Nutritional Intervention in IBD

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30 minute overview

- Malnutrition in IBD
- Roles of nutrition
  - Adjuvant
  - Primary
- Clinical evidence
- Patient selection
  - Case study
- Best practice guidelines
- Conclusion
Learning objectives

1. Consider the causes of malnutrition in IBD
2. Understand the different roles of nutrition
3. Learn the indications for primary therapy
4. Be aware of recent best practice guidelines
Questions

Can you use nutrition to treat active Crohn’s Disease?

What are the important nutritional issues in this patient group?
Malnutrition in IBD
Increased Nutritional Requirements
Inflammatory load
Disease exacerbation

Reduced Nutritional Intake
Anorexia, Nausea, Pain, Obstruction, Fasting for procedures, Fear of eating

Increased Nutrient Losses
Malabsorption, Intolerances, Vomiting, Fistulae

Drug therapy
Corticosteroids, MTX, Sulphasalazine

Surgery
Reduced absorptive area, Excisions, Stoma, Drains, Short bowel syndrome

Causes of Malnutrition in IBD

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

Source: O'Sullivan M, 2009
Disease process

Local inflammation
- Stool frequency
- Pain → Anorexia
  - Poor dietary intake
    - Nutrient availability
      - Altered body composition

Systemic inflammatory response
- Malaise
- Reduced activity → Energy deficit
  - Insufficient/inappropriate balance of nutrients
    - Altered inflammatory response

Growth failure

Nutrient absorption sites

- Iron and folate
- Same as jejunum, but distal ileum is specific for vitamin B12 and bile salts

Beginning of food breakdown

Carbohydrates, fats, proteins, calcium, magnesium, trace elements and vitamins

Water, electrolytes, and short chain fatty acids
Nutritional status – active phase

- Up to 85% Protein Energy Malnutrition in hospitalised pts\(^1\)

- Up to 75% experience weight loss & 50% present in negative nitrogen balance\(^2\)

\(^1\) Vagianos K et al 2007

\(^2\) Lochs H, 2004
Nutritional status - quiescent

- 40% overweight in quiescent disease\(^3\)
  - More prone to develop active CD\(^4\)
  - Require surgery sooner\(^5\)

- Lean body mass & muscle function are significantly reduced even in remission\(^6\)

- Body fat distribution differs – depletion of visible fat & increase in intra-abdominal fat \(\rightarrow\) ? role in inflammatory process\(^7\)

\(^3\)Nic Suibhne et al, 2009
\(^4\)Blain A et al, 2002
\(^5\)Hass DJ et al, 2006
\(^6\)Jahnsen J et al, 2003
\(^7\)Peyrin-Biroulet L et al, 2007
Micronutrient deficiencies

<table>
<thead>
<tr>
<th>Deficiency</th>
<th>Estimated Frequency %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone related:</td>
<td></td>
</tr>
<tr>
<td>● Calcium</td>
<td>13</td>
</tr>
<tr>
<td>● Magnesium</td>
<td>14-33</td>
</tr>
<tr>
<td>● Vitamin D</td>
<td>75</td>
</tr>
<tr>
<td>Anaemias:</td>
<td></td>
</tr>
<tr>
<td>● Iron</td>
<td>39</td>
</tr>
<tr>
<td>● Folate</td>
<td>54</td>
</tr>
<tr>
<td>● Vit B12</td>
<td>48</td>
</tr>
</tbody>
</table>

Source: O’ Sullivan MA & O Morain CA, 1998
Associated nutritional complications

- **Metabolic bone disease** -
  - Osteopenia/Osteoporosis/Osteomalacia

- **Lactose intolerance** -
  - Transient

- **Steatorrhoea** -
  - TI involvement/excision → reduced bile acid absorption → fat & fat sol vit malabsorption (Vit ADEK)

- **Micronutrient deficiencies** -
  - Magnesium & Zinc if excessive GI losses, Vit A, D & E, Vit B₆

- **Anaemia** -
  - iron, folate, Vit B₁₂

- **Thromboembolic complications** -
  - Excess plasma homocysteine in IBD. Pathway dependent on folate, B₁₂ and B₆
Role of Nutrition in IBD
Diet in IBD

- Dietary intervention depends on:
  - Disease location
  - Phase - active/quiescent
  - Nature - presence of strictures/fistulae
  - Current medical treatment
  - Surgical intervention
  - Individual symptoms

