The Gut Connection: Solutions for SIBO, IBS, IBD and GERD

Dr. Kim Bretz ND
And at that very moment, we heard a loud whack!
From outside in the fields came a sickening smack
of an axe on a tree. Then we heard the tree fall.
The very last Truffula Tree of them all!
GI – The Basics

One microbe = one disease?
GI – The Basics

Type of bacteria

vs

Function
How I think about treatment

1. **Diet** – not always curative but always important to health
2. **Microbiota** – almost always contributes to the problem (probiotics, prebiotics, occasionally killing)
3. **Nutrient deficiencies** – will make healing and repair, as well as feeling good impossible if there are major deficiencies
4. **Healing and repair**
5. **Help** – enzymes, HCl stimulators, HCl, prokinetics
...And Sleep Matters Too

Medscape Gastroenterology > GI Common Concerns – Computer Consult

COMMENTS

Treating Gastrointestinal Disorders Through Improved Sleep

David A. Johnson, MD

Disclosures | December 19, 2016

IN THIS PROGRAM

Sleep Fragmentation’s Considerable Costs

Identifying Sleep Disorders

Impact in GI Disease

Taking the Wider View
“In fact, if you start asking the IBD patients in your practice about sleep fragmentation, it may be a predictor for who in remission is going to go to a flare in the next 6 months, with odds ratios increasing anywhere from two to three times.”
Irritable bowel syndrome (IBS) is a group of symptoms—including abdominal pain and changes in the pattern of bowel movements without any evidence of underlying damage.
“One could make the case it is now time to drop the arguably pejorative term functional…”

“...a purely symptom-based classification of the FGIDs will be extinct in the next two decades…”
IBS – Diagnosis Rome IV

- Recurrent abdominal pain or discomfort at least 1 day a week in the last 3 months, associated with two or more of the following:
  - Symptoms improved by defecation
  - Onset associated with a change in frequency of stool
  - Onset associated with a change in form or appearance of stool
We herein showed that sensitivity to colonic distension of IBS patients can be transferred to rats by the fecal microbiota.
IBS – Microbial Dysbiosis

PI-IBS is common after gastroenteritis from water contamination and often is diarrhea-predominant.
IBS – Microbiota

Am J Gastroenterol 2015 Feb; 110(2):278-287
IBS - Diet

Most recently, and belatedly, the important role of the ubiquitous interloper into the gastrointestinal environment, food, has begun to be recognized and serious research efforts devoted to understanding its role in IBS and to the development of dietary approaches to the management of IBS.

Eamonn M.M. Quigley
IBS – Diet?

- Allergies
- Intolerances
- Elimination Diets
- Hypoallergenic Diets
- Rotation Diets
- Lactose, gluten, non-celiac wheat sensitivity...
Low-FODMAP Diet


# IBS – FODMAP Diet

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Patterns of malabsorption of FODMAPs</th>
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</table>
| **Oligosaccharides** | Fructans: no suitable small-intestinal hydrolases—negligible absorption  
Galacto-oligosaccharides: no human alpha-galactosidase—minimal absorption |
| **Disaccharides (lactose)** | No absorption if lactase is deficient |
| **Fructose** | Absorptive capacity limited when in excess of glucose—low in 30% (considered to have fructose malabsorption) |
| **Polyols** | Slow passive diffusion and absorption only (< 20%) |

FODMAPs = fermentable oligosaccharides, disaccharides, monosaccharides, and polyols
IBS – Low FODMAP Diet

**PROS**
- 70-86% success in patients – and fast

**CONS**
- Microbiota change - bad (and good?)
- Constipation
- Nutrient lack?
IBS symptoms are linked to FODMAP content and associated with alterations in the metabolome. In subsets of patients, FODMAPs modulate histamine levels and the microbiota, both of which could alter symptoms.
IBS – Low-FODMAP Diet

