Tried and True Secrets for Irritable Bowel Syndrome

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What is Irritable Bowel Syndrome?

Challenges in treating IBS

- Making the diagnosis
- Communicating the diagnosis
- Effective treatment
  - Constipation
  - Diarrhea
  - Refractory pain

"I'm afraid that your irritable bowel syndrome has progressed. You now have furious and vindictive bowel syndrome."
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Rome III definition of IBS

Recurrent abdominal pain or discomfort ≥ 3 days per month in
The past 3 months*

With 2 of 3 features:

- Improved with defecation
- Onset associated with a change in stool frequency
- Onset associated with a change in stool form

* Symptom onset at least 6 months before diagnosis
The **KISS** definition of Irritable Bowel Syndrome (IBS)?

- It is chronic and episodic
- Abdominal pain or discomfort
- Associated with altered bowel habit
  - Constipation
  - Diarrhea
  - Alternating/Mixed

### Which IBS Subtype?

<table>
<thead>
<tr>
<th>Constipation</th>
<th>Diarrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1: Long transit (e.g. &gt;100 hours)</td>
<td>Separate hard lumps, like nuts hard to pass</td>
</tr>
<tr>
<td>Type 2:</td>
<td>Sausage shaped but lumpy</td>
</tr>
<tr>
<td>Type 3:</td>
<td>Like sausage but with cracks on its surface</td>
</tr>
<tr>
<td>Type 4:</td>
<td>Like sausage or snake, smooth and soft</td>
</tr>
<tr>
<td>Type 5:</td>
<td>Soft blob with clear cut edges (assorted cash)</td>
</tr>
<tr>
<td>Type 6:</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td>Type 7:</td>
<td>Watery, no solid pieces (entirely liquid)</td>
</tr>
</tbody>
</table>
Challenges in treating IBS

• Making the diagnosis
• Communicating the diagnosis
• Effective treatment
  – Constipation
  – Diarrhea
  – Refractory pain

First things first!

• Establish a therapeutic relationship
• *Doesn’t take as long as you think!*
• Let the patient tell their complete story without interruption
  – Look at the patient
• Repeat back to the patient what you heard
• Identify what drove them to visit today
• Identify important quality of life implications
Remembering the basics

• Initial visit
  – Set the agenda
    • Educate regarding IBS
    • Mind body connection
    • Acknowledge role of stress without assessing blame
    • Disease management ---- not cure!
  – Identify therapeutic targets for the patient
    • Diet
    • Pharmacologic therapies
    • Non-pharmacologic approaches
      • Herbs, probiotics, cognitive behavioral therapy/hypnotherapy

Education

www.aboutibs.org
Patients are Worried!

- Convinced a diagnosis has been missed
- Cancer
- Colitis
- They lack digestive enzymes
- Their symptoms will worsen as they age
- Their lifespan will be shortened

Challenges in treating IBS

- Making the diagnosis
- Communicating the diagnosis
- Effective treatment
  - Constipation
  - Diarrhea
  - Refractory pain
**Treatment Goals**

- Reduce pain
- Normalize bowel habit
- Improve day to day functioning
- Improve quality of life

**Dietary Advice**

- Patient often relate their GI symptoms to certain foods
- Two large studies reported symptomatic improvement on elimination diets
  - Difficult to comply with
- Diet diary gets the patient involved with their treatment
- FODMAPS Diet (Fermentable Oligosaccharides, Difructose, Fructans, Raffinose, Polyols)
  - Some evidence to support
FODMAP Diet Restriction

- Oligosaccharides
  - Fructans – fructose chains w/glucose
    - Wheat, artichokes, onion
  - Galactans – galactose chains w/fructose
    - Soy, beans, cabbage

- Disaccharides
  - Lactose

- Monosaccharides
  - Fructose
    - Fruit sugars, apples, pears, high fructose corn syrup

