2020 Virtual Advocacy Event

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The following slides were presented during the educational portion of IFFGD's 2020 Virtual Advocacy Event. To view this presentation and the all videos available during this program, please visit https://bit.ly/Adv_Edu.

Be Active. Be Heard. Make a Difference.

1

Supplements for IBS: What is the Evidence?

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

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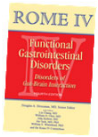
2



Functional GI Symptoms

- **Bothersome gut symptoms that reduce patient's quality of life and ability to carry out daily activities**
- **Can affect any part of the GI tract**
  - **Most common are functional dyspepsia and irritable bowel syndrome**
- **No obvious cause found by blood/radiology tests or endoscopy**
- **Affect between a quarter and a third of people**
- **Account for billions of dollars in health care expenditures**
- **FDA approved medical treatments:**
  - **Improve symptoms in fewer than half of patients**
  - **Can cause significant side effects**
  - **Often not covered by insurance**

Drossman et al, Gastroenterol May 2016
Shapiro, Deutsch, Chey. Neurogastro LATAM Rev. 2020

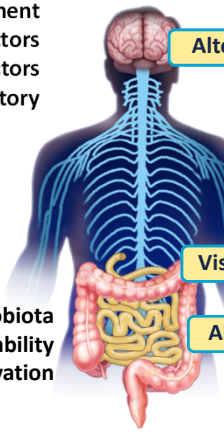
3

Proposed Etiologies of FGIDs

Environment
Genetic factors
Stress/psychological factors
Abuse history

Food sensitivity
Drugs
Acute enteric infection

Altered gut microbiota
Altered intestinal permeability
Mucosal immune activation



Altered perception

Altered brain-gut interactions

Visceral hypersensitivity

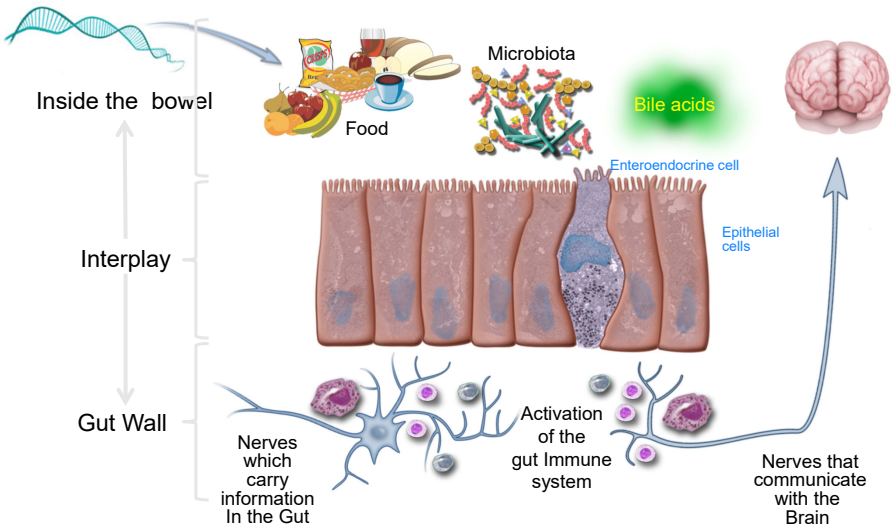
Altered GI motility

GI=gastrointestinal; IBS=irritable bowel syndrome.

Chey et al JAMA 2015

4

FGIDs: Outside-In?



Barbara G, et al. Gastroenterol 2016;150:1305

5

Step-wise Integrated Treatment of FGIDs

- Psychological treatments
- Continuing care
- Improve functioning

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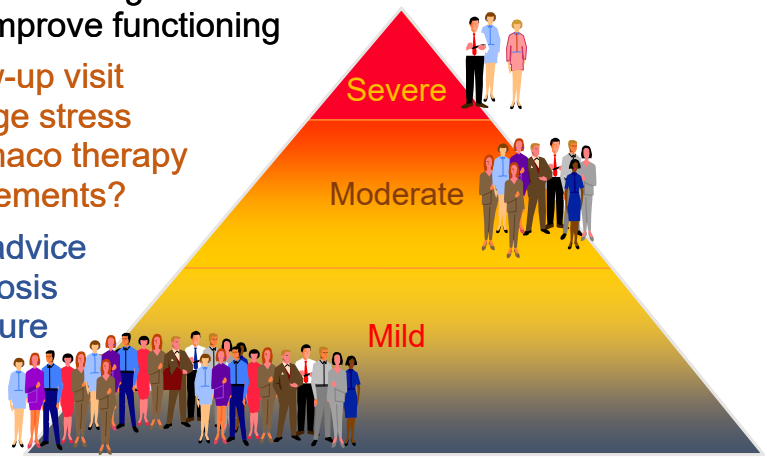
- Follow-up visit
- Manage stress
- Pharmaco therapy
- Supplements?

