Nutrition and IBD: Diet Matters!

Kelly Issokson, MS, RD, CNSC
Clinical Dietitian
Cedars Sinai Medical Center

@GIdietitian

Objectives

Participants will be able to:
• Understand dietary risk factors for IBD
• List one dietary approach for reducing inflammation
• List one dietary approach for management of GI symptoms
• List 3 common nutrient deficiencies associated with IBD

Case Study

• 50 y/o male with ileocolonic Crohn's disease
  - MRE 1/2015
    • Patchy pancolic wall thickening & hyperemia
    • Unremarkable appearance of the small bowel
  - Colonoscopy 1/2015:
    • Patchy moderate to severe active colitis
    • 2 inflammatory denosures at 30cm & 60cm due to severe inflammation
    • Anal ulcer/lesion
  - Labs 3/9/15: hgb 9.9, CRP 54 (nl <10), ESR 40
  - Rash on 6MP; attenuated to infliximab, lost response to adalimumab
  - Started vedolizumab + MTX, tapered off steroids
  - Flared shortly afterwards; d/c’d vedolizumab & MTX & self-resumed prednisone
  - Frequent ER visits for CD flare, dehydration

• No conflicts of interest to declare
Case Study

- Nauseated, poor oral intake, significant recent weight loss, muscle loss
- 12 BM daily (+ nocturnal)
- Severe protein-calorie malnutrition
  - Prolonged inadequate energy intake
  - Significant recent weight loss
- Iron deficiency anemia
- Wants to discuss ways to nutritionally manage his IBD

Nutrition & Integrative IBD Program

- Multidisciplinary nutrition program that integrates the expertise of an experienced IBD physician together with a GI/IBD focused registered dietitian
- Patients provide:
  - 1 or more written visit goals
  - Completed food/symptom logs
  - These direct medical and nutritional guidance

Nutrition & Integrative IBD Program

- Retrospective review found:
  - 77% had not previously met with an RD
  - Patient Goals:
    - Nutrition for symptom management (60%)
    - Nutrition for disease management (44%)
    - Nutrition for general health/cancer prevention (19%)
    - Nutrition for weight management (4%) (gain or loose)
  - Avoided: dairy (69%), fiber (40%), gluten (31%) and red meat (29%)
  - 40% of patients had 3 or more food avoidances
  - 58% of subjects did not take a daily multiple vitamin/mineral supplement
  - Vitamin D insufficiency and deficiency was common (44%)
  - Only 58% of D insufficiency/deficient pts were supplementing with vit D
  - 46% of patients had not previously had a bone density scan

Risk Factors for IBD

- MANY!
- Genetics
- Microbiota
- Environment/Diet - Food antigens trigger an immunologic response, specific pathogenic antigens have not been identified.
  - Data suggest a "Western" style diet (processed, fried, and sugary foods) is associated with an increased risk of developing Crohn’s disease, possibly ulcerative colitis.
Influence of Diet on Microbiota, IBD

Diet and IBD Relapse

- Jowett et al. UC had greater risk of relapse with higher intakes of meat, eggs, protein, alcohol
  - Association greater with red and processed meats; not linked to fish

Nutrition Therapy Goals

- Supportive or primary therapy to correct/prevent malnutrition, improve symptoms, improve QOL
  - PO diet (specific diets to reduce inflammation, diets for symptom management, ONS)
  - EN (EN if patient unable to eat adequate PO; EEN as primary therapy in CD)
  - TPN (if with non-functional gut)
Diets for IBD

Tailor Nutrition Therapy to Patient Goals

- **Reduce Inflammation**
  - Specific Carbohydrate Diet (SCD)
  - Induce remission → Exclusive Enteral Nutrition (EEN)
  - Maintain Remission → Semi-Vegetarian Diet (SVD); Partial Enteral Nutrition (PEN)

- **Symptom Management**
  - Low lactose, low fructose, low fat, low (insoluble) fiber
  - Gluten free
  - Low FODMAP

