William D. Chey, MD
Professor of Medicine
University of Michigan

Bloating and Distension: Blowing up the Old Dogma

Rome III

Functional Bowel Disorders

- Irritable bowel syndrome
- Functional Bloating
- Functional Constipation
- Functional Diarrhea
- Unspecified FBD
**Medical Definitions: Bloating vs. Abdominal Distension**

- **Functional Bloating – Rome III definition**
  - Abdominal fullness, bloating or distension unrelated to obvious maldigestion (e.g., lactose intolerance) or excess consumption of poorly digestible but fermentable food stuffs (e.g., sorbitol, beans, wheat bran), in the absence of functional dyspepsia or IBS

- **Bloating = subjective sensation of fullness**

*Longstreth G., Gastroenterology 2006; 130:1480*  
*Whorwell NGM 2012;24:301*
Medical Definitions: Bloating vs. Abdominal Distension

- Functional Bloating – Rome III definition
  - Abdominal fullness, bloating or distension unrelated to obvious maldigestion (e.g., lactose intolerance) or excess consumption of poorly digestible but fermentable food stuffs (e.g., sorbitol, beans, wheat bran), in the absence of functional dyspepsia or IBS
- Bloating = subjective sensation of fullness
- Distension = objective increase in abdominal girth

Bloating is Common in IBS

Ringel et al. CGH 2009:7:68
Bloating is Common in IBS

Order of Bothersome Symptoms (n=337)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cramping</td>
<td>47 (13.9)</td>
</tr>
<tr>
<td><strong>Bloating</strong></td>
<td><strong>43 (12.8)</strong></td>
</tr>
<tr>
<td>Loose/watery stool</td>
<td>38 (11.3)</td>
</tr>
<tr>
<td>Straining</td>
<td>33 (9.8)</td>
</tr>
<tr>
<td>Urgency</td>
<td>31 (9.2)</td>
</tr>
<tr>
<td>Fear of cancer</td>
<td>28 (8.3)</td>
</tr>
</tbody>
</table>

Symptoms that Made Participants Decide to See a Doctor During the Past 12 Months

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain/discomfort</td>
<td>125 (37.1)</td>
</tr>
<tr>
<td>Cramping</td>
<td>108 (32.0)</td>
</tr>
<tr>
<td><strong>Bloating</strong></td>
<td><strong>95 (28.2)</strong></td>
</tr>
<tr>
<td>Urgency</td>
<td>85 (25.2)</td>
</tr>
<tr>
<td>Fear of cancer</td>
<td>81 (24.0)</td>
</tr>
</tbody>
</table>

Bloating does not discriminate between Normals and FGIDs

- Cross sectional population based study of VA employees
- Completed BDQ, SF-36
- 72% response rate (723/1069)

Tuteja et al. Am J Gastroenterol 2008;103:1241
Pathogenesis of Bloating & Distension

- Microbiome Fermentation
- Abdominophrenic dyssynergia
- Delayed Transit
- Dyssynergic Defecation
- Visceral Hypersensitivity
- Abnl Gas Handling
- Air Swallowing

Villoria et al Am J Gastroenterol 2010;815
Whorwell Neurogastroenterol & Motil 2012;24:301

Comparison of LHBT Results Between IBS Patients and Healthy Controls

<table>
<thead>
<tr>
<th></th>
<th>IBS (n=277)</th>
<th>HC (n=64)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactase Malabsorption, n (%)</td>
<td>211 (76.2)</td>
<td>48 (75.0)</td>
<td>0.843</td>
</tr>
<tr>
<td>AUC, ppm.min</td>
<td>2,978 (1,058–5,693)</td>
<td>2,719 (1,071–5,366)</td>
<td>0.485</td>
</tr>
<tr>
<td>Lactose intolerance, n (%)</td>
<td>149 (53.8)</td>
<td>18 (28.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Intolerance symptoms

