(In)appropriate antibiotic self-treatment of traveller’s diarrhea

Jeroen C. H. van der Hilst, MD, PhD
Introduction

• Diarrhea is the most frequent medical problem encountered by travellers
• Most guidelines: self-treatment for TD
• Antibiotics are moderately effective in reducing length*
  • 0.7 – 1.5 days
  • ± 5 unformed stool less in 72 hour period
  • Significantly more side effects (OR 2.37)
• Even a single dose of antibiotics significantly increases the likelihood to become colonised with ESBL enterobacteriaceae
  • Kantele et al
  • See previous presentation

* de Bruyn G, Hahn S, Borwick A.
  Cochrane Database of Syst. Rev. 2000, 3
Introduction

• Until 2016: an antibiotic prescription for every traveller

• Independent of
  • Type of travel
  • Duration of travel
  • Age
  • Co-morbidities

• Ofloxacine 400 mg QD for max 3 days

• Azitromycine 500 mg QD for max 3 days
Self-treatment algorithm

Travel Diarrhea

Adequate intake of fluid and electrolytes

Mild diarrhea
- No additional measures
  - Or Loperamide
- Frequent watery stools without fever or abdominal cramps
  - ORS/Loperamide

Moderate severe diarrhea
- Fever and/or moderate abdominal cramps
  - Antibiotic 1 dose for maximum of 3 days and Loperamide

Severe diarrhea
- Feeling sick and/or Fever >38.5°C and/or Abdominal cramps and/or Blood or pus in feces
  - Consult a doctor
    - If not possible: antibiotics (3 days) avoid Loperamide
Introduction

• Shouldn´t we limit antibiotic prescriptions?

´We don´t believe that out travellers overuse their antibiotics´

´In my experience they only take it when necessary´
Study objectives

• How well do patients comply to the guideline?

• How many travelers have TD
  • Risk factors

• How many travelers use antibiotics for TD?
  • How many travelers use antibiotics appropriate according to guideline?
  • How many travelers use antibiotics inappropriate according to guideline?
  • How many travelers don’t use antibiotics inappropriate to guideline?

• Risk factors for suboptial antibiotic use
Methods

Inclusion/exclusion

- All travellers visiting travel clinic Dec 2015-Jun 2016
- Duration of ≤ 3 weeks
- Age > 18 years
- Able to understand Dutch
- Written informed consent

- Pre-travel survey
  - Demographics
  - Travel itinerary
  - Health status
  - Medication use
Methods

• Post-travel: questionnaire sent by email-link
  • Travel diarrhea
    • Durations of symptoms
    • Number of stools
    • Accompanying symptoms
  • Antibiotic
    • Got a prescription?
    • What antibiotic was prescribed, by who?
    • Brought the antibiotic during travel?
  • Antibiotic use
    • When started
    • How many days
    • For other indications?
  • Other medications use
    • Loperamide, domperidone
    • PPI, H2 I
  • level of education
Results

Questionnaire received
N= 587

Respons
N=353
(60.1%)

No TD
N=226
(64.0%)

TD
N=127
(36.0%)
Results
Antibiotic use for TD

- Of 28 patients that used AB for TD only 11 (39.3%) was in accordance with the guideline
<table>
<thead>
<tr>
<th>Age</th>
<th>Number of travellers</th>
<th>Travellers with TD N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>52</td>
<td>24 (46.2)</td>
</tr>
<tr>
<td>25-54</td>
<td>186</td>
<td>65 (34.8)</td>
</tr>
<tr>
<td>≥55</td>
<td>115</td>
<td>38 (33.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p=0.24</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>170</td>
<td>63 (37.1)</td>
</tr>
<tr>
<td>Female</td>
<td>183</td>
<td>64 (35.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p=0.68</td>
</tr>
<tr>
<td>Type of travel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tourist</td>
<td>169</td>
<td>69 (35.2)</td>
</tr>
<tr>
<td>Adventure</td>
<td>72</td>
<td>32 (44.4)</td>
</tr>
<tr>
<td>VFR</td>
<td>54</td>
<td>17 (31.5)</td>
</tr>
<tr>
<td>Business</td>
<td>15</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Other</td>
<td>12</td>
<td>6 (50)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p=0.22</td>
</tr>
<tr>
<td>Destination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Africa</td>
<td>201</td>
<td>75 (37.3)</td>
</tr>
<tr>
<td>South America</td>
<td></td>
<td>35 (36.8)</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td></td>
<td>10 (29.4)</td>
</tr>
<tr>
<td>Central America</td>
<td></td>
<td>3 (27.3)</td>
</tr>
<tr>
<td>South Asia</td>
<td>10</td>
<td>3 (30)</td>
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<tr>
<td></td>
<td></td>
<td>p=0.85</td>
</tr>
<tr>
<td>Duration of travel</td>
<td></td>
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</tr>
<tr>
<td>≤1 week</td>
<td>29</td>
<td>6 (20.7)</td>
</tr>
<tr>
<td>&gt;1 - ≤2 weeks</td>
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<td>63 (34.6)</td>
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<tr>
<td>&gt;2-3 weeks</td>
<td>142</td>
<td>58 (40.8)</td>
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<tr>
<td></td>
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<td>p=0.04</td>
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<tr>
<td>Use of PPI</td>
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<tr>
<td>Yes</td>
<td>41</td>
<td>15 (36.6)</td>
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<tr>
<td>No</td>
<td>312</td>
<td>112 (35.9)</td>
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<td></td>
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<td>p=0.93</td>
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</table>
Optimal vs suboptimal treatment

