Managing Inflammatory Bowel Disease: Optimizing Patient Outcomes Through Nutrition

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Disclosure

- The content of this program has met the continuing education criteria of being evidence-based, fair and balanced, and nonpromotional
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- Dr. Crandall and Jen Smith have participated in Abbott Nutrition speaking engagements

Objectives

- Describe inflammatory bowel disease (IBD), with a focus on Crohn’s disease (CD)
- Identify current treatment practices and/or recommended protocols for IBD/CD and the side effects associated with each treatment option
- Review the body of evidence supporting the role of nutrition therapy for improved patient outcomes
- Discuss the use of enteral therapy, perceived barriers, and the Crandall/Smith approach to implementation

What Is Inflammatory Bowel Disease (IBD)?

Uncontrolled inflammation of intestine
- Ulcerative colitis (UC): mucosal inflammation limited to the colon and rectum
- Crohn’s disease (CD): patchy transmural inflammation that may affect any part of the GI tract
- Indeterminate colitis (IC, IBD-U): features of both conditions; unclassifiable after investigations
Population-based studies suggest that IBD is unevenly distributed throughout the world, with the highest disease rates occurring in western countries.

In US:
- Inflammatory bowel disease
  - ~1 million affected
  - ~50,000 affected children
Treatment Goals

- MAXIMIZE therapeutic response
- MAXIMIZE adherence
- MINIMIZE toxicity
- IMPROVE quality of life
- PROMOTE physical growth
- PROMOTE psychological growth
- PREVENT disease complications

Treatment Goals: Old vs New

OLD TREATMENT GOAL
  - Clinical remission
    - No symptoms
    - Good growth and nutrition

NEW TREATMENT GOAL?
  - Mucosal healing

Why/Why Not Mucosal Healing?

- Improved symptoms do not equal mucosal healing!
- Better long-term outcomes?
- Best medications only achieve mucosal healing <50% of the time
  - Risk of serious complications
Evolution of Crohn’s Disease Over Time

- Disease Onset
- Diagnosis
- Early Disease
- Stricture
- Fistula/Abcess
- Surgery
- Mucosal Healing

Clinical Remission in Pediatric Crohn’s Disease

<table>
<thead>
<tr>
<th>Induction</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-TNFα Antibodies</td>
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</tr>
<tr>
<td>Corticosteroids</td>
<td>Azathioprine/6-MP</td>
</tr>
<tr>
<td>Enteral nutrition</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Sulfasalazine (5-ASA)</td>
<td>Methotrexate</td>
</tr>
</tbody>
</table>

Mucosal Healing in Pediatric Crohn’s Disease

- Induction
  - Anti-TNFα Antibodies
  - Corticosteroids
  - Enteral Nutrition
  - Sulfasalazine (5-ASA)
  - Methotrexate

- Maintenance
  - Anti-TNFα Antibodies
  - Azathioprine/6-MP
  - Methotrexate

Step-up Approach

- Biologics
- Steroids, Immunomodulators
- 5-ASAs, Antibiotics, Nutritional Therapy
**Rapid Step-up Approach**

- Biologics
- Steroids, Immunomodulators
- 5-ASAs, Antibiotics, Nutritional Therapy

**Top-Down Approach**

- Biologics
- Steroids, Immunomodulators
- Biotherapies
- Nutritional Therapy?

**Limitations of Medical Options for Induction Therapy**

- Steroids are “bad”
- Limited effectiveness of sulfasalazine
- Methotrexate is slow

**Steroids Are “Bad”**

- Effective for the induction of clinical remission
- Goal is to use “steroid-sparing” strategies
- Not effective maintenance therapy
- Multiple potential side effects
  - Eyes
  - Bones
  - Joints
  - Immune system
  - Cosmetic (weight gain, acne, stretch marks)
  - Diabetes
  - Depression
Limited Effectiveness of Sulfasalazine

• If effective, likely only for mild Crohn’s disease limited to the colon
• Limited side effects
  – Headache
  – Nausea
  – Rare kidney complications

Methotrexate Is Slow

• Often thought of more as maintenance therapy
  – Often paired with another induction therapy such as steroids
• ~6- to 8-week (or more) onset of action
• Requires that patient also takes folic acid supplement
• Potential side effects include
  – Bone marrow suppression
  – Liver injury
  – Immunosuppression
  – Nausea (vomiting); common
  – Teratogenic

Limitations of Medical Options for Induction Therapy

• Steroids are “bad”
• Limited effectiveness of sulfasalazine
• Methotrexate is slow

What about the anti-TNFs?

