Integrative Medical Approach To Care

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A 68 year old woman presents with 7 month history of

- History of recurrent, crampy pain in LLQ
- Bloating with abdominal distension and frequent loose stools.
- She spends long times in bathroom-worried about uncontrollable discomfort and fecal soiling.
- Feels anxious, fatigued and is frustrated that her previous physician did not take her distress seriously.
- Vitals-HR-70/min, BP-135/70mmHg, RR-16/min, Temp-98F.

Physical Exam is unremarkable except tenderness in LLQ.

How should her case be evaluated and treated?
Irritable Bowel syndrome is one of the several functional GI disorders seen by Primary Care physicians with worldwide prevalence of 10-15%\textsuperscript{(1)}.

Other functional disorders seen in the pts with IBS – fibromyalgia, chronic pelvic pain and interstitial cystitis \textsuperscript{(4,5)}.

Coexisting psychological conditions are also common.

Anxiety, somatization and symptom related fears.
The fears are

- I am worried that I will have severe discomfort during the day if I don’t empty my bowels completely in the morning.
- These contributes to impairment in quality of life and excessive use of health care associated with IBS.
Epidemiology

- The female to male ratio is 2:1 in population based samples and higher in those who seek health care.
- 10% of patients after bacterial or viral enteric infections.
- Risks factors for post infectious IBS include female sex, longer duration of enteritis and psychosocial factors (stress).
Pathophysiology

- IBS is often described as “Brain – Gut Disorder”
- But the pathophysiology is uncertain.
- Alterations in gastrointestinal motility and in the balance of absorption and secretion in the intestines may underlie irregularities in bowel habits (4)
Ask about the bowel habits and stool characteristics

Subclassified as

1. Diarrhea predominant
2. Constipation predominant
<table>
<thead>
<tr>
<th>Symptoms and Medication</th>
<th>Initial Dose</th>
<th>Target Dose</th>
<th>Common or Serious Side Effects</th>
<th>Evidence For the Symptom</th>
<th>Evidence For IBS</th>
<th>FDA-Approved For the Symptom</th>
<th>FDA-Approved For IBS</th>
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</thead>
<tbody>
<tr>
<td>Constipation</td>
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<td>Laxatives‡ and secretory stimulators</td>
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<tr>
<td>Polyethylene glycol 3350 (Miralax, Braintree Labs)</td>
<td>17,000 mg/day</td>
<td>up to 34,000, twice a day</td>
<td>Diarrhea, bloating, cramping</td>
<td>+++</td>
<td>–</td>
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<td>Lactulose (Kristolose, Cumberland Pharmaceuticals)</td>
<td>10,000–20,000 mg/day</td>
<td>20,000–40,000 mg/day</td>
<td>Diarrhea, bloating, cramping</td>
<td>+++</td>
<td>–</td>
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<td>Lubiprostone (Amitiza; Takeda, Sucampo)</td>
<td>24 μg, twice a day</td>
<td></td>
<td>Nausea, diarrhea, headache, abdominal pain and discomfort</td>
<td>+++</td>
<td>–</td>
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<td>No</td>
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<td>Prokinetics</td>
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<td>Tegaserod (Zelnorm, Novartis)</td>
<td>6, twice a day</td>
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<td>Initial diarrhea, abdominal pain, cardiovascular ischemia (rare)</td>
<td>+++</td>
<td>+++</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Diarrhea</td>
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<td>Loperamide (Imodium, McNeil)</td>
<td>2 mg</td>
<td>2–8 mg</td>
<td>Constipation</td>
<td>+++</td>
<td>–</td>
<td>Yes</td>
<td>No</td>
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<td>Alosetron (Lotronex, GlaxoSmithKline)</td>
<td>0.5 mg, twice a day</td>
<td>up to 1 mg, twice a day</td>
<td>Constipation, ischemic colitis (rare)</td>
<td>–</td>
<td>+++</td>
<td>No</td>
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<td>Bloating</td>
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<td>Antibiotics</td>
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<td>Rifaximin (Salix)</td>
<td>400 mg, three times a day</td>
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<td>Abdominal pain, diarrhea, bad taste</td>
<td>–</td>
<td>+</td>
<td>No</td>
<td>No</td>
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<td>Probiotics***</td>
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<td>Bifidobacterium infantis 35624 (Align, Procter &amp; Gamble)</td>
<td>1 capsule per day</td>
<td></td>
<td>None</td>
<td>+</td>
<td>+</td>
<td>No</td>
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<td>Pain</td>
<td></td>
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<td>Tricyclic antidepressants††</td>
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<td>Amitriptyline</td>
<td>10 mg, at bedtime</td>
<td>10–75 mg, at bedtime</td>
<td>Dry mouth, dizziness, weight gain</td>
<td>++</td>
<td>+</td>
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<tr>
<td>Desipramine</td>
<td>10 mg, at bedtime</td>
<td>10–75 mg, at bedtime</td>
<td></td>
<td>++</td>
<td>+</td>
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<td>Selective serotonin-reuptake inhibitors‡‡</td>
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<td>Paroxetine (Paxil CR, GlaxoSmithKline)</td>
<td>10–60 mg</td>
<td></td>
<td>Sexual dysfunction, headache, nausea, sedation, insomnia, sweating, withdrawal symptoms</td>
<td>–</td>
<td>+</td>
<td>No</td>
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<tr>
<td>Citalopram (Lexapro, Forest)</td>
<td>5–20 mg</td>
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<td>+</td>
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<td>Fluoxetine (Prozac, Eli Lilly)</td>
<td>20–40 mg</td>
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<td>Somnolence, dizziness, headaches, insomnia</td>
<td>+</td>
<td>–</td>
<td>No</td>
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</table>
Abstract