Do not let your patients find their own information online – make your own handouts based on Monash information or get them to buy them app themselves.
IBS – Low-FODMAP Diet

http://www.med.monash.edu/cecs/gastro/fodmap/
IBS – Low-FODMAP Diet

Even though your patients might feel better eliminating the foods in this diet, it is not the solution. Re-introduce foods, asap.
IBS – Low-FODMAP Diet

Re-introduction:

- Starting by week 6 – I often start earlier
- Remember, the food isn’t the problem
IBS - Prebiotics

Non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or the activity of a bacterium or a limited number of bacteria in the colon that can improve host health.
IBS - Prebiotics

Warning: These bars may cause your IBS patients to explode
IBS - Prebiotics

Are your patients avoiding all prebiotics?
IBS - PHGG

Beneficial Function

- Supports bifidogenic and lactogenic growth
- Increases the concentration of short chain fatty acids (SCFAs) in the distal intestine due to its fermentability
- Effective in the treatment of acute diarrhea in children and adult patients of intensive care units
- Alleviate irritable bowel syndrome (IBS) symptoms

Food Funct., 2016, 7, 1833
PHGG stimulates growth of Parabacteroides, a genus of bacteria that have been inversely associated with IBS and ulcerative colitis.
The results of this study support the administration of 6g/day PHGG for IBS patients with bloating.
Although the cause of pediatric functional gastrointestinal disorders is not known, the results show that the complementary therapy with PHGG may have beneficial effects on symptoms control.
Four-week PHGG use accelerates colon transit time in patients with chronic constipation, especially in those with slow transit, and improves many of their symptoms including frequency of bowel movements.
Prebiotics

Use caution (bloating likely)
- Inulin (including chicory root)
- Fructo-oligosaccharides (FOS)

Generally helpful
- Partially hydrolyzed guar gum
- Arabinogalactans
- Galacto-oligosaccharides
IBS - Probiotics

Stop saying you can recolonize the gut.

Seriously.
This systematic review of the pertinent literature demonstrates a lack of evidence for an impact of probiotics on fecal microbiota composition in healthy adults.
Further research will provide insight into the degree of permanence of probiotic-induced changes, although research to date suggests that continued probiotic consumption is needed for sustained impact.
IBS - Probiotics

Effects of Probiotics on the Microbiota:

- Production of inhibitory compounds (i.e. antimicrobial peptides)
- Producing substrates that might promote the growth of colonizing microbes
- Promoting immune responses against specific microbes

J Clin Gastroenterol Volume 45, Supp. 3,
IBS - Probiotics

Effects of Probiotics on the Microbiota:

- Inhibiting attachment through stimulated mucin production
- Decreased colonic pH
- Reinforcing gut barrier effects - repair of hyperpermeable epithelial barriers
- Increase production of SCFAs including butyrate
- Downregulation of gut inflammation

J Clin Gastroenterol Volume 45, Supp. 3,
Clinical Guide to Probiotic Supplements

Available in Canada: 2016 Edition
Indications, Dosage Forms and Clinical Evidence to Date

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Download PROBIOTIC GUIDE mobile app for free
IBS - Probiotics

- *L. plantarum 299v* – 10B/capsule (1-2 daily): level 1
- *L. acidophilus CUL60* – 10-25B/capsule (1-2 daily): level 2
  - *L. acidophilus CUL21*
  - *B. bifidum CUL20*
  - *B. lactis CUL34*
- *Saccharomyces cerevisiae I-3856* – 40B/capsule (1 daily): level 1
Digestive enzymes are classified based on their target substrates:

- **Proteases and peptidases** split proteins into small peptides and amino acids.
- **Lipases** split fat into three fatty acids and a glycerol molecule.
- **Amylases** split CHO such as starch and sugars into simple sugars such as glucose.
If your patient responds to a low-FODMAP diet, they don’t likely need amylases, lipases or proteases.
IBS - Enzymes