- Optimal: Mild TD, AB- and moderate-severe TD, AB+
- Suboptimal: Mild TD, AB+ and moderate-severe TD, AB-

<table>
<thead>
<tr>
<th></th>
<th>Optimal treatment N=99 (%)</th>
<th>Suboptimal treatment N=28 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
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<td>46.5</td>
<td>67.8</td>
</tr>
<tr>
<td>≥55</td>
<td>32.3</td>
<td>21.4, p=0.39</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>49.5</td>
<td>50</td>
</tr>
<tr>
<td>Female</td>
<td>50.5</td>
<td>50</td>
</tr>
<tr>
<td><strong>Type of travel</strong></td>
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<td></td>
</tr>
<tr>
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<td>54.1</td>
<td>53.6</td>
</tr>
<tr>
<td>Adventure</td>
<td>25.3</td>
<td>25</td>
</tr>
<tr>
<td>VFR</td>
<td>13.1</td>
<td>14.3</td>
</tr>
<tr>
<td>Other</td>
<td>7.1</td>
<td>7.1, p=0.99</td>
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<tr>
<td><strong>Education</strong></td>
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<td></td>
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<tr>
<td>High</td>
<td>72.7</td>
<td>64.3</td>
</tr>
<tr>
<td>Middle/low</td>
<td>27.3</td>
<td>35.7, p=0.38</td>
</tr>
</tbody>
</table>
Conclusion

• TD is frequent condition
  • Only duration of travel associated with risk
  • No association with PPI use

• Poor compliance with guideline
  • 39.3% of AB use in accordance with guideline
  • Both overuse and underuse of AB

• No subgroups with better or worse compliance
New Belgian guidelines

- No antibiotics prescribed except for:
  - Long-term travel
  - High risk for complications
    - Children <12 years
    - Pregnant women
    - Immunocompromised patients (diabetes, HIV, IBD, diabetes,..)
  - Decreased gastric acid production
  - Travel to Afrika and Asia for at least 16 days
  - Short term travel to Indian subcontinent
  - Adventurous travel

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**Het voorschrijfdagrad van stand-by antibiotica voor de behandeling van ernstige reizigersdiarree dient beperkt te worden.**

Azithromycine 1 g in stat (éénmalig) wordt als eerste keuze voorgesteld.

Azithromycine blijft aangewezen voor reizen naar twee continenten (Afrika en Azië) met als beperking een minimale reisduur van 16 dagen (o.b.v. Kantele et al).

Bepaalde risicogroepen dienen ongeacht hun reisbestemming en de duur te beschikken over azithromycine, zoals:
- kinderen onder 12 jaar
- zwangeren
- personen met een verminderde immunologische weerstand (diabetes, HIV, chronische inflammatoire darmziekten, chronisch gebruik van immunosuppressiva,..)
- personen met een verminderde/afwezige maagzuurproductie
- Avontuurlijke reizigers (trekking – jungle – hoogte – lange duur)
- Bij korte reizen naar het Indisch subcontinent

Er kan eveneens overwogen worden om voor personen die langdurig of zeer avontuurlijk gaan reizen (jungle/hoogte) azithromycine voor te schrijven ongeacht hun reisbestemming.
Discussion

• Data support the decision to limit antibiotic prescription

• Applying new guidelines
  • 62% of travellers in this cohort would not be eligible for antibiotic prescription

• In this group of 206 travellers
  • 70 had diarrhea
  • 4 took antibiotic according to guideline
Discussion

• Arguments for further restrictions of AB prescription
  • PPI / H2 receptor antagonist ?

• All destinations <16 days ?
Acknowledgements

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