+

- Diet, lifestyle advice
- Positive diagnosis
- Explain, reassure



6

Which supplements might be useful for FGIDs?

- Peppermint oil (RCTs)
- STW-5 (RCTs)
- Glutamine (1 RCT)
- Aloe Vera (RCTs)
- Melatonin (RCTs)
- Prebiotics (RCTs)

- Tumeric (Poor data)
- Artichoke Leaf Extract. (Poor data)
- Cannabis (Poor data)

Shapiro, Deutsch, Chey. Neurogastro LATAM Rev. 2020

7

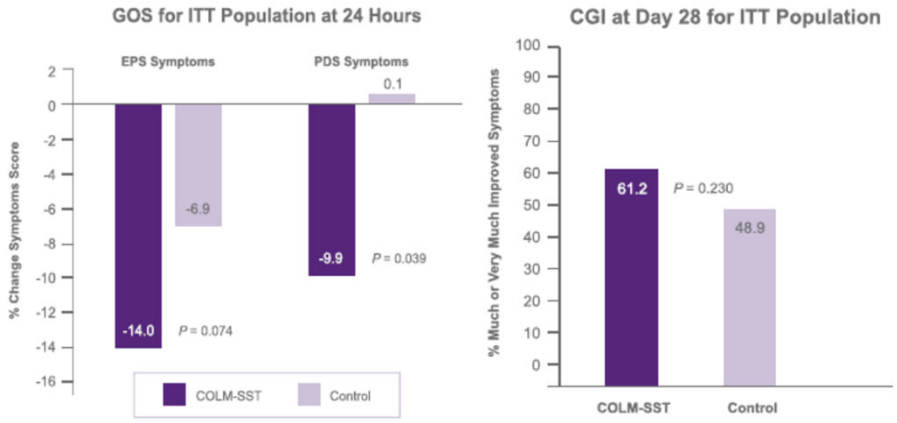
Peppermint Oil for FD and IBS

- From herb *Mentha peperta*
- Used to treat dyspepsia & IBS symptoms for centuries
- Effects:
  - Calcium channel blocker
  - Effects on 5-HT_3 receptor
- Liquid or capsule formulations
- Generally well tolerated
  - Heartburn, nausea, vomiting, diarrhea, allergy, asthma exacerbation, atrial fibrillation reported

Shapiro, Deutsch, Chey. Neurogastro LATAM Rev. 2020

8

Carraway Oil & L-menthol with SST for FD patients on usual care: A US RCT



95 FD patients randomized to COLM SST or placebo for 28 days. **All patients continued usual meds for their FD**

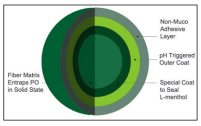
COLM-SST = 25 mg Caraway oil & 20.75 mg Menthol

SST – site specific targeting, FD – functional dyspepsia, RCT – randomized, controlled trial

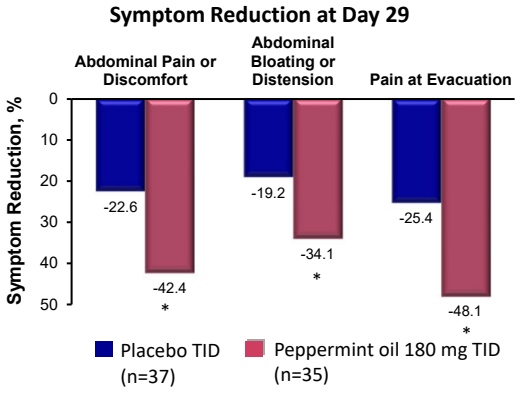
Chey et al. Clin Translational Gastroenterol 2019

9

Triple-Coated Peppermint Oil for IBS



- **RCT of triple-coated peppermint oil microspheres in IBS-M or IBS-D (N=72)**
  - **Randomized to peppermint oil 180 mg TID or placebo for 4 weeks**
  - **Primary analysis based on Total IBS Symptom Score**
- **Peppermint oil improved Total IBS Symptom Score (*P*<0.02) and frequency and intensity of individual IBS symptoms over 4 weeks**



***P*<0.05.**

AEs, adverse events; TISS, Total IBS Symptom Score; URT, upper respiratory tract.