Induce Remission: SCD
SCD

- Grain free, low dairy, diet limiting preservatives, additives, processed foods

SCD – Biochemical Improvement

- Suskind et al. 2014
  - Retrospective study with 7 pediatric CD patients
  - SCD for average 15 months, not on immunosuppressive meds
  - Complete resolution of symptoms within 3 months
  - CRP, Hct, alb, stool calprotectin overall improved (statistical significance not evaluated)

SCD – Growth Parameters

- [Table showing growth parameters]

SCD – Clinical Improvement

- [Table showing biochemical improvement]
SCD – Clinical/Mucosal Response

- Cohen et al. 2014
  - Prospective study, 9 pediatric active CD patients (4 on immunomodulators, 3 med naïve, 1 on mesalamine, 1 on budesonide)
  - Evaluated clinical and mucosal response
  - Improvement in symptom scores (HBI, PCDAI, LS) at weeks 12+52
  - Capsule endoscopy improved at wk 12, not 52
  - ESR, alb unchanged

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>CD duration, y</th>
<th>Disease location</th>
<th>Other CD medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>1.8</td>
<td>Rect, ileum, ileocecum</td>
<td>Azathioprine 50 mg</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>1.8</td>
<td>Rect, ileum</td>
<td>Not DAI</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>2</td>
<td>Colon, ileum, ileocecum</td>
<td>Metronidazole 75 mg</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>1.8</td>
<td>Colon, ileum, ileocecum, rectosigmoid</td>
<td>Aminosalicylate 75 mg</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>1.8</td>
<td>Colon, ileum, ileocecum</td>
<td>Aminosalicylate 75 mg</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>0.2</td>
<td>Rect, ileum</td>
<td>Not DAI</td>
</tr>
<tr>
<td>7</td>
<td>14</td>
<td>1</td>
<td>Rect, ileum, ileocecum</td>
<td>Vancomycin 300 mg</td>
</tr>
<tr>
<td>8</td>
<td>14</td>
<td>0.8</td>
<td>B, ileum, ileocecum, ileocolic</td>
<td>Budesonide 6 mg</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
<td>6</td>
<td>Colon</td>
<td>Budesonide 2.25 mg</td>
</tr>
<tr>
<td>Mean</td>
<td>13</td>
<td>1.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SCD = CDA, med = medications; T = treated them.

SCD – Clinical Improvement

- No published controlled trials of SCD + IBD yet
- CCFA to study effect of SCD + Mediterranean diet in CD
- Caution nutrient deficiencies: B vitamins, E, D, Ca
  - Freeda vitamins
  - Print resources: SCD guide, Recipe books
  - Online resources: scdshoppingcart.com, breakingtheviciouscycle.info

Induce Remission – EEN

- EEN = 100% of nutrient needs provided by a formula
  - EEN is routinely used in pediatric and adult CD in Japan
  - Not indicated for use in UC
  - EEN in CD has been shown to induce remission, heal mucosa (endoscopic and histologic), reduce pro-inflammatory cytokine levels (Fell et al. 2000; Yamamoto et al. 2005)
  - Study participants were not on immunosuppressive meds
- ESPEN (2006): In adults, EN should be used to address undernutrition, and used as sole therapy when corticosteroids are not feasible.
EEN – Mucosal Healing

Mucosal healing and a fall in mucosal pro-inflammatory cytokine mRNA induced by a specific oral polymeric diet in pediatric Crohn’s disease

Yamamoto et al.

- Affect of Polymeric EEN on mucosal inflammation on children with CD (29)
- 79% were in complete clinical remission after 8 weeks on EEN
- Polymeric EEN was associated with mucosal healing and a down regulation of mucosal pro-inflammatory cytokine mRNA in both the terminal ileum and colon. In the ileum there was also an increase in transforming growth factor β1 mRNA.

EEN – Yamamoto et al.

