Nutritional Requirements for Inflammatory Bowel Disease

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No disclosures
Objectives

1) Review the biological mechanisms disturbed in inflammatory bowel disease (IBD)

2) Review the association between diet and the risk of developing IBD

3) Discuss the evidence for unique nutritional requirements in IBD

4) Discuss the role of nutritional therapy in IBD
Inflammatory Bowel Disease (IBD)

• Definition: **chronic** inflammatory condition affecting the gastrointestinal tract
  – Symptoms: abdominal pain, diarrhea, bloody stool
  – Systemic manifestations: fever, rash, growth delay

• Two types of IBD:
  – Crohn’s disease (CD)
    • Can affect any portion of GI tract
  – Ulcerative colitis (UC)
    • Confined to colon
IBD Pathogenesis

Are Diet/Nutrients Important?

Dietary exposures are associated with incidence of IBD

Immigration studies implicate environment/diet

Exclusion diets can be effective therapy for IBD (i.e. EEN)

“Western diet”

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Protective factor</th>
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<tbody>
<tr>
<td>Saturated fat</td>
<td>Fiber</td>
</tr>
<tr>
<td>Total PUFA</td>
<td>Fruits</td>
</tr>
<tr>
<td>Omega-6 PUFA</td>
<td>Vegetables</td>
</tr>
<tr>
<td>Meat</td>
<td>Omega-3 PUFA</td>
</tr>
</tbody>
</table>

Hou JK. Am J Gastro 2011.
## Nutrient deficiencies in IBD

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Resultant Nutrient deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia</td>
<td>Global (macro, micronutrients)</td>
</tr>
<tr>
<td>Malabsorption</td>
<td>Global; fat soluble vitamins, zinc</td>
</tr>
<tr>
<td>Intestinal blood loss</td>
<td>Iron</td>
</tr>
<tr>
<td>Chronic systemic inflammation</td>
<td>Anemia*</td>
</tr>
<tr>
<td></td>
<td>1,25-OH Vitamin D†</td>
</tr>
<tr>
<td>Ileal inflammation</td>
<td>Vitamin B12</td>
</tr>
</tbody>
</table>

*Anemia of chronic disease—abnormal utilization of iron
†Decreased PTH \(\rightarrow\) decreases renal 1α-hydroxylase activity

Augustine MV. J Clin Endo Metab 2014.
Role of Nutrient supplementation in IBD

Current approach:

a) Focus on control of active inflammation

b) As an adjunct, specific supplementation:
   - Vitamin D
   - Iron
   - B12 injections
   - Zinc, other B vitamins
Vitamin D and Risk of Developing IBD

• Nurses’ Health Study: prospective cohort study with ~1.5 million person years follow-up

<table>
<thead>
<tr>
<th>Median 25-OH Vit D (ng/mL)</th>
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<tbody>
<tr>
<td>Lowest quartile</td>
<td>22.3</td>
</tr>
<tr>
<td>Highest quartile</td>
<td>32.2</td>
</tr>
</tbody>
</table>

– Crohn’s disease: Compared to lowest quartile, highest quartile had **lower risk** of developing disease
  • Hazard ratio: 0.54 (95% CI 0.3 - 0.99); p-trend: 0.02

– Ulcerative colitis: no significant association

Ananthakrishnan A. Gastroenterology 2012.
Vitamin D: Clinical Trials in IBD

63 children with IBD: 12 mo trial

IL-6 > 3 pg/mL
CRP ≥ 1 mg/dL

Arm A: Vit D2 400 IU/d
Arm B: Vit D2 1000/2000 IU/d

Vit D3 supplemented group: Decreased risk of disease relapse (13% vs. 29%; p=0.056)

94 adults: Crohn’s in remission

D3 1200 IU/d
Placebo

Jorgensen SP. Aliment Pharm Therapeut 2010.
Pappa HM. J Clin Endocrin Metabolism 2014.
Iron in IBD: IV is Superior to Oral

20 Week Randomized Trial
• 91 adults with mild active IBD

IV iron sucrose: 200 mg q1-2 weeks (until total of 1000 mg)
PO: Ferrous sulfate 200 mg BID

Hg response > 2 g/dL
Anemia at EOT
Reaching mean Hg
Reference values

n=45
n=46

Additional effects of oral iron:
1) Change in microbiome
2) Increase in intestinal oxidative stress and inflammation

Hepcidin: Decreases absorption of enteral iron

*FPN: ferroportin—iron export protein

Strategies for Treating IBD

• **Immunosuppression**
  – Corticosteroids
  – **Immunomodulators**: azathioprine, methotrexate
  – **Biologics**: anti-TNF-alpha, anti-adhesion

• **Nutrition**
  • **Exclusive Enteral Nutrition (EEN)**
  • Exclusion diets
    • Specific carbohydrate diet (SCD)
    • Crohn’s disease exclusion diet
    • “Anti-inflammatory” diet
    • Semi-vegetarian diet
What is Exclusive Enteral Nutrition (EEN)?