- **Alpha-galactosidase** – beans, veg, whole grains (esp. cruciferous)
- **Lactase** – milk lactose
- **Hemi-cellulase & cellulase** – plant cell wall/fiber
- **Pectinase** – breaks down pectin (polysaccharide) found in cell walls (fruits/veg)
- **Xylanase** – structural components of cell walls (fruits, veg, nuts, grains)
Visceral pain modulation represents another potential health benefit attributed to bifidobacteria and other GABA-producing species of the intestinal microbiome.
GABA selectively increases the expression of MUC1, a cell surface mucin that prevents the adhesion of microorganisms, because of its size and negative charge, and therefore propose that the well-described positive effects of glutamine on enterocytes and intestinal integrity are partly attributable to effects of its metabolite GABA.
Melatonin has been studied as a co-adjuvant treatment in several gastrointestinal diseases including irritable bowel syndrome (IBS), constipation-predominant IBS (IBS-C), diarrhea-predominant IBS (IBS-D), Crohn's disease, ulcerative colitis, and necrotizing enterocolitis.
SIBO

Condition in which there is overgrowth of bacteria in small bowel in excess of $10^5$ colony forming units per milliliter on culture of the upper gut aspirate.
111 IBS subjects (55 neomycin, 56 placebo) entered the study, with 84% having an abnormal LBT, compared with 20% in healthy controls (p < 0.01)
Irritable bowel syndrome and small intestinal bacterial overgrowth: Meaningful association or unnecessary hype?
SIBO – Fad or Fact?

2014 review of studies on SIBO among patients with IBS

- Patients with IBS: 4% to 78%
- Controls: 1% and 40%

World J Gastroenterol 2014 Mar 14;20(10):2482-91
SIBO – Fact...But...

Stop saying 84% of people with IBS have SIBO
SIBO - Treatment

- Reduce the bacteria
- Dietary components
- Gut healing

DEAL WITH THE CAUSE!
High dosage rifaximin for the treatment of small intestinal bacterial overgrowth.
Scazzellini E, Gabrielli M, Lauritano CE, Lupascou A, Merola G, Cammareri G, Cazzato IA, Gasbarrini G, Gasbarrini A.

**Abstract**
BACKGROUND: Rifaximin is a broad spectrum non-absorbable antibiotic used for treatment of small intestinal bacterial overgrowth. Doses of 1200 mg/day showed a decontamination rate of 60% with low side-effects incidence.

AIMS: To assess efficacy, safety and tolerability of rifaximin 1600 mg with respect to 1200 mg/day for small intestinal bacterial overgrowth

**Conclusions**: Rifaximin 1600 mg/day showed a significantly higher efficacy for small intestinal bacterial overgrowth treatment with respect to 1200 mg with similar compliance and side-effect profile.
The combination of rifaximin with partially hydrolysed guar gum seems to be more useful in eradicating SIBO compared with rifaximin alone.
SIBO - Eradication

Herbal therapies are at least as effective as rifaximin for resolution of SIBO by LBT.

Herbal therapy is equivalent to rifaximin for the treatment of small intestinal bacterial overgrowth.

RESULTS: Three hundred ninety-six patients underwent LBT for suspected SIBO, of which 251 (63.4%) were positive. 165 underwent treatment and 104 had a follow-up LBT. Of the 37 patients who received herbal therapy, 17 (46%) had a negative follow-up LBT compared to 23/67 (34%) of rifaximin users (P = .24). The odds ratio of having a negative LBT after taking herbal therapy as compared to rifaximin was 1.85 (CI=0.77-4.41, P = .17) once adjusted for age, gender, SIBO risk factors and IBS status. Fourteen of the 44 (31.8%) rifaximin non-responders were offered herbal rescue therapy, with 8 of the 14 (57.1%) having a negative LBT after completing the rescue herbal therapy, while 10 non-responders were offered triple antibiotics with 6 responding (60%, P = .85). Adverse effects were reported among the rifaximin treated arm including 1 case of anaphylaxis, 2 cases of hives, 2 cases of diarrhea and 1 case of Clostridium difficile. Only one case of diarrhea was reported in the herbal therapy arm, which did not reach statistical significance (P = .22).