Impact of Elemental Diet on Mucosal Inflammation in Patients with Active Crohn’s Disease: Cytokine Production and Endoscopic and Histological Findings

Yamamoto, M., Hagiwara, K., Uehara, H., Tani, T., Eto, K., and Kishi, M.

- Affect of Elemental EEN on cytokine levels in CD adults (n=28)
- 71% achieved clinical remission after 4 weeks on EEN
- Elemental diet reduced cytokine production and lead to more favorable ratio of pro-inflammatory: anti-inflammatory cytokines

EEN vs Corticosteroids

Table 1. Cytokine concentration results in EEN and placebo groups

Table 2. Body weight, BMI, and laboratory parameters before and after treatment

*Values are the means ± standard error
EEN vs Corticosteroids

- Type of formula can be polymeric, semi-elemental, or elemental
  - No significant difference in inducing remission (Grogan et al. 2012; Ludvigsson et al. 2004; Zachos et al. 2007)
  - EEN formula types:
    - Polymeric
    - Semi-Elemental
    - Elemental
  - Gluten free, low residue, lactose free, and Kosher (except Modulen, Peptamen).

EEN

- Use predictive equations to measure energy needs
  - Mifflin St. Jeor (BMR x 1.2-1.3), Penn State Equation 2003b, or Modified 2010 in obese >60yrs old
  - Add calories for weight gain if needed
- Protein 1-1.5 g/kg
- Surgery, corticosteroid use, high output fistulas, large wounds, non-healing wounds
- Recommended duration of therapy varies (4-12 weeks)
- Social impact, palatability, taste fatigue can influence patient success rate
- How to improve compliance?
  - Discuss risks and benefits, expectations
  - Provide samples
  - Work with formula reps, attempt insurance reimbursement
  - Have a strategy in place
  - Provide encouragement! Be enthusiastic! Approach as a team - MD and RD support are essential.

EEN in Practice

- Use predictive equations to measure energy needs
- Protein 1-1.5 g/kg
- Recommended duration of therapy varies (4-12 weeks)
- Social impact, palatability, taste fatigue can influence patient success rate
- How to improve compliance?
- Discuss risks and benefits, expectations
- Provide samples
- Work with formula reps, attempt insurance reimbursement
- Have a strategy in place
- Provide encouragement! Be enthusiastic! Approach as a team - MD and RD support are essential.

Case continued

- EEN trial (Boost, Ensure, Modulen) x 9 weeks
- Gained 18#
- Symptom improvement, less ER visits, less need for IVF
Maintain Remission – PEN

- **PEN**: 30-50% of nutrient needs delivered by formula, remainder via diet
- Can be helpful for maintaining remission in CD
- PEN is more effective than regular diet, as effective as some medications (mercaptopurine, 5-ASA) in maintaining remission in inactive CD (El-Matary et al, 2015)

PEN – Lower Relapse Rates

- Lower relapse rates in PEN vs no EN CD patients (Takagi et al. 2006)
  - RCT, free diet + PEN elemental formula, 30% needs vs free diet on mesalamine or azathioprine
  - Relapse rates significantly lower in PEN group (34% vs 64%)

PEN – RCT

Table 1: Randomised Controlled Trial Assessing Effectiveness of Enteral Therapy in Maintaining Remission in Adult CD

<table>
<thead>
<tr>
<th>Group</th>
<th>Elemental Formula Use</th>
<th>Relapse Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>EN group</td>
<td>50%</td>
<td>40%</td>
</tr>
<tr>
<td>Non-EN group</td>
<td>30%</td>
<td>60%</td>
</tr>
</tbody>
</table>

El-Matary et al, 2015

PEN – Clinical and Endoscopic Remission

- Nocturnal elemental PEN and low fat diet vs No intervention (Yamamoto et al. 2007)
  - Quiescent CD; No steroids or immunosuppressive agents
  - Group on unrestricted diet/no PEN had significantly higher rates of relapse at 1 yr, higher endoscopic inflammation scores, and higher pro-inflammatory cytokines.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>EN group</th>
<th>Non-EN group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical recurrence</td>
<td>1 (2)</td>
<td>7 (2)</td>
<td>0.048</td>
</tr>
<tr>
<td>Endoscopic recurrence</td>
<td>6 months after operation</td>
<td>9 (1)</td>
<td>14 (1)</td>
</tr>
</tbody>
</table>
PEN

A retrospective study showing maintenance treatment options for paediatric CD in the first year following diagnosis after induction of remission with EEN: supplemental enteral nutrition is better than nothing!

