Diet, Fecal Microbiota Transplant (FMT), and Other Non-Pharmacological Management Options for Irritable Bowel Disease (IBD)

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Agenda

- Dietary Influences on IBD
- FMT in IBD +/- Clostridium difficile Infection (CDI)
- Alternative Medicine Options in IBD
Diet and IBD
Important Concerns

- Nutritional Support
- Symptom Control
- Diet During Flares
- Maintenance of Medical Therapy
- Cost of Unproven Dietary Therapies

Diet and IBD

- No definitive dietary cause of either Crohn’s Disease (CD) or Ulcerative Colitis (UC) to date
- Randomized Controlled Trial (RCT) with diet extremely difficult
- Dietary influences on IBD have been shown
- Many patients suspect dietary influences and may alter their diet after diagnosis
Diet and IBD Goals

- Nutritional Support
- Symptom Control
- Maintenance of Remission

Nutritional Support

- Elemental diet, especially in CD
- Poorly tolerated, usually requires NG at night
- Mainly for young patients needing weight gain
- Has been shown to induce remission in CD, but 3 times less effective as steroids
- Not effective in UC
- Enteral Feeds no better than Total Parenteral Nutrition (TPN)
Treat Nutritional Deficiencies

- Iron
- Vitamin B12
- Vitamin D

- Test regularly, treat if abnormal
- Reassure patient when normal

Calories Important

- Patients need to continue caloric intake even when ill
Diet and IBD

- Dietary influences on symptoms and flares
- Diet treatment options

Diet and Microbiota

Source: Curr Opin Gastroenterol © 2015 Lippincott Williams & Wilkins
Diet and Inflammation

- Potential mechanisms
- Various foods may lead to dysbiosis and changes in gut permeability leading to inflammation
- Genetic susceptibility

Fermentable Oligosaccharides, Disaccharides, Monosaccharides And Polyols (FODMAP) Diets

- Some evidence for symptom control
- No evidence on inflammation improvement

Low FODMAP Benefits in Patients with:

- Bloating
- Distention
- Gas/Flatus
- Strictures/Adhesions
- Ileocecal (IC) Valve Surgery

Diet During Flares

- Patients feel better eating less during flares
- Less input = less output - fewer symptoms
- Bland foods/liquid diets better tolerated
- Avoid foods that have caused issues in the past (spicy, fats etc.)
- Avoid caffeine and alcohol
Diet During Flares Continued:

- Keep hydrated
- MAINTAIN CALORIES
- Maintain protein intake
- Try inexpensive supplements
- Continue medications
- Gradually return to regular diet as flare improves

Diet with Strictures or Obstruction

- Low residue items
- Avoid:
  - Raw vegetables
  - Beans
  - Tough meats/sausages
  - Skinned fruits
Fiber and IBD 2016

- 1619 patients; 1130 CD, 489 UC
- CCFA (Crohn’s and Colitis Foundation of America) Partners Diet Survey, Dietary Screener Questionnaire
- 6 month survey follow up to assess for flare based on Short CDAI (Crohn’s Disease Activity Index) and Simple Clinical Colitis Index (<150 or <2)
- Flare defined as activity index exceeding remission cutoff and/or need for IBD related surgical procedure or IBD related hospitalization


IBD and Fiber Results

- High Fiber quartile in CD had a 40% lower odds for flare than low fiber patients
- UC patient consumed more fiber than CD patients.
- Men ate more fiber than women
- No difference in flare with UC patients and amount of fiber
- May want reconsider fiber recommendations for CD patients

Diet and IBD

- Council patients on Extreme and Fad Diets
- Specific Carbohydrate Diet (SCD), Paleo Diet (ancient human diet), macaroon and macrobiotic diets (whole grains, vegetables, and beans) and nutraceutical or medical foods
- Can be expensive
- May restrict nutrients
- Patient may stop effective therapy in lieu of diets without good evidence of effectiveness

FMT and IBD

- FMT and Recurrent *Clostridium difficile* Infection (RCDI) and IBD
- High success rate of CDI clearance
- Not without risk, some IBD flares
- Success in CDI prompted study for FMT in IBD without CDI
FMT and IBD Continued:

• Fecal Bacterial Flora of IBD Patients differ from healthy patients
• RNA sequencing has shown an increase of pathologic *E. coli, Campylobacter* and *M. avium* in CD and decreased *Bacteroidetes* and *Firmicutes*
• Bacterial invasion of mucosa seen in both CD and UC but rare in health
• Increased enteroadherent bacteria and decrease of health promoting bacteria in IBD

FMT and IBD Continued:

• Early studies, small case reports
• Mixed results
• Some side effects with fevers, UC flares
FMT and IBD
Meta Analysis 2014

- 18 studies (9 cohort, 8 case studies, 1 RCT)
- FMT primary therapeutic agent and CR and/or mucosal healing primary endpoints
- 122 pts with 45% remission rate
- 36% remission after removing case reports
- 61% in CD vs 22% in UC
- Appears safe with no significant adverse events