CONCLUSION: SIBO is widely prevalent in a tertiary referral gastroenterology practice. Herbal therapies are at least as effective as rifaximin for resolution of SIBO by LBT. Herbs also appear to be as effective as triple antibiotic therapy for SIBO rescue therapy for rifaximin non-responders. Further, prospective studies are needed to validate these findings and explore additional alternative therapies in patients with refractory SIBO.
SIBO – Eradication SE

- **Rifaximin**
  - Anaphylaxis (1)
  - Hives (2)
  - Diarrhea (2)
  - C. diff infection (1)

- **Herbal Therapy**
  - Diarrhea (1)
SIBO – Herbal Eradication

- **Hydrogen SIBO**
  - Berberine herbs (2000-5000mg/d)**
  - Oregano (50 mg tid)

- **Methane SIBO**
  - Allicin extract (450 mg tid)
SIBO - Diets

- Nothing has been proven as a gold standard
- Not to be done in isolation
- Usually done after microbe eradication (many symptoms should be gone BEFORE starting)
SIBO – Diet Options

1. Specific Carbohydrate Diet
2. GAPS diet
3. Low FODMAP diet
4. SIBO Specific Food Guide (Dr Allison Siebecker)**
5. Cedars-Sinai Diet (Dr Pimentel)
During the fasting state the upper gastrointestinal tract exhibits a specific periodic migrating contraction pattern that is known as the migrating motor complex (MMC).
SIBO - Motility

- Prokinetic options to help motility:
  - Medications: erythromycin, low dose naltrexone
  - Iberogast
  - 5-HTP**
  - Melatonin**
Melatonin plays an important part in gastrointestinal physiology which includes regulation of gastrointestinal motility, local anti-inflammatory reaction as well as moderation of visceral sensation.
Additionally, melatonin an important mediator of brain gut axis, has been shown to exhibit important protective effects against stress-induced lesions in the gastrointestinal tract.
GERD

Backwards movement of stomach acid secretions or bile/gastric acid secretions into the esophagus, causing symptoms (with or without esophagitis)
GERD - Symptoms

- A burning sensation in the chest, can spread to the throat
- Sour taste in the mouth
- Chest pain
- Dry cough
- Regurgitation of food or sour liquid (acid reflux)
- Sensation of a lump in your throat
GERD - Symptoms

Less common:

- Hoarseness and sore throat
- Difficulties swallowing
- Asthma
- Sinusitis
- Nausea and vomiting
A diagnosis of refractory GERD is made if no other causes are identified and a patient’s symptoms persist in spite of proton pump inhibitor dose escalation to twice daily; typically, this represents 19% to 32% of GERD patients.
Is It Really GERD?

**Functional heartburn**: the same heartburn symptoms that are caused by GERD without any evidence of abnormal esophageal acid exposure, physiologic acid reflux exposure that highly correlates with symptoms and recognized esophageal motility disorders.
GERD – Causes

- Peristaltic motility disorders
- Valve incompetency
- Delayed gastric emptying
- Hiatal hernia
- Poor dietary habits
- Obesity, pregnancy
- Medications
GERD – Medications

- Anti-cholinergic drugs
- Birth control pills
- Ca channel blockers
- Diazepam, TCA
- Cholestryamine
- Bisphosponates
- α and β adrenergic agonists
GERD-IBS Overlap

Of individuals meeting the criteria of one or more of the conditions GERD, FD and IBS, about one-third are suffering from at least **two** of them.
IBS overlaps more frequently with FH than with GERD and HE, suggesting common pathways and treatment.
Don’t Make Your Patients Worse!