Objective

To review the evidence supporting selected complimentary and alternative medicine approaches used in treatment of irritable bowel syndrome.
Quality of evidence

Medline (from Jan 1966), and Cochrane database of systemic reviews were searched combining the terms irritable bowel syndrome or irritable colon with complementary therapies, alternative medicine, acupuncture, fiber, peppermint oil, yoga, massage, hypnotherapy and cognitive behavioral therapies.

Level I evidence was available for most interventions.
Summary of evidence for CAM treatments for IBS

Intervention
- Peppermint oil
- Probiotics
- Soluble fiber
- Tong Xie Yao Fang
- Hypnotherapy
- CBT

Body of evidence
- 2 meta analysis of 5 and 4 RCTs\(^\text{(6)}\)
- Meta-analysis of 23 RCTs\(^\text{(7)}\)
- Meta-analysis of 9 RCTs\(^\text{(8)}\)
- Meta-analysis of 12 prospective trials\(^\text{(9)}\)
- 1 Cochrane and 3 other systematic reviews\(^\text{(10-13)}\)
- 5 RCTs (3 individual CBT and 2 group CBT)\(^\text{14-17}\)
Complimentary and Alternative Therapies

Interventions

1. Fiber-Increasing fiber intake through diet or supplementation is often the first advice given to IBS patients.
2. Soluble vs insoluble Fiber
Found 2 systemic reviews that examined the role of fiber in IBS. A Cochrane review of randomized control trials (RCTs) limited to bulking agents (4 trials using wheat bran and 7 trials using soluble fiber) failed to demonstrate any effect on abdominal pain (RR 1.2, global assessment (RR) 1.09 or symptoms score. Overall the trials indicated improvement of global IBS symptoms (RR) 1.33, 95% CI 1.19 to 1.50, especially in IBS related constipation. Soluble fiber fared better than insoluble fiber, which had no effect. In summary there is good evidence that soluble but not insoluble fiber improves constipation and IBS symptoms.
Peppermint Oil