- Polyols
  - Sorbitol, Xylitol, Mannitol, Glycerol
Dietary Advice for IBS

- Reduce fat/caloric load
- Sorbitol
- Dairy
- Fructose
- Gluten

Add fiber if constipation

Avoid triggers

Pharmacological Therapy for IBS

<table>
<thead>
<tr>
<th>Pain/Bloat</th>
<th>Diarrhea</th>
<th>Constipation</th>
</tr>
</thead>
</table>
| • Antispasmodics  
  - Anticholinergics  
  - Peppermint oil  
  - Calcium channel blockers  
  - Anti-depressants  
  - TCAs  
  - SSRI’s  
  • 5HT3 antagonists  
  • 5HT4 agonists  
  • Antibiotics  
  • Probiotics |
| • Loperamide  
  • Diphenoxylate  
  • Cholestyramine  
  • Bismuth  
  • 5HT3 antagonists  
  • Antibiotics  
  • Probiotics |
| • Fiber  
  • Osmotic laxatives  
  • Polyethylene glycol  
  • Stool softener  
  • Misoprostol  
  • Prokinetics  
  - 5HT4 agonist  
  • Chloride channel  
  • Guanylate cyclase C  
  • Antibiotics  
  • Probiotics |
Effective of Agents for IBS - C

- Fiber
  - Decreases whole gut transit time, eases stool passage
  - No change in contractile activity
  - May exacerbate gas, abdominal pain and bloating
  - Soluble fiber better than insoluble

- 10 grams psyllium
- Symptom relief 57% vs 35%

Bijkerk CJ et al BMJ 2009
Chloride Channel Agonist

- Lubiprostone
- Prostaglandin derivative
  - Enhances movement of Na, Cl and water into lumen
- 8 mcg BID
- Dose with meals to reduce side effect of nausea

Lubiprostone

NNT = 12.5
Drossman et al APT 2009
Linaclotide

- Pro secretory agent
- Similar to guanylin peptides
- Activate guanylate cyclase C receptors
- Three randomized controlled trials
- NNT = 6

Linaclotide

Linaclotide

Pain and Constipation

- Treat the constipation first
- Exclude dyssynergic defecation
  - Anorectal manometry and balloon expulsion testing
- If pain still present add a low dose TCA
Tricyclic antidepressants

• ~10 RCTs in IBS
  – Imipramine, amitriptyline, desipramine, doxepin, trimipramine
• Three meta-analyses
  • Demonstrate efficacy for improved abdominal pain
  • OR 4.2 (95% CI: 2.3 – 7.9)
  • TCAs improve global IBS symptoms more in IBS-D

TCA Meta-Analysis

• TCAs improve symptoms IBS
  – Pooled RR = 1.93
  – 95% CI: 1.44 – 2.6
  – p< 0.0001
• TCAs improve symptoms in IBS
  • Rahimi et al, World J GE 2009; 15: 1548
TCA Effect Not Dose Related

- Scatter plot of despiramine dose and composite score
  - Spearman correlation coefficient -0.04; p=0.7
- Halpert et al, AJG 2005 100: 664

SSRIs in IBS

- SSRIs with RCTs in IBS – few in number and with few numbers
  - Paroxetine
  - Citalopram
  - Fluoxetine
- Reduced days with abdominal pain
- Improved health related QOL
  - Stool pattern was not changed
- Promote global well-being
  - Whether depressed or not
SSRIs

- Meta-analysis 5 studies, 230 patients
- RR that symptoms remain: 0.62 (95% CI: 0.45 – 0.87)
- NNT = 3.5

Ford et al Gut 2008

Which SSRI?

- Fluoxetine, Citalopram and Paroxetine are generic
- Citalopram and escitalopram have low GI side effect profiles
  - Conflicting data on benefit overall
  - No effect on colon compliance or visceral pain (rats)
- Consider fluoxetine in constipation
  - Improved stool frequency and consistency
- Consider paroxetine in diarrhea
  - Data support global improvement
- Duloxetine seems to help pain (open label)
  - Exacerbates constipation
Peppermint Oil

- Antispasmodic properties
- Active ingredient is menthol
  - Relaxes smooth muscle by blocking Ca influx
- Seven randomized controlled trials
- Superior to placebo at 1 month in male VA pts
- Superior to placebo at 2 weeks in children
- NNT = 3

Diarrhea
Symptom Relief: Diarrhea

• Loperamide
  – Use before meals or other inciting events
  – Has not been shown to help overall IBS symptoms!