Hazel Duncan1, Claire Buchanan1, Tracey Ong2, Jane Garcia2, Lee Carse2, Karen McGinnigle2, Andrew Bartley1 and Richard K Russell1

- Newly dx peds CD, given EEN x 8 weeks (n=59)
  - 81% achieved clinical remission (mostly Modulen)

PEN – Clinical Remission

- MEN (maintenance enteral nutrition) → 31%
  - MEN median 10.8 months (4-12 months)
- 6 months:
  - significantly more remission in MEN vs no treatment (p<0.003)
  - All MEN vs all not on MEN: significantly more remission at 6 mos, not at 1 yr
- 1 year remission rates:
  - 50% in MEN group
  - 15% in those on no treatment
  - 65% in those on azathioprine only

<table>
<thead>
<tr>
<th>Treatment option</th>
<th>N</th>
<th>Remission 6 mos</th>
<th>p-value of others at 6 mos</th>
<th>Remission 1 year</th>
<th>p-value of others at 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEN + azathioprine</td>
<td>9</td>
<td>6/9 (66.6%)</td>
<td>0.11</td>
<td>5/9 (55.5%)</td>
<td>0.48</td>
</tr>
<tr>
<td>5/9 azathioprine</td>
<td>8</td>
<td>6/9 (66.6%)</td>
<td>0.11</td>
<td>4/5 (80%)</td>
<td>0.08</td>
</tr>
<tr>
<td>2/5 azathioprine</td>
<td>13</td>
<td>1/5 (20%)</td>
<td>0.001</td>
<td>0/3 (0%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Azathioprine only</td>
<td>20</td>
<td>1/20 (5%)</td>
<td>0.001</td>
<td>0/18 (0%)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Maintain Remission – SVD

- Prospective study (Chiba et al., 2010)
- Aim was to assess affect of SVD on relapse in CD
  - Everyday: fruits, vegetables, legumes, potatoes, yogurt
  - Once weekly: fish
  - Once every two weeks: meat
- Only meds used were mesalazine and sulfasalazine
- Clinical remission defined as absence of GI sx

SVD

16 patients remained on SVD for 2 yrs and had 92% remission rate
- Of the 6 who went back to omnivorous diet, remission rate was 25%
Nutrition and IBD

- **Up to 85% of adults with IBD are malnourished**
  - Patients with Crohn’s disease in remission can have a normal BMI, but reduced handgrip muscle strength consistent with loss of protein muscle mass
  - Screen patients: SGA, MUST
- **Risk of malnutrition higher in CD**
- **Causes for malnutrition:**
  - Inadequate intake
  - Increased needs
  - Increased losses
  - Malabsorption (from active disease or intestinal surgery)
  - Medications
  - Surgery

Malnutrition Impact

- **Increased rate of post-op complications**
- **Increased mortality** (sepsis, MRSA, PNA, other resistant infections)
- Impaired immune function, impairment of mucosal barrier, bacterial translocation
Biochemical Markers of Nutrition

Common deficiencies:
Vitamin D, Calcium, B12, B6, Iron, Zinc

• Can impact bone health, inflammation, response to medication, VTE, taste acuity/appetite, QOL
• Lower vitamin D levels linked with >morbidity, >disease in IBD

