Rifaximin Use in IBS Symptoms

TESSA WILEY
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UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES
COLLEGE OF PHARMACY
Disclosure

The individual reported that no relevant financial relationship exists.
Objective

- Describe the safety and effectiveness of rifaximin in patients with irritable bowel syndrome (IBS) diarrhea symptoms
Irritable Bowel Syndrome

- IBS affects between 25 and 45 million people in the United States
- IBS is unpredictable
  - Symptoms vary
  - Diarrhea can alternate with constipation
- What are options for treatment?

Rome Diagnostic Criteria for IBS

**Rome III criteria (2006)**
- At least 3 months, with onset at least 6 months previously of recurrent abdominal pain or discomfort** associated with 2 or more of the following:
  - Improvement with defecation; and/or
  - Onset associated with a change in frequency of stool; and/or
  - Onset associated with a change in form (appearance) of stool

**Discomfort means an uncomfortable sensation not described as pain.

**Rome II criteria (1999)**
- 12 weeks or more in the last 12 months of abdominal discomfort or pain with 2/3 of the following:
  - Relieved by defecation
  - Associated with a change in frequency of stool
  - Associated with a change in consistency of stool

The second group of criteria included in Rome I are now considered supportive rather than mandatory in the diagnosis.
Rifaximin

- Recently approved for use in patients with IBS diarrhea symptoms
- Target 1 and Target 2
  - Two identically designed, phase 3, double blind, placebo controlled trials
- Patients were given either rifaximin 550 mg or placebo three times daily
  - 2 weeks of treatment
  - 10 week follow up

Study Endpoints

- The primary endpoint was the proportion of patients that had adequate relief of global IBS symptoms
  - Abdominal pain and discomfort
  - Bloating
  - Diarrhea
  - Gas
  - Altered bowel function

- Secondary endpoints
  - Relief of IBS-related bloating
  - Daily assessment of IBS symptoms

Results

## Safety

<table>
<thead>
<tr>
<th>Event</th>
<th>Rifaximin (N=624)</th>
<th>Placebo (N=634)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>38 (6.1)</td>
<td>42 (6.6)</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>29 (4.6)</td>
<td>35 (5.5)</td>
</tr>
<tr>
<td>Nausea</td>
<td>27 (4.3)</td>
<td>24 (3.8)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>27 (4.3)</td>
<td>22 (3.5)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>15 (2.4)</td>
<td>9 (1.4)</td>
</tr>
<tr>
<td>Flatulence</td>
<td>10 (1.6)</td>
<td>14 (2.2)</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>6 (1)</td>
<td>3 (0.5)</td>
</tr>
</tbody>
</table>

Other Rifaximin Data

- Randomized, double-blind, placebo-controlled trial of rifaximin in patients with abdominal bloating and flatulence
  - Treatment of rifaximin 400 mg or placebo twice daily
- Used Rome II criteria
- Patients who used rifaximin had an improvement in global symptom relief
  - Mean bloating-specific scores were lower for the rifaximin group
  - H2-breath excretion also lower for rifaximin group

Where do we go from here?

- Both trials were based on self-reported symptom relief
  - Heavily subjective
  - No actual lab values
- Cost
  - 2 week course of treatment = $1,295.00
- IBS symptoms vary
  - Treatment is very patient specific
## Other Treatment Options for IBS-D

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Generic name (dose)</th>
<th>Key points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidiarrheals</td>
<td>Loperamide (1–8mg four times daily in divided doses)</td>
<td>Useful for the treatment of diarrhea but no global symptom relief shown. Titrate dose to desired effect and avoid constipation.</td>
</tr>
<tr>
<td></td>
<td>Diphenoxylate (5mg up to four times daily)</td>
<td></td>
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<tr>
<td>5-HT₃ antagonist</td>
<td>Alosetron (0.5–1.0mg twice daily)</td>
<td>Efficacious for IBS-D. Only available for treatment of severe IBS-D in women under a risk management program. Concerns of serious complications of constipation and ischemic colitis.</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Amitriptyline (10–150mg at night)</td>
<td>Post hoc analysis of an IBS trial suggests greater efficacy in IBS-D. Initiated at lower dose than usual dose for mood disorders. Recommend titrating dose for desired effect and to minimize adverse effects.</td>
</tr>
<tr>
<td></td>
<td>Doxepin (10–150mg at night)</td>
<td></td>
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<td></td>
<td>Imipramine (10–150mg at night)</td>
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<td></td>
<td>Clomipramine (25–100mg at night)</td>
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<td>Trimipramine (10–150mg at night)</td>
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<td>Desipramine (10–150mg at night)</td>
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<td></td>
<td>Nortriptyline (10–150mg at night)</td>
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<tr>
<td>Antibiotics</td>
<td>Rifaximin (400–550mg three times daily)</td>
<td>Global efficacy demonstrated in nonconstipating IBS. Improvement in bloating also demonstrated.</td>
</tr>
</tbody>
</table>

Abbreviation: IBS-D, diarrhea-predominant IBS.
IBS can be predominately:

a) Constipation
b) Diarrhea
c) Both
Rifaximin is FDA approved in IBS with:

a) Constipation
b) Diarrhea
c) Both
Thank you for your attention!

Questions?

2. http://www.aboutibs.org/site/what-is-ibs/facts/