An extract of plant- mentha Piperita has been used to treat stomach upset for thousand of years.
Relaxes smooth muscle cells by interfering with calcium channels.
Short term trials suggest daily use of 3 to 6 enteric coated capsules containing 0.2 to 0.4 ml of peppermint oil each improves IBS symptoms.
Herbal Formulas

- In traditional Healing systems combination of several herbs has been used to achieve therapeutic effect.
- One of the most extensively studied herbal therapies for IBS is Tong xie yao fang (TXYF).
- A systemic review of 12 randomized trials included 1,125 IBS patients found that TXYF was more effective than control treatments (RR 1.35 with 95% CI, 1.21 to 1.50; p <0.05. (18)
- But caution that the trials were heterogeneous and of poor quality and formula itself was inconsistent.
Two herbal formulas known as STW 5 (iberogast) and STW 5-2 contain several known herbal digestive aids. In a recent trial, 208 pt’s with IBS received STW 5, STW 5-2, a single plant extract or placebo. Pain and symptoms scores were significantly improved among pts receiving STW formulas (p <0.001). Safety is common concern with herbal medicines. A systemic review of 22 RCTs of herbal medicines for IBS reported adverse events in 2.97% of patients (95% CI 2.04% to 3.90%), none of them were considered serious. (21)
Probiotics

- Are live microorganisms which when taken in sufficient quantities confer health benefits.
- Mechanism
  
  1. Modification of Gut mucosal barrier function.
  2. Mucosal immune system.
  3. Visceral sensation as well as alterations in fermentation and
  4. Production of bacteriocins or substances with neurotransmitting properties.
In a recent systemic review, Brenner and colleagues reported that of 16 RCT’s evaluating probiotics in the treatment of IBS, Bifid bacterium infantis 35624 was the only one which provided significant improvement in IBS symptoms in short term studies.

In the study of O’Mahony et al, IBS patients were randomized to receive B infantis, Lactobacillus salivarius UCC4331, or placebo, pts randomized to B infantis 35624 experienced a greater reduction in symptom scores for abdominal pain/discomfort/bloating and BM compared to placebo.\(^{(22)}\)
There was another dose ranging study by Whorwell et al, which found that *B. infantis* 35624 at a dose of 10^8 CFU/ml was significantly more likely than placebo to improve IBS symptoms (P – 0.014).
Based on the hypothesis that treatments designed to improve the ability of mind to influence or control bodily functions may be effectively used to relieve IBS symptoms.

The 2 most studied techniques are
- CBT (cognitive behavioral technique)
- GDH (Gut directed hypnotherapy)
Most treatment trials involving psychological therapies in IBS have featured a specific treatment called CBT.

Protocols include
1. Info about stress and its relation to IBS.
2. Self monitoring of events before and after IBS flare ups.
3. Problem solving strategies about stressors.
Evidence

- A recent meta-analysis of 17 studies regarding CBT for IBS that defined efficacy as >50% reduction in symptoms yielded an ODD ratio of 12 with a mean NNT vs control subjects of approx 2.
- This may be compared with another meta-analysis of 6 RCTs of Alosetron that showed odd ratio of 1.8 with NNT of 7 as well as similar analysis of 8 studies regarding Tegaserod showed odd ratio of 1.2 with NNT of 17.
Gut Directed Hypnotherapy

- It is a form of hypnosis that has been frequently reported to have beneficial effect on IBS symptoms.
- Includes education about self hypnosis, which enable pt to manage their symptoms without reliance of care providers.
Evidence

- The first study to evaluate GDH in the management of IBS was published in 1984.
- Only 4 studies including the original article in 1984 have used randomized and controlled treatment trials, but the reported success rate > 75% in all studies. All 4 studies reported improvement in GI symptoms.
- In a controlled but non randomized trial of GDH vs standard care with 12 months follow up, GDH was much more effective in reducing IBS symptoms.
- Pts included in these trials had refractory IBS, so not possible to generalize the result.
References

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22. O mahony L lactobacillus and bifido bacterium in IBS gastroenterology 2005;128;541-551