Warn your patients about rebound when stopping their PPIs
Acid hypersecretion after PPI therapy is more pronounced, lasts longer, and could possibly be the cause of acid-related symptoms.
Treatment with GAS medications is associated with the occurrence of food allergy, an effect not apparently related to a diagnosis of GERD alone.
GERD - Diet

Commonly considered foods:
- Fatty or fried foods
- Tomato sauce, citrus, spicy
- Alcohol
- Chocolate
- Mint
- Garlic, onions – especially raw
- Coffee, tea
GERD - Diet

Poor habits

- Over-eating
- Eating late at night
- Eating too quickly, not chewing enough
- Lying down after eating
- Smoking
GERD - Diet

Biggest successes

- Gluten-free
- Alcohol decrease, especially if excessive
- Mint – watch toothpastes, gums, candies
- Low FODMAP diet – especially for refractory cases/functional heartburn or those with IBS-type symptoms**
GERD – Treatment and Healing

Acute Care:

- 2 Tbsp aloe vera juice in water or chamomile tea
- Slippery elm gruel or tea
- DGL tablets –1-2 tabs, as needed (max qid)
- 1 Tbsp ACV in large glass of water
- Alginates
- Chewing non-mint gum
GERD – Treatment and Healing

- Melatonin (5-10g)
  - Gastroprotective
  - Inhibits NO production
  - Healing
  - Increases LES pressure
- Demulcents (capsules or slippery elm gruel)
- Aloe vera juice (1-3 oz before meals) or in smoothie
- HCl stimulator (instead of HCl) – gentian, ACV, dandelion, chamomile, bitters combo
In infants with functional GER, *L. reuteri* DSM 17938 reduce gastric distension and accelerate gastric emptying. In addition, this probiotic strain seems to diminish the frequency of regurgitation.
The sequential treatment regimen achieved a significantly higher eradication rate of *H. pylori* compared with standard 7-d regimen. *L. reuteri* supplementation could reduce the frequency and the intensity of antibiotic-associated side-effects.
L. reuteri combination alone is able to exert an inhibitory effect on *H. pylori* growth, and when administered with eradication therapy, it determines a significant reduction in antibiotic-associated side effects.
**GERD/H. pylori – Probiotics**

- **L. reuteri DSM 17938 (Adjunctive with some eradication)**
  - 100M/tab – daily

- **L. rhamnosus GG (Adjunctive)**
  - 10B/cap – daily

- **Saccharomyces boulardii lyo (Adjunctive)**
  - 5B/capsule – 1-2 daily
Inflammatory Bowel Disease

- Group of inflammatory autoimmune disorders affecting the gut – anywhere from mouth to rectum
- Most common types: Crohn’s Disease and Ulcerative Colitis
Inflammatory Bowel Disease

Symptoms related to inflammation of the GI tract:
- Diarrhea
- Rectal bleeding
- Urgent need to move bowels
- Abdominal cramps and pain
- Sensation of incomplete evacuation
- Constipation (can lead to bowel obstruction)

General symptoms that may also be associated with IBD:
- Fever
- Loss of appetite
- Weight Loss
- Fatigue
- Night sweats
- Loss of normal menstrual cycle
IBD: Physiology

- Increased paracellular permeability
- Tight junction abN
- TNF-α
  - altered permeability
  - apoptosis of enterocytes
  - increased rate of shedding, and hindering the redistribution of TJs that should seal the gaps left

Mediators Inflamm. 2015; 2015: 628157.
IBD: History Of Antibiotic Use

UK study following a total of 1,072,426 subjects from 1994-2009

- IBD rates: **anti-anaerobic antibiotic** unexposed and exposed subjects were 0.83 and 1.52/10000 person-years, respectively
- 84% relative risk increase
- Dose-response effect existed with more than 2 courses of antibiotics

The dysbiosis of CD patients is characterized by reduced abundance of multiple butyrate-producing bacteria species.
IBD - Diet

A low-FODMAP diet does not seem to improve IBD
These data suggest that a diet low in FODMAPs is an efficacious treatment solution in the management of functional bowel symptoms for IBS and IBD patients.
IBD - Diet

Clinical and mucosal improvement with specific carbohydrate diet in pediatric Crohn disease; N = 9

METHODS: Eligible patients with active CD (Pediatric Crohn’s Disease Activity Index [PCDAI] ≥ 15) underwent a patency capsule and, if passed intact, capsule endoscopy (CE) was performed. Patients taking SCD were monitored for 52 weeks while maintaining all prescribed medications. Demographic, dietary, and clinical information, PCDAI, Harvey-Bradshaw Index (HBI), and Lewis score (LS) were collected at 0, 12, and 52 weeks. CEs were evaluated by an experienced reader blinded to patient clinical information and timing.

