The Older Traveller—Pharmacist Provided Care
Symposium—Pharmacist Professional Group
CISTM 16
WASHINGTON DC

Pharmacokinetic and Metabolic Pathways: The Science Behind Drug and Disease Interactions commonly found in elderly travellers.

Provide insight into age-related changes in pharmacodynamics and drug metabolism in older patients

Derek Evans, FRPhS, FRGS, MFTM RCPS(Glasg)
Independent Prescriber
Adjunct Clinical Professor
Keck Graduate Institute, School of Pharmacy and Health Science

Disclosures: none

Pharmacokinetics Versus Pharmacodynamics

What the body does to the drug
What the drug does to the body

From Basic and Clinical Pharmacology, 13th Ed

Pharmacokinetics

Conversely

Anticipated age related Pharmacokinetic changes in the older Traveller

Pharmacokinetic pathways of travel-related medications
- Absorption- water soluble drugs have smaller volumes of distribution giving higher serum levels
- Distribution- More protein binding and extended half life.
- Metabolism- reduced blood flow and liver mass generally reduces or slows drugs with first-pass activation
- Excretion—expected reduction in renal and hepatic clearance

CONVERSELY

Age-related changes in pharmacokinetics
- Cytochrome P450 enzymes are preserved in normal aging
- One third of the elderly show no decrease in renal function (GFR > 70ml/min)


Pharmacokinetic cytochrome enzyme pathways

Human cytochrome P450 enzymes are present in most body tissues and have important roles in
- Hormone synthesis, breakdown and metabolism (CYP1, CYP2, CYP3)
- Cholesterol synthesis (CYP4, CYP7, CYP46, CYP51)
- Vitamin D metabolism (CYP24)
- Drug metabolism (CYP2C)

Pharmacokinetics and Antimalarials

<table>
<thead>
<tr>
<th>Absorption</th>
<th>Metabolism</th>
<th>Excretion</th>
<th>Risk of ADR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapidly absorbed</td>
<td>Glucuronidated by CYP2C19, half-life 2-3 days</td>
<td>Mostly excreted in urine and faeces</td>
<td>Hepatotoxic or urticaria, rash, fever, or anaphylaxis</td>
</tr>
<tr>
<td>Poorly absorbed</td>
<td>Metabolised by CYP2C19, half-life 72h, enzyme inducer</td>
<td>Absorbed from GI tract</td>
<td>Acute plasma sickness, other drug effects, others</td>
</tr>
<tr>
<td></td>
<td>Metabolised by CYP3A4, half-life 4-8 days, enzyme inducer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metabolised by CYP2C19, half-life 21 days, does not induce or inhibit enzymes.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Antimalarials**
- Doxycycline
- Mefloquine
- Atovaquone/proguanil
- Azithromycin
- Rifaximin
- Ciprofloxacin

**Risk of ADR**
- Hepatotoxicity, rash, hypoglycaemia, anticoagulants.
- Hepatitis, NAFLD, steroid-induced diabetes.

**Metabolism**
- Most frequently undertaken in the liver via different transferases.
- Therapeutic levels can be adjusted when in combination with other medication using CYP450 or CYP2C19.

**Excretion**
- Mostly in urine, some in the faeces, renal or bile.
- Renal associated problems may affect urinary excretion.

**Summary**
- Drugs are well or rapidly absorbed.
- Drugs or conditions that alter the rate of absorption of GI movement.

**Drugs**
- Antimalarials:
  - Doxycycline
  - Mefloquine
  - Atovaquone/proguanil
  - Azithromycin
  - Rifaximin
  - Ciprofloxacin

**Absorption**
- Rapidly absorbed, 50% bioavailable.
- Slowly absorbed from small intestine, biavailability 30%.

**Distribution**
- Peak plasma concentration, 2-3hrs.
- Plasma protein binding 10%.
- Low-protein binding (20%) distributed in plasma.

**Metabolism**
- Metabolised (small amounts) by CYP2C19 in plasma, half-life 6-8 hours.
- Inhibited or reduced by other drugs or enzyme-inducing drugs.

**Excretion**
- Mostly excreted in urine and unchanged in the bile.
- Acute plasma sickness, other drug effects, others.