Cash BD, et al. Dig Dis Sci. 2016;61:560-571

10

STW-5 (Iberogast) for FD and IBS

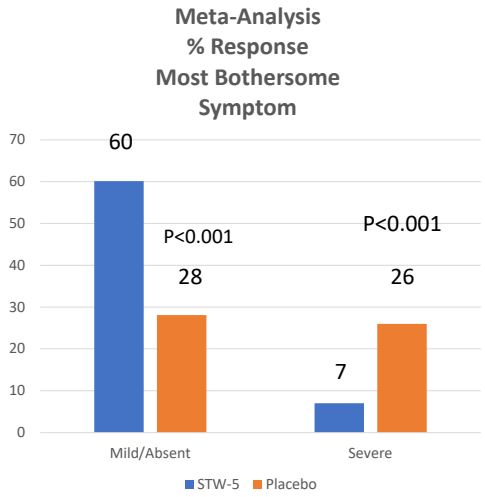
- Combination supplement containing:
  - angelica root (*Angelica archangelica*)
  - bitter candytuft (*Iberis umbellata*)
  - caraway (*Carum carvi*)
  - celandine (*Chelidonium majus*)
  - chamomile (*Matricaria chamomilla*)
  - lemon balm leaves (*Melissa officinalis*)
  - licorice root (*Glycyrrhiza glabra*)
  - milk thistle (*Silybum marianum*)
  - peppermint (*M. piperita*)

- Anti-spasmodic effects & effects on visceral afferent nerves

Shapiro, Deutsch, Chey. Neurogastro LATAM Rev. 2020

11

STW-5 for Functional Dyspepsia



- 3 placebo-controlled trials, 273 pts
- STW-5, 20 drops (1 ml) TID x 4 weeks
- All trials evaluated another alternative formulation
- Symptoms assessed: regurgitation, epigastric pain, ”dysmotility” symptoms, vomiting
- AEs similar to placebo, No SAEs

Meltzer et al. Aliment Pharmacol Ther 2004;20:1279

12

STW-5 for IBS

- 208 IBS patients (all subtypes) randomized to
  - STW-5 = 51
  - STW-5 II = 52
  - Bitter tuft abstract = 53
  - Placebo = 52
- STW-5 better than placebo for:
  - Abdominal pain score (p=0.001)
  - IBS-SS score (p=0.001)
- Rare cases of hepatotoxicity
- Can interfere with drugs metabolized by CYP3A4 (acetaminophen diazepam, codeine)

Madish et al. Aliment Pharmacol Ther 2004;19:271
Shapiro, Deutsch, Chey. Neurogastro LATAM Rev. 2020

13

Glutamine for PI-IBS

- Essential amino acid and energy source for rapidly dividing cells
- 106 PI-IBS-D pts randomized to glutamine 5g tid or placebo x 8 wks
- Primary endpoint: >50 point reduction on IBS-SS score

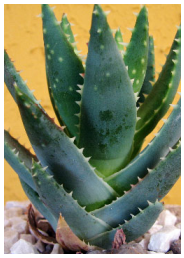
Outcome	Glutamine	Placebo	P value
Primary Outcome	**80%**	**6%**	**<0.001**
IBS-SS score	**173**	**295**	**<0.0001**
Stool Frequency	**2.9**	**4.3**	**<0.0001**
BSFS	**3.5**	**6.8**	**<0.0001**

Improvements in intestinal permeability noted with glutamine

Zhou et al. Gut 2019;68:996-1002

14

Aloe Vera and IBS



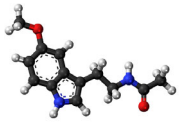
- Succulent has 2 components: Gel and Latex
- Possible health effects:
  - Known stimulant laxative properties
  - Possible anti-inflammatory properties
  - Possible analgesic properties
- Meta-analysis of 3 studies, 151 IBS pts
  - ITT analysis for improvement in IBS symptoms (RR = 1.69, 1.05-2.7, p=0.03)
- Diarrhea & melanosis can occur, acute hepatitis reported
- Can affect absorption of anti-coagulants & oral diabetic meds
- 2002, FDA removed aloe latex products from US market

Shapiro, Deutsch, Chey. Neurogastro LATAM Rev. 2020
Hong et al. J Neurogastroenterol Motil. 2018;24:528-35

15

Melatonin for IBS

- Neurohormone released by pineal gland in a circadian pattern related to light exposure
- Exerts local effects in the GI tract
- Structurally similar to serotonin