• Other options:
  – Probiotics
  – Antispasmodics
  – Antibiotics
  – Bile acid binding
  – Mesalamine
  – Purified bovine serum immunoglobulin

Efficacy of IBS Therapies

<table>
<thead>
<tr>
<th>Agent</th>
<th>Drug</th>
<th>Placebo</th>
<th>Therapeutic Gain</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antispasmodic</td>
<td>61</td>
<td>44</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>58</td>
<td>35</td>
<td>23</td>
<td>4</td>
</tr>
<tr>
<td>Alosetron</td>
<td>51</td>
<td>34</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Psychological</td>
<td>49</td>
<td>37</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Rifaximin</td>
<td>42</td>
<td>32</td>
<td>10</td>
<td>11</td>
</tr>
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</table>
Anti Spasmodics

- Agents with best evidence not available in the US
- Hyoscyamine 0.125 mg
- Dicyclomine 10 mg
- Methscopalamine 2.5 – 5 mg

- Best used intermittently
- Before meals
- Frequent side effects

IBS and Diarrhea

- Generally use amitriptyline as a first choice
- If too sedating, desipramine + anti-diarrheal
- Anxiety mediated symptoms or failure to response to TCA, try paroxetine
- Don’t forget Alosetron
5-HT₃ receptor antagonists

- Anti-nociceptive effects on GI tract
- Increase right colon compliance
- Reduce colon transit and improve stool form
  - reduced post-prandial colonic motility
- Alosetron was taken off the market “voluntarily” by the company
  - ischemic colitis, severe constipation, deaths
  - Reapproved 7/2002, restricted program

Clinical Trials With LOTRONEX™ (alosetron HCl): Effect on IBS Pain and Discomfort in Diarrhea-Predominant Female Patients

*P<0.05
S3BA3002

**P<0.001
S3BA3001

ACG Women in Gastroenterology Forum - Chicago, IL
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Alteration of Gut Microflora

• Complex relationship between host and enteric microflora
• Evidence of altered gut microbiota

Probiotics

• **Bifidobacter infantis 35624**
  – RCT - mild to moderate IBS
  – Improved abdominal pain and bowel habit
• **Lactobacillus plantarum**
  – 2 positive and 1 negative trial
  – RCT
  – Improved flatulence, abd pain at 6 and 52 weeks
• **Lactobacillus GG, reuterii or Salivarius (3 different trials)**
  – No effect
• **VSL #3**
  – Decreased flatulence and bloating
• **Saccharomyces cerevisiae**
Rifaximin

- Antibiotic with low systemic absorption
  - FDA approved hepatic encephalopathy and traveller’s diarrhea
- 550 mg TID x 14 days “nonconstipated” IBS
  - 40.7% improved rifaximin
  - 31.7% improved placebo
- Improvement persistent for up to 12 weeks
- No data on retreatment

Rifaximin RCT

NNT = 9
**Rifaximin Effect on Bloating**

- **Overall Study Population**
  - Rifaximin (n=83) vs Placebo (n=81)
  - Graph comparing baseline, after treatment, and post-treatment values for bloating.

- **IBS only**
  - Rifaximin (n=37) vs Placebo (n=33)
  - Graph comparing baseline, after treatment, and post-treatment values for bloating.

* P < 0.05

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**Bifidobacter infantis 35624**

- Probiotic
- Excellent safety data
- Dose finding data
- Randomized controlled trial
- Placebo controlled
- Also evaluated lactobacillus
  - Lactobacillus wasn’t effective
Bifidobacter infantis 35624

Psychological Therapies

- Cognitive behavioral therapy
- Medical hypnotherapy
Psychological Therapies

- Cognitive behavioral therapy \textit{NNT 3}
- Medical hypnotherapy \textit{NNT 2}

- High response rate (~70%)
- Evidence of sustained benefit
- No drug related side effects
- Requires a motivated patient
- Dependent on local expertise
- May not be covered by insurance

Final Pearls

- Determine why the patient is in your office \textit{today}
  - Assess psychological co-morbidities
  - Provide reassurance
- Provide dietary advice
- Determine if patient is interested in pharmacologic therapy
  - Symptomatic relief of main symptom
  - Provide non-narcotic pain relief
- Give non pharmacologic therapies a try!