RESULTS: Sixteen patients were screened; 10 enrolled; and 9 completed the initial 12-week trial receiving 85% of estimated caloric needs before, and 101% on the SCD. HB significantly decreased from 3.3 ± 2.0 to 1.3 (P = 0.007) as did PCDAI (21.1 ± 5.9 to 7.8 ± 7.1; P = 0.011). LS declined significantly from 2153 ± 732 to 960 ± 433 (P = 0.012). Seven patients continued the SCD up to 52 weeks; HB (0.1 ± 0.4) and PCDAI (5.4 ± 5.5) remained improved (P = 0.016 and 0.027 compared to baseline), with mean LS at 1046 ± 372 and 2 patients showed sustained mucosal healing.

CONCLUSIONS: Clinical and mucosal improvements were seen in children with CD, who used SCD for 12 and 52 weeks. In addition, CE can monitor mucosal improvement in treatment trials for pediatric CD. Further studies are critically needed to understand the mechanisms underlying SCD’s effectiveness in children with CD.
This retrospective review provides evidence that the SCD can be integrated into a tertiary care center and may improve clinical and laboratory parameters for pediatric patients with nonstructuring, nonpenetrating CD as well as UC.
After following the IBD-AID, all (100%) patients were able to discontinue at least one of their prior IBD medications, and all patients had symptom reduction including bowel frequency.
IBD-AID Nutritional Regime

There are 4 basic parts to the diet that need to be included on a daily basis + texture changes to food:

1. Prebiotic food
2. Probiotic food
3. Good balanced diet
4. Avoidance of certain foods (modified specific CHO diet)
   - No processed foods, trans, refined sugar, grains (except oats), lactose

http://www.umassmed.edu/nutrition/ibd/ibdaid/
**IBD – Strain Specific Probiotics**

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<tr>
<th>Strain</th>
<th>Form</th>
<th>Dose</th>
<th>Quantity</th>
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<tr>
<td><em>Saccharomyces boulardii</em> lyo</td>
<td>Capsule/Sachet</td>
<td>5B/capsule</td>
<td>1-2 capsules</td>
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<tr>
<td><em>Escherichia coli</em> Nissle 1917</td>
<td>Capsule</td>
<td>2.5-25B/capsule</td>
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Clinical Guide to PROBIOTIC SUPPLEMENTS AVAILABLE IN CANADA: 2016 Edition
PHGG promotes colonic epithelial cell wound. These findings indicate that PHGG could be utilized as a therapeutic agent for patients with intestinal mucosal damage such as those with IBD.
These findings suggest that microbial metabolites of PHGG reduce intestinal barrier defects and inflammation in colitic mice.
IBD - Melatonin

Shown to block the induction of drug-induced colitis in mice if premedicated with melatonin.

BMC Gastroenterol. 2002 Apr 24;2:

Melatonin reduces TNF-a induced expression of MAdCAM-1 via inhibition of NF-kappaB.

METHODS: We examined how different doses of melatonin reduced endothelial MAdCAM-1 induced by TNF-a in an in vitro model of lymphatic endothelium. Endothelial monolayers were pretreated with melatonin prior to and during an exposure to TNF-a (1 ng/ml, 24 h), and MAdCAM-1 expression measured by immunoblotting.

RESULTS: MAdCAM-1 was induced by TNF-a. Melatonin at concentrations over 100 microm (10(-4) M) significantly attenuated MAdCAM-1 expression and was maximal at 1 mM.

CONCLUSIONS: Our data indicate that melatonin may exert therapeutic activity in IBD through its ability to inhibit NF-kappaB dependent induction of MAdCAM-1.
The majority of these studies indicate that melatonin has a positive impact on IBD with no or negligible side effects. Such results have been mostly explained through free radical scavenging and diminishing inflammation.