- Bloating, n (%) | 108 (39.0) | 9 (14.1) | <0.001 |
- Diarrhea, n (%) | 79 (28.5)  | 6 (9.4)  | 0.001  |
- Pain, n (%)     | 87 (31.4)  | 7 (10.9) | 0.001  |
- Borborygmi, n (%) | 108 (39.0) | 14 (21.9) | 0.010  |
- Nausea, n (%)   | 16 (5.8)   | 2 (3.1)  | 0.586  |

AUC, area under the curve; HC, healthy control; IBS, irritable bowel syndrome; LHBT, lactose hydrogen breath test. AUC is expressed as median (interquartile range), comparisons made by Mann-Whitney U test. Other variables are reported as number (Percentage), comparisons done using Pearson chi-square test.
Treatment Options for Bloating & Distension

Diet

Antibiotics

Probiotics

Prosecretories

Prokinetics

Biofeedback

Scmulson & Chang. Aliment Pharmacol Ther 2011;33:1071

Gluten Causes Symptoms in IBS Patients Without Celiac Disease

Mean Change in Symptoms Over 6 Weeks

*P-value for analyses at Week 1 and entire study period.
Reprint permission has been requested.
**FODMAPs: Mechanism of Action**

![Diagram showing the mechanism of FODMAPs in the small and large intestine.]

- Water delivery
- Gas production
- Luminal distension
- Altered motility
- Pain, bloating, distension, wind, constipation +/- diarrhea

(Courtesy of Sue Shepherd, Ong, 2010, Barrett, 2009)

**Impact of FODMAP Diet on Breath Hydrogen Production and Symptoms**

- **Design**
  - Single-blind crossover study in 15 controls and 15 IBS patients
  - 2-day consumption of high-FODMAP diet (50 g/d) or low-FODMAP diet (9 g/d)

- **Results**
  - Higher levels of breath hydrogen with high FODMAP diet
  - GI symptoms and lethargy induced by high FODMAP diet in IBS patients but not controls

![Graph showing breath hydrogen production over time for different diets.]

N=29

HFD=high-FODMAP diet; LFD=low-FODMAP diet

Daily Symptom Scores on low-FODMAP vs. Control Diet


Treatment of Bloating & Distension

Scmulson & Chang. Aliment Pharmacol Ther 2011;33:1071
Mean score changes at 4 weeks: *B. infantis 35624 vs. Placebo for IBS*

![Graph showing mean score changes at 4 weeks for B. infantis 35624 vs. Placebo for IBS. The graph displays significant improvements in abdominal pain, bloating, incomplete evacuation, gas, straining, bowel satisfaction, and a composite score. The *P < 0.05 for Bifantis compared to Placebo.](image)

Probiotic VSL#3 Improves Flatulence and Retards Colon Transit in IBS

![Graph showing the improvement of flatulence and retardation of colon transit with VSL#3 compared to Placebo. The VAS score shows significant reductions in average symptom scores over 4-8 wk treatment period.](image)

*Whorwell, Am J Gastroenterol 2006; 101:1581
Kim HJ et al. NGM 2005; 17:687*
**Pathogenesis of Bloating & Distension**

- **Diet**
- **Probiotics**
- **Prosecretories**
- **Antibiotics**
- **Prokinetics**
- **Biofeedback?**

*Scmulson & Chang. Aliment Pharmacol Ther 2011;33:1071*

---

**Rifaximin Reduces Gas-related Symptoms in Bloating Patients Without SIBO***

**Overall Study Population**

- Baseline: 22.9% (Rifaximin) vs. 41.3% (Placebo)
- End of Treatment: 28.6% (Rifaximin) vs. 11.5% (Placebo)
- Post-treatment (10 days): 18.2% (Rifaximin) vs. 9.1% (Placebo)

