Specific needs of patients with chronic disease

Drug – Nutrient interactions

R. Witkamp (NL)
Drug – Nutrient interactions
The menu of the day for mrs. B.
And I also seem to lose my appetite...

> 15 Different medicines

> 3 Guidelines

> 3 Physicians

X Nurses & caregivers

Dietician (?)
Key messages

- Chronic drug use is often associated with malnutrition and deficiencies

- *Polypharmacy* is an important risk factor and elderly are specifically at risk

- Causality is often not (yet ?) clear

- Awareness of apparent drug-food interactions can help to improve patient care
Food – Drug interactions
5 mg felodipine combined with 250 mL grapefruit sap or water.
Abiraterone 1,000 mg dose level; Ryan et al. JCO 2010;28:1481-1488
Drug-Food interactions
Elderly: at risk for ADRs in general
Increased risk of adverse drug reactions

Increased number of drug reactions
More drugs, longer treatment duration

Changes in external and internal environment
Physical, physiological, psychological, cognitive

Increased vulnerability
Decreased adaptability, more health problems

Adverse drug reactions
Altered pharmacokinetics and pharmacodynamics

Péter et al., Eur J Nutr. 2017
High incidence of polypharmacy among older persons

Foundation for Pharmaceutical Statistics (Netherlands), 2014
Medication-related causes of malnutrition

- Oral health and functioning
- Taste, smell
- Appetite and satiation (+ or -)
- GI physiology
- General metabolism
- Micronutrient absorption and metabolism
- Microbiota
Gingiva swelling due to Nifedipine (GEBU, Oct 2012)
Drug-induced smell and/or taste disorders

Highly common
Mechanisms rather diverse
e.g.
Cytotoxicity
Neurotoxicity
Taste aversion
Effects on food reward
Effects on saliva
Bad taste

<table>
<thead>
<tr>
<th>Medications that reportedly alter smell and/or taste [16-20].</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug class</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Antianxiety agents</td>
</tr>
<tr>
<td>Antibacterials</td>
</tr>
<tr>
<td>Antidepressants</td>
</tr>
<tr>
<td>Antiepileptic drugs</td>
</tr>
<tr>
<td>Antifungals</td>
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<tr>
<td>Antihistamines and decongestants</td>
</tr>
<tr>
<td>Antihypertensives and cardiac medications</td>
</tr>
<tr>
<td>Anti-inflammatory agents</td>
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<tr>
<td>Antimanic drugs</td>
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<tr>
<td>Antimigraine agents</td>
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<tr>
<td>Antineoplastics</td>
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<tr>
<td>Antiparkinsonian agents</td>
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<tr>
<td>Antipsychotics</td>
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<tr>
<td>Antiviral agents</td>
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<tr>
<td>Bronchodilators</td>
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<tr>
<td>CNS stimulants</td>
</tr>
<tr>
<td>Hypnotics</td>
</tr>
<tr>
<td>Lipid-lowering agents</td>
</tr>
<tr>
<td>Muscle relaxants</td>
</tr>
<tr>
<td>Pancreatic enzyme preparations</td>
</tr>
<tr>
<td>Smoking cessation aids</td>
</tr>
<tr>
<td>Thyroid drugs</td>
</tr>
</tbody>
</table>
Xerostomia

- Common in elderly
- Often associated with / caused by drug use
- Long list of compounds potentially involved*, in particular; tricyclic anti-depressants, SSRIs (less), anti-cholinergics, beta-blockers, opiates, some antihistaminics etc.

* > 500; e.g. Crit Rev Oral Biol Med 2004: 15 (4): 221
Effects on appetite

• CNS compounds but also others e.g.:
  • TCAs, benzodiazepines, corticosteroids and valproate stimulate appetite
  • SSRIs and topiramate inhibit appetite

• Be aware of indirect effects (nausea, other GI complaints)
## Drugs that can cause constipation

<table>
<thead>
<tr>
<th>Category</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiates</td>
<td>Morphine, Codeine</td>
</tr>
<tr>
<td>CNS drugs</td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Haloperidol, Risperidone</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Amitriptyline, Nortriptyline</td>
</tr>
<tr>
<td>Serotonin reuptake inhibitors</td>
<td>Paroxetine</td>
</tr>
<tr>
<td>Anti-Parkinson drugs</td>
<td>Amantadine</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Butylscopolamine</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Hydrochloorthiazide</td>
</tr>
<tr>
<td>NSAID’s</td>
<td>Diclofenac, Ibuprofen</td>
</tr>
<tr>
<td>Calcium-antagonists</td>
<td>Verapamil, Diltiazem</td>
</tr>
<tr>
<td>Antihistaminics</td>
<td>Levocetirizine</td>
</tr>
</tbody>
</table>
Effects on absorption or elimination of nutrients

- Mg ↓ with proton pump inhibitors (omeprazole a.o.)
- Vit B12 ↓ with metformin and proton pump inhibitors
- Vit B6 and B12 ↓ with certain anti-epileptic drugs
- Vit D ↓ with different medicines
Polypharmacy and deficiencies of micronutrients in Dutch geriatric outpatients (*PanDeMic* study)

<table>
<thead>
<tr>
<th>Polypharmacy</th>
<th>Prevalence of malnutrition*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>men</td>
</tr>
<tr>
<td>no (&lt;5 med)</td>
<td>22%</td>
</tr>
<tr>
<td>yes (≥5 med)</td>
<td>31%</td>
</tr>
</tbody>
</table>

- MNA screening
- 65+ geriatric outpatients (N=1078)
# Medication and vitamin B12-status