• Also known as the “defined formula diet”
  – Formula provides nearly 100% of nutritional needs
  – Exclusion of table foods
• Formula can be consumed by mouth or via tube
• Does not require a specific formula
• Uses:
  – Calories
  – Therapy to control inflammation in Crohn’s
    • Efficacy in children: ~80%

Day AS. World J Gastro 2015.
Therapy with EEN is Effective

– 37 children with newly diagnosed Crohn’s disease
– 10 week randomized trial: steroids vs. EEN

Is it all about nutrients in the formula?

PLEASE study (n=90)

- Children with active Crohn’s disease
- 8 week trial:
  - Pediatric Crohn’s disease activity index (PCDAI)
  - Fecal calprotectin (FCP)
- Three arms:
  - Partial Enteral Nutrition (PEN) –50% calories by formula
  - Exclusive Enteral Nutrition (EEN)
  - Anti-TNF-alpha

Lee D. Inflamm Bowel Dis 2015.
Formula *and* Food are Important

<table>
<thead>
<tr>
<th></th>
<th>PEN</th>
<th>EEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>%EER</td>
<td>150.8 ± 36.2</td>
<td>128 ± 19.9</td>
</tr>
<tr>
<td>%EER from formula</td>
<td>77.7 ± 14.2</td>
<td>115.3 ± 20.8</td>
</tr>
<tr>
<td>%EER from food</td>
<td>72.9 ± 25.5</td>
<td>12.9 ± 6.9</td>
</tr>
</tbody>
</table>

EER: estimated energy requirement
Route of Nutrition and Disease Activity

- **NPO + Total Parenteral Nutrition**
  - Benefits malnourished patients
  - **No benefit** on eventual need for surgery

- **Luminal constituents are important for intestinal health**
  - Fiber is fermented $\rightarrow$ short chain fatty acids (SCFA)
  - **SCFA:**
    - Energy source to colonocytes
    - Role in promoting immune tolerance

Thornburn AN. Immunity 2014.
Food-based dietary therapy for IBD

- Specific carbohydrate diet (SCD)
- Crohn’s disease exclusion diet
- Semi-vegetarian diet
- “Anti-inflammatory” diets

Each of these diets involves the restriction of specific foods
- Commonly: bread/gluten, “processed foods”
- Some variance: dairy, sugar, animal fat
The specific carbohydrate diet (SCD)

- Restricted foods on the SCD:
  - All grains
  - Refined sugars
  - Cow’s milk products (fully fermented yogurt ok)
  - “Processed foods”

- Popular following in the community for variety of GI illnesses
  - Anecdotal evidence plentiful

- Concerns:
  - Elimination of whole food groups from diet
  - Inadequate calories
  - Emotional well-being
Studies on the SCD

<table>
<thead>
<tr>
<th>Author</th>
<th>Study design</th>
<th>n</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suskind DL, J Clin Gastro (2018)</td>
<td>Prospective case series</td>
<td>13</td>
<td>Clinical + laboratory improvements; significant microbiome shifts</td>
</tr>
<tr>
<td>Obih C, Nutrition (2016)</td>
<td>Retrospective case series</td>
<td>26</td>
<td>Improved clinical and laboratory parameters for Crohn’s disease and UC</td>
</tr>
<tr>
<td>Suskind DL, Dig Dis Sci (2016)</td>
<td>Patient survey</td>
<td>417</td>
<td>Majority of respondents perceive clinical benefit to SCD</td>
</tr>
<tr>
<td>Burgis JC, World J Gastro (2016)</td>
<td>Retrospective case series</td>
<td>11</td>
<td>Improved labs, growth parameters</td>
</tr>
<tr>
<td>Kakodkar S, J Acad Nut Diet (2015)</td>
<td>Retrospective case series</td>
<td>50</td>
<td>SCD is effective for some adults with IBD; High quality of life reported</td>
</tr>
<tr>
<td>Suskind DL, JPGN (2014)</td>
<td>Retrospective case series</td>
<td>7</td>
<td>Improvement in clinical + lab parameters (Hct, CRP)</td>
</tr>
<tr>
<td>Cohen SA, JPGN (2014)</td>
<td>Prospective case series</td>
<td>16</td>
<td>Clinical and mucosal improvements seen</td>
</tr>
</tbody>
</table>
Potential complexities

• Nutrition therapy in Crohn’s vs. ulcerative colitis
  – EEN effective for Crohn’s only

• Genetic polymorphisms and efficacy of EEN
  – Nod2 gene polymorphisms associated with efficacy of EEN

• Active inflammation vs. quiescent disease
  – Vitamin D: decreased activation of Vit D (decreased PTH and 1α hydroxylation)
  – Iron: oral iron poorly absorbed; oral iron may worsen disease activity

Gaps in understanding

1) Elucidating the role of specific dietary components on IBD pathogenesis

2) Developing better methodologies (including biomarkers) to assess dietary exposures

3) Understand the interplay between diet, intestinal microbiome, and metabolome - And utilizing this to intervene on an individual basis
Conclusion

• Diet is a risk factor for developing IBD
  – Diet can also be used as therapy for IBD

• IBD can result in nutrient deficiencies
  – Inflamed state important to consider

• Further research is needed to better understand how to best utilize diet as therapy for IBD
Thank you

David Suskind, MD
Johanna Lampe, PhD