Common deficiencies:
Vitamin D, Calcium, B12, B6, Iron, Zinc

• Can impact bone health, inflammation, response to medication, VTE, taste acuity/appetite, QOL
• Lower vitamin D levels linked with >morbidity, >disease in IBD

Kabbani et al 2016

Association of Vitamin D Level With Clinical Status in Inflammatory Bowel Disease: A 5-Year Longitudinal Study

Kabbani J, Kabbani M, MPM, Zarrin E, Nourouzzadeh MD, PhD, Noha E, Ghanem, MD, MP, Claudia Gomez-Alora, MD; Nino Brink, PhD; Joan Berger, MD, MPH; Miguel Bagilhole, MD; Arthur Borra, MD, PhD; Mari Schwartz, MD; Ione D. Kabbani, MD; Leonard Tabib, MD, Michael A. Dunn, MD, and David E. Brisco, MD

• 965 IBD patients
• Approximated clinical status based on medication use, healthcare utilization, biochemical parameters, pain/clinical disease activity scores, health-related QOL
• 29.9% had low mean vitamin D levels (<30ng/mL)
  o More deaths, biologics, narcotics, CT scans, ED visits, hospital admissions, and surgery (p<0.05)
  o Worse pain, disease activity scores, QOL (p<0.05)
• Those who received supplementation/correction of vit D levels had reduced healthcare utilization

Table 1: Fatality-free survival curves in inflammatory bowel disease patients stratified by vitamin D status. Black line normal vitamin D group, gray line vitamin D group.

<table>
<thead>
<tr>
<th>Disease status</th>
<th>Low vitamin D (n=106)</th>
<th>Normal vitamin D (n=317)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (%)</td>
<td>39.3</td>
<td>29.5</td>
<td>0.006</td>
</tr>
<tr>
<td>Disease duration (y)</td>
<td>3.6 ± 1.4</td>
<td>3.3 ± 1.3</td>
<td>0.007</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>11.4 ± 7.8</td>
<td>8.0 ± 5.2</td>
<td>0.007</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (mm/h)</td>
<td>126 ± 36</td>
<td>106 ± 31</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Table 2: Medication use, disease activity scores, quality of life, and healthcare utilization during the study period in CD and UC patients stratified by vitamin D status.

<table>
<thead>
<tr>
<th>Disease status</th>
<th>Normal vitamin D (n=317)</th>
<th>Low vitamin D (n=106)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids (mg/y)</td>
<td>0.8 ± 1.4</td>
<td>2.0 ± 2.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Biologics (units/y)</td>
<td>8 ± 5.5</td>
<td>34 ± 21.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nutrition support (y)</td>
<td>0.8 ± 1.4</td>
<td>2.0 ± 2.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>39.3</td>
<td>29.5</td>
<td>0.006</td>
</tr>
<tr>
<td>Disease duration (y)</td>
<td>3.6 ± 1.4</td>
<td>3.3 ± 1.3</td>
<td>0.007</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>11.4 ± 7.8</td>
<td>8.0 ± 5.2</td>
<td>0.007</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (mm/h)</td>
<td>126 ± 36</td>
<td>106 ± 31</td>
<td>0.007</td>
</tr>
</tbody>
</table>
Biochemical Markers of Nutrition

Consider monitoring:
- **25-OHD**
- Vitamin B12/methylmalonic acid
- **B6 (pyridoxine)**
- Ferritin, %saturation
- High stool output? Potassium, Serum zinc, Mg
- Restrictive diet? Consider checking thiamine, folate, pyridoxine, vitamin E, zinc, selenium
- Consider others depending on medications, length of remaining/functional bowel

