware of the cost of the prescription and of cheaper alternative therapies.
- Noncompliance may result from forgetfulness (retrograde amnesia) or confusion.
- Noncompliance may also be deliberate.
- Some errors in drug taking are caused by physical disabilities.
General principles

- 1. Take a careful drug history
- 2. Prescribe only for a specific and rational indication
- 3. Define the goal of drug therapy
- 4. Maintain a high index of suspicion regarding drug reactions and interactions
- 5. Simplify the regimen as much as possible
Key line

1. what are the major pharmacokinetic changes in elderly?
2. what are the general principles that drug used in elderly?
3. what are the major characteristic of central nervous system drugs used in elderly?
Thank you for your attention!