SONIC Trial: Clinical Remission Without Corticosteroids at Week 26

- Primary Endpoint

  - Proportion of Patients [%]
  - AZA + Placebo: 30
  - IFX + Placebo: 44
  - IFX + AZA: 57

- Statistical Significance
  - IFX + Placebo vs Placebo: P<.001
  - IFX + Placebo vs AZA: P<.002
  - IFX + AZA vs Placebo: P<.006
SONIC Trial: Mucosal Healing

Complete Mucosal Healing at Week 26

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Proportion of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZA + Placebo</td>
<td>16</td>
</tr>
<tr>
<td>IFX + Placebo</td>
<td>30</td>
</tr>
<tr>
<td>IFX + AZA</td>
<td>44</td>
</tr>
</tbody>
</table>

P<.001

P<.023

P<.055

Cost
Infusion/Injection site reactions
Immunogenicity
Infectious complications
Opportunistic infections (including tuberculosis, histoplasmosis, coccidioidomycosis, listeriosis)

Drug-induced lupus
Demyelination
Psoriasiform skin lesions
Increased risk of neoplasia, including lymphoma

Risk of Hepatosplenic T Cell Lymphoma

- 37 cases of IBD (35 male)
- 18 on anti-TNF therapy + thiopurine (17 male)
- 19 on thiopurine therapy alone
- Aged 12 to 58 years (mean, 26 years)
- 1 to 24 infusions (8 had <3 infusions)

Estimated Risks
- Males <35 years on thiopurines: 1/7404
- Males <35 years on thiopurines + anti-TNF: 1/3534

Nutritional Therapy: Primary Treatment of Active Crohn’s Disease

- Therapeutic efficacy in pediatrics
  - Remission in 50% to 80% of patients
  - Mucosal healing in 75%?
- Controversy regarding influence of anatomic location: colon vs small intestine
- Value of elemental vs polymeric
Mucosal Healing: Polymeric Enteral Nutrition vs Corticosteroids (CS)

- Increased caloric intake
- Anti-inflammatory properties
  - Decrease in inflammatory markers during therapy
- Modification of gut microflora

Nutritional Therapy for CD: Rationale

Maintenance Enteral Therapy

Less Evidence of Efficacy
  - Repeated induction
  - Minimum weekly requirement (5-6 days)

Treatment Goals

- MAXIMIZE therapeutic response
- MAXIMIZE adherence
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Enteral Therapy for Crohn’s Disease

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Columbus, Ohio

Treatment Goals

- MAXIMIZE therapeutic response
- MAXIMIZE adherence
- MINIMIZE toxicity
- IMPROVE quality of life
- PROMOTE physical growth
- PROMOTE psychological growth
- PREVENT disease complications

Multidisciplinary Team

- Ideally, a team approach to enteral therapy is preferred
- As it is not always feasible (eg, dietitian not available), enteral therapy treatment plan should be as simple as possible
  - Practitioner: help determine treatment strategy, implement plan, assess efficacy
  - Nurse: education, nasogastric (NG) placement as needed
  - Dietitian: education, modification of enteral therapy plan as needed
  - Patient/Parent: coaching, mentoring
  - Others: SW, office staff, insurance specialists, psychology

Definitions

- Enteral nutrition (EN) or enteral therapy: using liquid formulas to treat Crohn’s disease
- Exclusive enteral nutrition (EEN): using enteral nutrition as a sole source of providing nutrition to induce remission in Crohn’s disease
- Partial enteral nutrition (PEN): using enteral nutrition as the majority or portion of nutrition (in addition to regular foods) to induce remission, maintain remission, or improve nutrition status
Background

- European, Japanese, and British societies recommend considering EN as first-line induction therapy\(^1\)-\(^3\)
- 62% of European pediatric gastroenterologists regularly use EEN\(^4\)
- 4% to 12% of North American pediatric gastroenterologists regularly use EEN\(^4,5\)

Side Effects

Possible GI side effects\(^1\):
- Nausea, diarrhea, less commonly constipation
- Loose or runny bowel movement, typically in the morning

Refeeding syndrome\(^1,2\):
- If a patient is severely malnourished, initiation of EEN should be monitored closely, perhaps in inpatient setting

References:
NASPGHAN formed Enteral Nutrition Working Group (ENWG) and published report in 2012

- Goal to support physicians in developing and promoting an enteral nutrition therapy program
- Reviewed current literature for efficacy of therapy and assessment of variations in treatment

Recommendations (EN to Induce Remission)

EEN vs PEN

- 3-fold greater remission rate using EEN vs 50% PEN

Recent study (2013) showed 65% achieved remission with 80% and 90% EN

Recommendations (EN to Induce Remission)

Formula composition

- No significant difference in outcome (polymeric vs semi-elemental vs elemental)
- Significant difference in cost and taste

Recommendations (EN to Induce Remission)

Duration

- 8 to 12 weeks
- Inflammatory markers may improve within 1 week
- Remission may be seen in as little as 1 to 2 weeks; however, for some patients, it may take more than 2.5 weeks
- 3- to 4-week trial, and if no improvement, then may wish to change treatment plan

4-6 weeks is suggested by some experts
Recommendations (EN to Induce Remission)

Route
• Oral or NG

Restarting foods
• No studies
• Committee recommends introducing 1 meal every 2 to 3 days while gradually decreasing volume of formula