512 geriatric patients

<table>
<thead>
<tr>
<th>Medication (yes, no)</th>
<th>Vitamin B12 blood level (nmol/l)</th>
<th>mean difference (exposed – unexposed)</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td></td>
<td>- 51</td>
<td>0.002</td>
</tr>
<tr>
<td>PPI’s(^1)</td>
<td></td>
<td>- 33</td>
<td>0.096</td>
</tr>
<tr>
<td>Beta blockers</td>
<td></td>
<td>- 29</td>
<td>0.070</td>
</tr>
<tr>
<td>Statins</td>
<td></td>
<td>+ 22</td>
<td>0.246</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td></td>
<td>- 28</td>
<td>0.083</td>
</tr>
</tbody>
</table>

1. Proton pump inhibitors
2. Time period electronic patient records: August 1 – October 25, 2011
3. Time period electronic patient records: August 1 – November 15, 2011
Vitamin D deficiency as adverse drug reaction? A cross-sectional study in Dutch geriatric outpatients

A. C. B. van Orten-Luiten¹,² • A. Janse² • R. A. M. Dhouwes-Rutten³ • R. F. Witkamp¹

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Abstract
Purpose Adverse drug reactions as well as vitamin D deficiency are issues of public health concern in older people. However, relatively little is known about the impact of drug use on vitamin D status. Our primary aim is to explore associations between drug use and vitamin D status in older people. Furthermore, prevalences of drug use and vitamin D deficiency are estimated.
Methods In a population of 873 community-dwelling Dutch geriatric outpatients, we explored the cross-sectional relationships of polypharmacy (≥5 medications concomitantly used), severe polypharmacy (≥10 medications), and use of twenty-one specific drug groups, with serum 25-hydroxyvitamin D (25(OH)D) by analysis of covariance.

Results Overall prevalence of polypharmacy was 65 %, of severe polypharmacy 22 %. Depending on the cut-off value, prevalence of vitamin D deficiency was 49 % (<50 nmol/l) or 77 % (<75 nmol/l). Of the patients using a vitamin D supplement, 17 % (<50 nmol/l) or 49 % (<75 nmol/l) were still deficient. In non-users of supplemental vitamin D, after adjustment for age and gender, negative associations were found for severe polypharmacy, metformin, sulphonamides and urea derivatives (SUDs), vitamin K antagonists, cardiac glycosides, loop diuretics, potassium-sparing diuretics, ACE inhibitors, and serotonin reuptake inhibitors; for non-selective monoamine reuptake inhibitors (NSMRIs) the association was positive. The most extreme impacts of drug use on adjusted mean 25(OH)D were −19 nmol/l for SUDs and +18 nmol/l for NSMRIs.

Conclusion Drug use should be considered a risk factor for vitamin D deficiency amongst geriatric outpatients.
Vit D associations with drug use

*PAnDeMic study*

<table>
<thead>
<tr>
<th>Rank</th>
<th>Medication</th>
<th>User subgroup</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PPIs</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>2</td>
<td>platelet aggregation inhibitors</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>3</td>
<td>selective beta blocking agents</td>
<td>males</td>
<td>↓</td>
</tr>
<tr>
<td>4</td>
<td>statins</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>5</td>
<td>ACE inhibitors</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>6</td>
<td>thiazide diuretics</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>7</td>
<td>anilides (paracetamol)</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>8</td>
<td>angiotensine-2 antagonists</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>9</td>
<td>loop diuretics</td>
<td>≥79 yr</td>
<td>↓</td>
</tr>
<tr>
<td>10</td>
<td>benzodiazepines</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>11</td>
<td>dihydropyridines</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>12</td>
<td>vitamin K antagonists</td>
<td>females</td>
<td>↓</td>
</tr>
<tr>
<td>13</td>
<td>biguanides (antidiabetic)</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>14</td>
<td>osmotically acting laxatives</td>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>15</td>
<td>sulfonamides &amp; urea derivatives</td>
<td>males</td>
<td>↓</td>
</tr>
<tr>
<td>16</td>
<td>SSRIs (antidepressive)</td>
<td>&lt;79 yr</td>
<td>↓</td>
</tr>
<tr>
<td>17</td>
<td>potassium sparing diuretics</td>
<td>males</td>
<td>↓</td>
</tr>
<tr>
<td>18</td>
<td>NSMRIs (antidepressive)</td>
<td>&lt;79 yr</td>
<td>↑</td>
</tr>
<tr>
<td>19</td>
<td>cardiac glycosides (digoxin)</td>
<td>males</td>
<td>↓</td>
</tr>
</tbody>
</table>

(* Polypharmacy and deficiencies of micronutrients in Dutch geriatric outpatients*)
The impact of drug use on Magnesium status
A cross-sectional study in Dutch geriatric outpatients

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Methods

Background: Magnesium depletion is an important risk factor for the development of fractures. Various factors influence magnesium intake, such as diet, age, and medication use. In the Netherlands, dietary calcium intake is lower than recommended, and magnesium intake is even lower than dietary calcium intake. Therefore, the aim of this study was to investigate the relationship between magnesium status and medication use in Dutch elderly patients.

Results:

- Table 1: Association between magnesium status and number of medications used.
- Figure 1: Association between the number of different medications used and blood magnesium level adjusted for age, gender, and BMI, in 351 Dutch geriatric outpatients.

Figure 1

Association between the number of different medications used and blood magnesium level adjusted for age, gender, and BMI, in 351 Dutch geriatric outpatients.
Medication can play a role in malnutrition, in particular with chronic use of multiple drugs.

Elderly are at risk. Drug-induced malnutrition is often unrecognized as side-effect.

Effects and mechanisms are diverse and causality is often not (yet?) clear.

Prediction, alertness and timely intervention needed; consider measuring nutrient levels.

Summary & take home points