Pro: Patients with Crohn’s disease and growth failure should be managed with “step up” therapy: Nutrition, steroids and immunomodulators before biologics

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I have the following financial relationships to disclose

• In the past 12 months, I have had the following relevant financial relationships with the following manufacturers:
  
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  Celgene                  Advisory Board
  AbbVie, Inc.            Advisory Board
  Abbott Nutrition        Speaker Board

*Products or services produced by this company are relevant to my presentation*
Effect of Daily Corticosteroid Therapy on Growth in Children with IBD

A stunted, cushingoid child without gastrointestinal symptoms is not a success story

Increased Effectiveness of Early Therapy With Anti–Tumor Necrosis Factor-α vs an Immunomodulator in Children With Crohn’s Disease


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Effect of Early Therapy on Growth Parameters at 1 Year

No linear growth on thiopurines

Mean change z score

Anti TNF monotherapy: p=.002
IM monotherapy: p=.NS
No Immunotherapy: p=.NS

(68 triads)

Walters TD, et al, Gastro 2014;146:383
Management of Growth failure

Steroids

Thiopurines
Methotrexate Induces Steroid Free Remission in Children with 6-MP Intolerant/Resistant CD


Turner, et al. AJG; 2007:1572
Let’s talk about Nutrition!
Etiology of Growth Failure in IBD

- Increased needs
- Suboptimal intake
- Malabsorption
- Increased GI losses

MALNUTRITION

GROWTH FAILURE

- Pubertal Delay
- Corticosteroids
- Inflammation
Management of growth retardation in the young patient with Crohn’s disease

Caloric intake for CD with growth failure is 60% RDA

Formula given to achieve RDA

Changes in growth velocity before and after 1 year of nutritional supplementation

Ballinger A. Expert Opin. Pharm, 2002
Simple nutritional hypothesis does not explain growth failure in CD

- Undernutrition
  - Pair-fed group are healthy but food intake is matched to the colitic group

- Inflammation

* p=0.02 vs pair-fed
** p<0.002 vs controls

Ballinger A. Expert Opin. Pharm, 2002
Management of growth failure in IBD

• The ultimate therapy:
  - Corrects nutritional deficits
  - Anti-inflammatory effects
  - Heals mucosal inflammation
  - Stimulates growth
  - No serious adverse effects
Polymeric Diet Alone vs. Steroids for Active Pediatric CD (Induction Therapy)

• Methods (n=37)
  - Prospective 10 week randomized controlled open-label trial
  - Newly diagnosed children receive:
    • polymeric formula (n=18) or steroids (n=19)

  - Primary outcomes at 10 weeks
    • Clinical remission (PCDAI≤10)
    • Mucosal healing
      - Decrease in both endoscopic and histologic scores by > 50% when compared to baseline
Polymeric Diet Alone vs. Steroids for Active Pediatric CD (Induction Therapy)


*Clinical improvement*

- Enteral nutrition: n=19
- Corticosteroids: n=18

*Healing of GI tract*

- P<0.05
Induction Therapy with Polymeric Diet for Active Pediatric CD

Study Design:
- Open-label, 8-week trial (n=29)
- Polymeric diet was sole source of nutrition

Results:
- Clinical remission: 79%
- Mean weight gain: 3.2 kg
- Improved endoscopic and histologic scores
- ↓ mucosal inflammatory cytokines
- Relapse: 39% relapse (by 10 months after stopping formula)

Greater Mucosal Healing with More Restrictive Diet During Induction Phase

PLEASE Study: An 8-week Prospective Cohort Study Among Children with Crohn’s

** p<0.05 PEN vs. EEN and PEN vs. anti-TNF

Significant improvements occurred
- Inflammatory markers by day 7
- Nutritional parameters after day 14

Conclusion
- Early increases in IGF-1 are attributable to the anti-inflammatory effect of EN

Horizontal solid line arrows indicate the days of significant change from day 0

Bannerjee k, et al. JPGN2004;38:270
Maintenance Therapy with Enteral Nutrition for CD

• Inclusion
  - Adult patients in remission at the beginning of trial (CDAI<150)

• Methods (prospective study)
  - 50% of caloric needs from an elemental diet (Elental®) by overnight NG feed for 1 year (n=20)
    VS
  - Normal diet (n=20)

Yamamoto T et al. Inflamm Bowel Dis 2007;13:1493
Maintenance Therapy with Enteral Nutrition for CD

Severity of mucosal inflammation was graded 0-3

Conclusion: Endoscopic inflammation was significantly higher in the normal diet group at 12 months*

## Maintenance Therapy with Enteral Nutrition for CD

### Table

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>EN Group</th>
<th>Normal Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IL-1(^2) (pg/mg)</strong></td>
<td>P = 0.32</td>
<td>P = 0.02*</td>
</tr>
<tr>
<td>At Entry</td>
<td>102</td>
<td>104</td>
</tr>
<tr>
<td>12 months</td>
<td>110</td>
<td>150</td>
</tr>
<tr>
<td><strong>IL-6 (pg/mg)</strong></td>
<td>P = 0.18</td>
<td>P = 0.002*</td>
</tr>
<tr>
<td>At Entry</td>
<td>810</td>
<td>900</td>
</tr>
<tr>
<td>12 months</td>
<td>900</td>
<td>1300</td>
</tr>
<tr>
<td><strong>TNF-± (pg/mg)</strong></td>
<td>P = 0.2</td>
<td>P = 0.001*</td>
</tr>
<tr>
<td>At Entry</td>
<td>135</td>
<td>160</td>
</tr>
<tr>
<td>12 months</td>
<td>150</td>
<td>215</td>
</tr>
</tbody>
</table>

Conclusion: Pro-inflammatory mucosal cytokines were significantly higher in the normal diet group at 12 months.*

Nutrition as Primary Therapy for Growth Failure in IBD

• Minimize disease activity
• Encourage positive nitrogen balance
• Enhance growth
• Promote normal sexual development
• Corticosteroid sparing