Nationwide Children's Hospital Approach (Induction)

<table>
<thead>
<tr>
<th>Amount</th>
<th>100% for 1 to 2 weeks until meeting with RD, then consider 90% EN and 10% conventional foods if compliance or adherence an issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route</td>
<td>PO preferred</td>
</tr>
<tr>
<td>Type</td>
<td>Polymeric</td>
</tr>
<tr>
<td>Duration</td>
<td>4-6 weeks after initiation to see if improvement; if improvement, then another 6-8 weeks (12 weeks total)</td>
</tr>
</tbody>
</table>
| Taper           | After 12 weeks, if not using EN to maintain remission
• Add 1 meal every 3 days, gradually decreasing supplement by 1 to 2 cans at a time |

Nationwide Children's Hospital Approach (Remission)

• No clear recommendations from the committee
• After 12 weeks of EN (EEN or 90% EN), if patient wishes to use EN as maintenance
  • 6 days of EN per week for 12 weeks (1 day per week of conventional foods allowed)
  • Weight and inflammatory status check
    • If remission, change to 5 days of EN per week
    • If active disease, return to 7 days of EN per week

Perceived Barriers

Physician challenges
• EN may delay treatment
• No clear process or criteria for initiation and management
**Enteral Nutrition Flowchart**

**Induction**
- Begin exclusive EN (see table)
- Establish plan for maintenance therapy
- Schedule practitioner visit at 4-6 weeks to determine response
- Note: Dietitian visit at 1-2 weeks (if available)
- Determine 90% vs. 100% EN

**Maintenance**
- EN for a total of 12 weeks
- \( \text{Extra Water (Cups/Day)} \)

**Initiation of EEN**

**Typical Regimen**

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Male (Cans Formula/Day)</th>
<th>Female (Cans Formula/Day)</th>
<th>Extra Water (Cups/Day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-5</td>
<td>4-5 Standard Pediatric</td>
<td>4-5 Standard Pediatric</td>
<td>1-2</td>
</tr>
<tr>
<td>6-9</td>
<td>5 Standard Pediatric</td>
<td>5 Standard Pediatric</td>
<td>2-3</td>
</tr>
<tr>
<td>10-13</td>
<td>4-5 Adult High Calorie</td>
<td>4-5 Adult High Calorie</td>
<td>3-4</td>
</tr>
<tr>
<td>14-17</td>
<td>6 Adult High Calorie</td>
<td>5 Adult High Calorie</td>
<td>3-4</td>
</tr>
<tr>
<td>18-21</td>
<td>6-7 Adult High Calorie</td>
<td>5 Adult High Calorie</td>
<td>3-4</td>
</tr>
</tbody>
</table>

- Individualized recommendations made based on patient needs
- Adjust recommendations to height age if significant growth delay

**Enteral Nutrition Flowchart: Induction**

- **Significant response or remission at 4-6 wks?**
  - **YES**
    - Continue EN for a total of 12 weeks
  - **NO**
    - \( \text{Continue EN for maintenance therapy?} \)
      - **YES**
        - Continue EN for a total of 12 weeks
      - **NO**
        - \( \text{Consider additional or alternate therapy} \)

- **Taper EN 3 days by adding 1 regular meal in place of 1-2 cans of formula**
We are going to treat your Crohn’s disease with nutrition therapy for the first 3 months.

- Regular food
- Patient insurance may not cover
- Medicaid or other supplemental state-funded programs may cover

We want you to do this for at least 4 weeks to see if there is improvement.

If there is, we will continue for a total of 12 weeks.

Then, after the 3 months, you may be able to have 1 or 2 days off, which would allow you to eat your usual foods.
Perceived Barriers

Quality of Life

- Limited studies looking at quality of life and EEN
  - 92% treated with EEN for 8 weeks had improved quality of life scores
- Start a mentoring program
  - Parents of the young patients
  - Teenage patients

Experience to Date

- 14 patients started EN
- 3 complete
  - 5 in p
  - 6 did not complete
- 1 patient continuing EN for maintenance
- Reasons for stopping
  - 4 unable to take PO
  - 2 did not respond within 3-4 weeks and changed therapy
- All 3 patients that completed EN feel it was successful and agreed to be mentors

Quality of Life

- Social eating
  - Allowing patients to eat a small amount of food with friends and family (10%)

Thank you for your participation in this program.

Questions and Answers

Discussion Question #1

There are good data that enteral therapy is effective in Crohn's disease and has minimal side effects, yet it is underutilized in the US. What do you think is the biggest barrier to its use in your practice?

Discussion Question #2

How can we increase our comfort with using enteral therapy, and therefore increase our patients' willingness to use it as primary therapy?

Discussion Question #3

Although the perceived barriers to using enteral therapy are often greater than the actual barriers, there are certainly real challenges that should be addressed. What information and tips can you give patients to help them with the process?
Discussion Question #4

In what patients should I consider recommending enteral therapy?

References


References