- RCT #1: 40 IBS pts randomized to melatonin 3 mg qHS or placebo x 2 weeks
  - Mean abd pain scores improved more with melatonin vs. placebo (p<0.001)
  - No changes in bloating, BSFS score, stool frequency, anxiety/depression, sleep
- RCT #2: 18 IBS pts randomized to melatonin 3 mg qHS v placebo
  - Improvements in IBS symptoms and QOL
- RCT #3: 60 IBS pts received melatonin 3/5 mg v placebo x 6 months
  - Visceral pain improved at months 4 & 6 in IBS-C patients (p<0.05)

Shapiro, Deutsch, Chey. Neurogastro LATAM Rev. 2020

16

Prebiotics, Synbiotics and Postbiotics for IBS

- **Prebiotics:** Poorly absorbed selectively fermented short-chain carbohydrates which allow targeted changes in GI microbiota which confer a health benefit
  - Bran, lactulose, sorbitol are examples
  - FOS & galacto-oligosaccharides increase concentrations of luminal and mucosal *Bifidobacteria*
- **Synbiotics:** preparations containing both a prebiotic and probiotic in order to improve GI probiotic colonization
- **Postbiotics:** isolated bacterial components which are administered as therapeutics

Parkes et al. Am J Gastroenterol 2008;103:1557
Neish. Et al. Gastroenterol 2009;136:65

17

Food as Medicine…

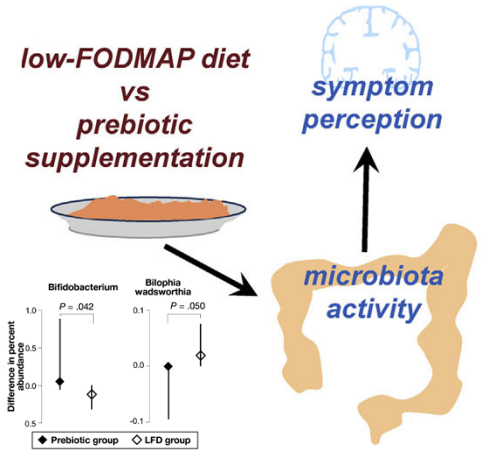
- **Functional Food: "**A modified food that claims to improve health or well-being by providing benefit beyond that of the traditional nutrients it contains"
- **Personalized Nutrition:** "An approach that uses information on individual characteristics to develop targeted nutritional advice, products, or services".
- **Precision Nutrition:** "Suggests that it is possible to have sufficient quantitative understanding about the complex relationships between an individual, his/her food consumption, and his/her phenotype (including health) to offer nutritional intervention/advice, which is known to be individually beneficial."

Ordovas JM, et al. Br Med J 2018;361:k2173

18

Low-FODMAP diet vs. Prebiotic for FGID Patients

RCT: Prebiotic (1.37 g beta-GOS) plus placebo Mediterranean diet (n =19) vs placebo prebiotic (2.8 g xylose) plus low-FODMAP (n=21) for 4 weeks; patients followed for additional 2 weeks.



By 4 weeks administration, both treatments had opposite effects on intestinal microbiota but a similar clinical benefit in patients with functional gut disorders.

After treatment discontinuation the decrease in symptoms persisted in the prebiotic group, but reappeared immediately in the low-FODMAP group.

Intermittent prebiotic administration might be an alternative to continuous dietary restrictions for patients with functional gut symptoms.

Huaman et al. Gastroenterol 2018;155:1004-7

19

Cannabis for FGIDs

- *Cannabis sativa* plant
- Recreational and medicinal uses
- >100 Chemicals – "cannabanoids"
  - THC, CBD, CBG
- Receptors found in the brain, periphery including nerves and muscles in the gut
- No studies of marijuana or CBD oil for FGIDs
- Marijuana can cause CNS symptoms and cannabinoid hyperemesis syndrome
- Studies ongoing with a CB2 agonist for IBS

Shapiro, Deutsch, Chey. Neurogastro LATAM Rev. 2020

20

Take Home Messages

- FGIDs have many causes
- Because of this, there are many possible solutions
- Though patients often use supplements, doctors are rarely knowledgeable or recommend them
- Peppermint oil offers benefits for functional dyspepsia and IBS
- STW-5 may offer benefits for functional dyspepsia and IBS
- Glutamine may offer benefits for PI-IBS
- Aloe vera possesses laxative properties and may benefit IBS
- Melatonin may improve IBS symptoms, especially pain
- Prebiotics may be similarly effective to the LFD in IBS patients

21