Are We Able to Treat IBD with Diet?

Consultant Gastroenterologist, Adelaide and Meath Hospital Incorporating The National Children’s Hospital.
Dean of Health Sciences and Professor of Medicine, Trinity College Dublin.
President-Elect, United European Gastroenterology Federation.
Overview of Presentation

- Diet & Malnutrition
- Enteral Diet Therapy
  - Evidence
  - Side effects
  - Mode of action
- Diet - the Future
Diet as a Risk Factor in IBD

Incidence of CD in Japan

Shoda et al, 1996
Diet as a Risk Factor in I.B.D.

- Incidence of I.B.D. in Europe:
  - 0.81 / \(10^5\) in Galicia Spain.
  - 4-6 / \(10^5\) in Northern Europe.
Diet as a Risk Factor in I.B.D.

E.C.I.B.D.

- Northern Europe (7.0)
- Southern Europe (3.9)

(Shuhaibar, M. 2011)
Incidence of I.B.D. in Ireland

- U.C. (M: F = 18.6 :11.6 / 100,000)
- C.D. (M: F = 4.5 :5.9 / 100,000)

(Shuhaibar, M. 2011)
Diet in IBD

- Nutritional role
- Primary therapeutic role
Increased Nutritional Requirements
Inflammatory load

Reduced Nutritional Intake
Anorexia, poor appetite, nausea, vomiting, pain

Increased Nutrient Losses
Nutrient malabsorption, diarrhoea, vomiting, fistulae, intestinal protein losses

Drug Therapy
Corticosteroids, 

Surgery
Reduced absorptive area, short bowel syndrome

Causes of Malnutrition in IBD

Prevention Strategy
Nutritional monitoring and appropriate intervention as part of the multidisciplinary management of CD

Diet and Osteoporosis - General Guidelines

General Advice: all IBD: BSG: Gut 2000

Diet
- Adequate dietary calcium; add calcium tablets if necessary to ensure daily intake of 1500 mg
- Seek and treat vitamin D deficiency

Lifestyle
- Exercise
- No smoking
- No alcohol excess
Diet and Osteoporosis - General Guidelines

**Steroids:** BSG, Gut 2000

- Lowest dose for as short as possible
- Concurrently 800 units vitamin D daily
- Measure BMD, repeat each year in which steroids are given
- If T score < 1.5 offer bisphosphonate (in addition to vitamin D)

**AGA, Gastroenterology, 2003**

- Ensure adequate calcium
- At-risk Sub-groups
Vitamin D and Inflammation in CD

25 (OH) D and IL-10 in CD

Kelly P, Nic Suibhne T, Ó'Moráin C, O’Sullivan M; IJVNR 2010 in press
Vitamin D Deficiency is Common in CD

N=200

(a) Prevalence of insufficiency

(b) Serum 25-OH-D levels

Vitamin D criteria Lips 2004

Nic Suibhne, Ó'Moráin, O’Sullivan 2009
Vitamin D Therapy in IBD?

IRCSET funding – novel roles of vitamin D in inflammation in IBD
O’Sullivan, Raftery 2010-13
Iron Deficiency in IBD

- Iron deficiency occurs in 45% of patients with IBD and is higher among CD than UC.

- Anaemia is present in 35% of IBD patients in OPD and has a significant impact on QOL.
Iron Replacement and I.B.D.

- A recent literature review concluded that iv iron is:
  1. More effective.
  2. Better tolerated.
  3. Improves quality of life to a greater extent.

- The mean response of iv iron is 72.5% vs 58.2% for oral iron.
Iron Replacement in I.B.D.

- Ferric carboxymaltose versus Iron Sucrose (n=475) in IBD

### Haematologic parameters

- **Hb (g/dL)**
  - Week 0: 10.5
  - Week 4: 11.2
  - Week 8: 12.1
  - Week 12: 13.0

- **TSAT (%)**
  - Week 0: 18.5
  - Week 4: 22.0
  - Week 8: 25.5
  - Week 12: 28.0

- **Ferritin (ng/mL)**
  - Week 0: 50
  - Week 4: 60
  - Week 8: 70
  - Week 12: 80

---

*FCM* - *IS* ; *p <0.001 and **p ≤0.015 for change vs. baseline*
Both treatments showed significant improvement in quality of life.

Fewer infusion site reactions 0.4 vs 2.5%.