*Vagianos et al 2007*

Vitamin/Mineral | Amount | Daily Deficiency Symptoms | When Needed
--- | --- | --- | ---
Calcium | 1000-1500 mg | Osteoporosis, osteopenia, muscle cramps | If avoiding dairy or diet inadequate; if on high dose steroids (>7.5 mg/day)
Vitamin D | 600IU daily (200-5000IU/day may be needed); repletion dose 50,000IU D2 x 12 wks | Osteoporosis, osteopenia, increase in inflammation, decreased response to anti-TNF | If deficient; if on high dose steroids (>7.5 mg/day)
Zinc | RDA. If deficient, 50mg elemental x 15 days | Red rash on palms of hands, hair loss, decreased taste | Vegetarian/Vegan diet, high vitamin C food output
Folic Acid | RDA. If on certain meds, or risk for deficiency, 1 mg/dl | Anemia, hyperhomocysteinemia | If on MTX/auranofin, disulfiram/selected distal lesions, restrictive diet
B12 | RDA. If risk for deficiency, 100 mcg daily sublingual or monthly IM | Anemia, hyperhomocysteinemia, neuroanomaly, neurologic impairment | IF disease/worsening >50%, or if has significant gastric resection
Iron | 100 mg oral iron daily or CRF normal, in active disease; IV iron | Fatigue, RES, cognitive impairment, lassitude, hair loss | If on cholestyramine, or if fat malabsorption present, consider water miscible form

Study Highlights

**WHAT IS CURRENT KNOWLEDGE**
- Low vitamin D is common in patients with inflammatory bowel disease (IBD).
- Epidermolysis data suggests a role for low vitamin D and the development of IBD.
- Low vitamin D is associated with increased risk of surgery in IBD.
- There is limited data suggesting low vitamin D is associated with increased overall activity in IBD, particularly Crohn’s disease.

**WHAT IS NEW**
- We used a prospective longitudinal, observational, IBD network study to conduct a multinational cohort study to evaluate the relationship between serum vitamin D status and clinical course over a 5-year time period in IBD patients.
- IBD patients with low vitamin D status (25(OH)D <30 ng/mL) had more steroid exposure, anti-TNF tolerance, more months of hospitalization, more hospital admissions, and surgery compared with IBD patients with normal vitamin D levels.
- IBD patients with low-vitamin D status had more chronic abdominal pain, disease activity and worse quality of life.
- IBD patients who received supplementation and corrected vitamin D status had a significant reduction in healthcare utilization.
Nutrition Therapy - other considerations

- SIBO – small intestinal bacterial overgrowth (Bures 2010, Grace 2013)
  - 25-48% prevalence in CD
  - 81% prevalence in UC

- Bone health
  - In cross-sectional studies of patients with IBD, the prevalence of osteoporosis ranges from 18% - 42% (Bernstein 2003; van Hoeijzen 2006)
  - The prevalence of osteopenia 22 - 77% (Ali 2009)
  - In newly diagnosed IBD, the prevalence is 0 - 5% (Bernstein 2009)
  - Osteitis multifactorial: corticosteroid therapy, disease-related inflammatory activity, malabsorption, and hypogonadism (Compston 2003; Ali 2009)

- Fat malabsorption: consider PERT

Summary

- Nutrition therapy in IBD is probably both undervalued & underused

- While the mechanisms of action of EEN/PEN/Real Food Diets are not well understood, mounting evidence suggests diet can affect:
  - the gut microbiome
  - patient symptoms/QOL
  - disease activity

- Consider Nutrition Therapy for remission induction/maintenance:
  - EEN, SCD as induction therapy in CD
  - PEN, SVD as maintenance therapy
  - Stress monitoring - symptoms, labs, mucosal healing, dysplasia

- Symptom management: (low fiber, low fat, low FODMAP)

- Nutritional deficiencies in IBD remain common in both the inpatient & outpatient setting - many often go unrecognized

References

- CDC http://www.cdc.gov/ibd/ibd-epidemiology.htm
- Kotsouri M, Panagiotopoulos K, Chaniotis A, Oikonomou E, et al. Nutritional deficiencies in IBD remain common in both the inpatient & outpatient setting - many often go unrecognized
Questions?

Contact Info:
Kelly Issokson, MS, RD, CNSC
issoksonk@cshs.org
310-423-2762