**Patients With IBS (Rome II)**

- Baseline: 41.3% (Rifaximin) vs. 40.5% (Placebo)
- End of Treatment: 28.6% (Rifaximin) vs. 18.2% (Placebo)
- Post-treatment (10 days): 11.5% (Rifaximin) vs. 9.1% (Placebo)

Symptoms evaluated included abdominal pain, distension, number of bowel movements, stool consistency, and feeling of incomplete evacuation

*As determined by breath test.
Efficacy of Rifaximin for Bloating in IBS

<table>
<thead>
<tr>
<th>Measure Outcomes</th>
<th>Response rates (%)</th>
<th>Weight</th>
<th>ARR</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rifaximin</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pimental</td>
<td>41.8</td>
<td>15.9</td>
<td>2.5%</td>
<td>25.9</td>
</tr>
<tr>
<td>Lembo</td>
<td>46.1</td>
<td>39.6</td>
<td>26%</td>
<td>6.5</td>
</tr>
<tr>
<td>Target 1</td>
<td>39.5</td>
<td>28.7</td>
<td>33.9%</td>
<td>10.8</td>
</tr>
<tr>
<td>Target 2</td>
<td>41.0</td>
<td>31.9</td>
<td>37.5%</td>
<td>9.1</td>
</tr>
<tr>
<td>Overall</td>
<td>41.6</td>
<td>31.7</td>
<td>100%</td>
<td>9.9</td>
</tr>
</tbody>
</table>

OR = 1.55; 95 % CI = 1.23, 1.96; P < 0.001


Pathogenesis of Bloating & Distension

Bloating Distension

Diet

Probiotics

Prosecretories

Antibiotics

Prokinetics

Biofeedback?

Chloride Channels in Intestinal Transport

Enterocytes

**Ion Transport**

- $H_2O$ (Water)
- $Na^+$ (Sodium)
- $Cl^-$ (Chloride)
- $K^+$ (Potassium)

**Ion Transport**

- CFTR Channel
- Linaclotide
- Plecanatide
- CIC Channel
- Lubiprostone
- Tight junction

Lubiprostone Symptom Change: Responder vs Nonresponder

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Baseline Score</th>
<th>Mean Change From Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Discomfort/Pain</td>
<td>2.08</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Bloating*</td>
<td>2.26</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Constipation Severity*</td>
<td>2.23</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Stool Consistency†</td>
<td>2.76</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Straining*</td>
<td>2.39</td>
<td>P &lt; 0.001</td>
</tr>
</tbody>
</table>

*0 (absent), 1 (mild), 2 (moderate), 3 (severe), 4 (very severe)
†0 (very loose [watery]), 1 (loose), 2 (normal), 3 (hard), 4 (very hard [little balls])

Effect of Linaclotide on Bloating in Chronic Constipation

- Very severe
- Severe
- Moderate
- Mild
- None

*p ≤ 0.0001 vs. placebo*

Linaclotide Phase 3 IBS-C Trial
Weekly Change in Abdominal Symptoms

Discomfort
Bloating
Fullness
Cramping

p < 0.01 for each of the 26 Weeks in the Treatment Period.
Evidence-based Treatment of Bloating & Distension

**Bloating & Distension**

**General Measures:**
- Lifestyle
- Diet
- Probiotics

**Diarrhea**
- Antibiotics

**Constipation**
- ClC₂ activator
- GCC agonists
- Prokinetics
- Biofeedback

MBCP
877.462.6935
Functional Bowel Disorders Clinic
888-229-7408
Fecal *Bifidobacteria* Concentration in IBS Patients

Baseline [Bifidobacteria] log10/g

Change in [Bifidobacteria] log10/g

\[ r = -0.54 (P = 0.033) \]

Effect of Linaclotide on Change in Bloating Severity from Baseline to 12 Weeks in IBS-C

Phase 3 trials

Very severe

None

Placebo (n=797) | Linaclotide, 290 ug (n=805)

-1.0 | -1.9*  

*p=0.0001 vs. placebo*