FCM also required fewer infusions and better adherence.
Enteral Nutrition as Primary Therapy in CD

Primary Therapy

1. **Elemental Diet**
   nutrients in simplest form
   (protein as aa, short chain fatty acids, glucose)

2. **Semi-Elemental**
   (peptide)

3. **Polymeric**
   (whole protein, routine use, cheap)
Landmarks in Diet Therapy

- 1970s  Uncontrolled trials
- 1984   Controlled trial
- 1990s  Meta analyses
- 2000   Reviews
- 2000+  Guidelines; Era of Biologics
Elemental Diet v. Steroids in CD

Change in clinical score (neg. score indicates clinical improvement)

Weeks

O’Morain et-al Digestive diseases and sciences 1987
Primary Therapy:
Enteral Nutrition v Steroids in CD
Enteral Diets as Primary Therapy
Meta-analysis

- Steroids are superior
- Enteral better than placebo (60%)
- No difference between polymeric v elemental: peptide inferior
- Not essential to be elemental
- Diet more suited to some subgroup

Messori 1990, Fernandez-Banares 1995
Enteral Diets - Efficacy

- Elemental diets induced remission in 77-100% of compliant patients (4 trials; n = 111),

*Elemental diets are as effective as steroids*

O’Morain ‘84, Hunt ‘89 Seidman ‘91, Gorard ‘93
# Drug Therapy – Side Effects

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td>Bone disease, growth suppression, Cushings</td>
</tr>
<tr>
<td>Newer steroids</td>
<td>Fewer side-effects</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Bone marrow suppression, abnormal LFT’s</td>
</tr>
<tr>
<td>Cyclosporin</td>
<td>Nephrotoxicity, hypertension</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Pancreatitis, Bone marrow suppression</td>
</tr>
<tr>
<td>Sulphasalazine</td>
<td>Rashes, allergy</td>
</tr>
</tbody>
</table>
Nutritional Therapy - Side effects

- Free from major side effects.
- Safe therapy.
- Diarrhoea, nausea, headaches.
Nutrition - End-Points for Clinical Trials?

- Drop in CDAI - 70 points.
- Improved Quality of Life.
- Changes in inflammatory cytokine levels.
Nutrition - End-Points for Clinical Trials?

Endoscopic healing

Histological healing
Elemental Diet - Mode of Action

- Nutritional Effect
- Fat composition
- Glutamine / Arginine
- Gut Permeability
- Gut Flora
- Antigenic Load
- Luminal pH
- Bowel Rest

ELEMENTAL DIET
Mode of Action: Intestinal Permeability
crEDTA Before and After Rx with an Elemental Diet

Teahon et al 1990
Mode of Action: Anti-Inflammatory

Mucosal Cytokine (mRNA) Response to Polymeric Diet CT3211

Fell, 2000
Mode of Action: Anti-inflammatory

Effects of an enteral diet on CD-affected tissues in vitro

\[ P < 0.05 \]

Meister, et al 2001
Mode of Action: Glutamine

Glutamine-enriched polymeric diet in active CD

N=18

P= 0.5; NS

Akobeng, 2000
Mode of Action: Role of Fat

Gassull et al, 2002
Mode of Action: Role of Fat

Bamba et al, 2003
### Fat: Fish Oil in Crohn’s Disease

**Remission at 1 Year**

<table>
<thead>
<tr>
<th></th>
<th>Remission at 1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fish Oil</strong></td>
<td>23 (59%)*</td>
</tr>
<tr>
<td>(2.7g n-3 FA)</td>
<td></td>
</tr>
<tr>
<td><em>n = 39</em></td>
<td></td>
</tr>
<tr>
<td><strong>Placebo</strong></td>
<td>10 (26%)*</td>
</tr>
<tr>
<td><em>n = 39</em></td>
<td></td>
</tr>
</tbody>
</table>

*P = 0.003

Elemental Diet and Infliximab

N=75

■ With ED treatment;

□ without ED treatment

*OR: 4.5

Torao Tanaka et al. J Gastroenterol Hepatol. 2006;21(7):1143-9
EN as Primary Therapy: Guidelines

- **Europe - ESPEN (2006)**
  - First line therapy in *children*
  - Therapy in *adults* in whom steroids are not suitable

- **UK - BSG (2004)**
  - First line in *children* with impaired growth/malnutrition
  - *Adults* – specific cases

Enteral Diets In CD - Summary

**INDICATIONS**

- Active disease
- Paediatric patients
- Conventional treatment failure
- Steroid dependence
- Steroids poorly tolerated / side-effects
- Strictures due to oedema
- Pregnancy
Diet and IBD - The Future

- Basic research
- Clinical trials
- Multidisciplinary
- Disease specific formula
Dublin, Ireland

6th Congress of ECCO
10 year ECCO anniversary
February 24-26, 2011