RCT in UC 2015

- 75 pts with active UC (38 FMT; 37 Placebo)
- Mayo score ≥4 and Endo ≥1
- FMT and water enemas weekly for 6 wks
- Stable medical therapy maintained
- Endpoints remission with Mayo score ≤2 and Endo score 0
- Study terminated due to futility

Results

- Only 37 of pts included in per protocol analysis
- 7/17 (41%) vs 5/20 (25%)  p=0.29 NS
- Recipient resembled donor at week 12
- No donor effect
- 2 pts with fevers

Results Continued:

- 9/27 (24%) FMT vs 2/26(5%) placebo
- 7 of the 9 responders had the same donor
- Remission in 3 of 4 pts with disease less than 1 year vs 6 of 34 with disease >1 year
- ? More effective early in disease process
Netherlands Study 2015

- 50 pts with moderately active UC
- FMT via NG and week 1 and 3 wks later
- Placebo was patients own stool
- Primary endpoints colitis activity score <2 and >1 point decrease in Mayo endo score
- Secondary endpoints of safety and microbiota composition


Comparison of the 2 Studies

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Moayyedi et al</th>
<th>Rossen et al</th>
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<tbody>
<tr>
<td>Study design</td>
<td>Double-blind, randomized (1:1), controlled</td>
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<tr>
<td>Study population</td>
<td>Adult patients with mild to moderate UC</td>
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<tr>
<td>Subjects randomized (n)</td>
<td>136</td>
<td>60</td>
</tr>
<tr>
<td>Comparing therapy (W)</td>
<td>placebo</td>
<td>placebo</td>
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<tr>
<td>Anti-TNF permitted?</td>
<td>Yes, at stable disease for ≥12 weeks</td>
<td>No</td>
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<tr>
<td>Route of FMT delivery</td>
<td>Parenteral</td>
<td>Autologous FMT</td>
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<tr>
<td>Placebo</td>
<td>Water</td>
<td>15 donors, fresh</td>
</tr>
<tr>
<td>Donor stool</td>
<td>Unidentified, fresh or frozen</td>
<td>2 doses (2 and 3 weeks)</td>
</tr>
<tr>
<td>Dosage schedule</td>
<td>Weekly for 6 weeks</td>
<td>Remission (Mayo score ≤2 with an endoscopic score ≤1 at week 7.</td>
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<tr>
<td>Primary endpoint</td>
<td>Remission (Mayo score ≤2 with an endoscopic score ≤1 at week 7.</td>
<td>Remission (simple clinical colitis activity score ≤2 combined with &gt;1-point decrease in Mayo endoscopic score at week 72.</td>
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<tr>
<td>Subjects who achieved primary endpoint</td>
<td>50/81 (61%) treated with FMT vs 23/71 (31%) controls (P = .00)</td>
<td>7/25 (28%) treated with FMT vs 5/25 (20%) controls (P = .51)</td>
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<td>Microbiome analysis</td>
<td>Yes, increased diversity in FMT treated subjects compared with the control group.</td>
<td>Yes, increased diversity of responders in both groups. FMT treated group developed similar microbiota profile to respective donor.</td>
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FMT, fecal microbiota transplantation; TNF, tumor necrosis factor; UC, ulcerative colitis.
• 81 pts with active UC (Mayo score 4-10)
• Pts had been resistant to standard therapy
• Single FMT vs placebo colonoscopy on day one followed by FMT vs placebo enemas 5 days a week for 8 weeks
• Active enemas from 3-7 unrelated donors
• Primary endpoint, steroid free remission together with endo remission or response (total Mayo score <2 with subscores <1)


DDW 2016 Continued:

• Secondary endpoints steroid free with combined total Mayo endo score ≤1 for both bleeding and stool frequency Mayo subscores; Endo remission - Ulcerative Colitis Endoscopic Index of Severity (UCEIS) score of 1, quality of life and safety
• Placebo treated pts offered 8 wk open label treatment after blinded therapy
Results DDW 2016

• 11/41 (27%) FMT vs 3/40 (8%) p=0.02, meeting primary endpoint of steroid free clinical remission and endo remission or response
• Steroid free remission 44% vs 20% p=0.02
• Clinical response 54% vs 23% p<0.01

Results DDW 2016 Continued:

• Steroid free endo remission 17% vs 8% p=0.19
• Endo response 37% vs 10% p<0.01
• No difference in adverse events but 3 serious events comprising worsening colitis (2 active FMT, 1 required colectomy)
• Placebo pts (37) entering open label phase 27% met primary endpoint
FMT Conclusions

• Very effected for RCDI
• Studies show promise in IBD
• Much more data needed, multiple RCT ongoing
• Guidelines needed that standardize the collection, preparation, dosing and delivery.
• Safety data still scarce
• At present, would not treat with FMT outside of a clinical trial

Complementary and Alternative Medicine (CAM) and IBD

• Fish Oil and Omega-3
• Aloe Vera
• Turmeric
• Acupuncture
• Probiotics and Prebiotics
• Yoga, Biofeedback, Meditation
• Biofield and Bioelectromagnetic Therapy
CAM and IBD

- Complementary not Replacement
- Avoid any potential harmful modalities
- Again maintain effective medical therapy

When all else fails...