No clear nutrition ‘formulation’ that works for all patients
Adjuvant Therapy

Basic nutrition support to prevent or treat malnutrition

- Supplemental NG feeding for weight gain
- Micronutrient replacement if deficiency
- Parenteral nutrition (PN) if small bowel obstruction

For **correction and maintenance** of nutritional status in both Crohns and Ulcerative Colitis

Targeting nutritional status - weight, nutrient deficiencies, functionality
Primary treatment

Using nutrition to **achieve remission** in patients with an acute exacerbation of Crohn’s disease

- Exclusive liquid diet/Total Enteral Nutrition (TEN)
- Polymeric or elemental type formula
- Orally or via nasogastric tube (NGT)
- Min 10 days - Approx 4-6 weeks
- Commence reintroduction diet (e.g. LOFFLEX) when established on medical treatment
  - Draft British Dietetic Association (BDA) GSIG consensus guidelines 2010

**Targeting disease activity & inflammation**
**Formulae**

<table>
<thead>
<tr>
<th>Categories refer to nitrogen source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Polymeric = whole protein</strong></td>
</tr>
<tr>
<td>e.g. Osmolite (<em>Abbott</em>)</td>
</tr>
<tr>
<td>Nutrison (<em>Nutricia</em>)</td>
</tr>
<tr>
<td>Fresubin (<em>Fresenius Kabi</em>)</td>
</tr>
<tr>
<td>Modulin IBD (<em>Nestle</em>)</td>
</tr>
<tr>
<td><strong>Semi-elemental = polypeptides</strong></td>
</tr>
<tr>
<td>e.g. Perative (<em>Abbott</em>)</td>
</tr>
<tr>
<td>Peptisorb (<em>Nutricia</em>)</td>
</tr>
<tr>
<td>Survimed OPD (Fresenius Kabi)</td>
</tr>
<tr>
<td><strong>Elemental = amino acids</strong></td>
</tr>
<tr>
<td>e.g. E028 (<em>Nutricia</em>)</td>
</tr>
</tbody>
</table>
Reintroduction diets

- Elimination diets
  - 1 new food per day, 2-3 times daily
  - Concurrent reduction in sip feed volume
  - Food diary
    - If symptom free, allow food ad libitum
    - If provokes reaction, exclude and retest later
  - 2 days rest after 7 days testing (delayed reactions)
  - Process takes ~ 3 months even with daily testing
  - Continue for 2-3 symptom-free years before retesting intolerances

- ‘LOFFLEX’
  - ‘Low fat, fibre limited, exclusion diet’
  - Based on foods least likely to cause intolerance
  - Start with more foods \(\rightarrow\) more acceptable
  - Process takes ~ 2-4 weeks
<table>
<thead>
<tr>
<th>Not allowed</th>
<th>Allowed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pork, meat products</td>
<td>All other lean meat &amp; poultry</td>
</tr>
<tr>
<td>Fish in batter/crumb/tinned in oil/tomato</td>
<td>All other types of fish/shellfish</td>
</tr>
<tr>
<td>Cow/sheep/goat milk, dairy products, eggs, chocolate</td>
<td>Soya milk &amp; products</td>
</tr>
<tr>
<td>Wheat, rye, barley, corn, oats, yeast</td>
<td>Rice, tapioca, sago, arrowroot</td>
</tr>
<tr>
<td>Corn &amp; vegetable oil</td>
<td>Sunflower &amp; olive oils in moderation</td>
</tr>
<tr>
<td>Pulses, onion, tomato, sweetcorn</td>
<td>Potato &amp; all other veg, 2 portions a day, no skins/seeds</td>
</tr>
<tr>
<td>Citrus, apple, banana, dried fruit</td>
<td>All other fruit, 2 portions per day, no skins/seeds</td>
</tr>
<tr>
<td>Tea, coffee, alcohol, squash, cola</td>
<td>Fruit/herbal teas, water, ribena, non-citrus fruit juice</td>
</tr>
<tr>
<td>Gravy mixes, salad dressings, nuts, seeds</td>
<td>Salt, pepper, herbs, spices, sugar, honey, jam</td>
</tr>
</tbody>
</table>
Clinical Evidence
Evidence - inducing remission

- 3 meta-analyses & 1 cochrane review conclude steroid therapy is more effective than liquid diets at inducing remission 8,9,10,11

8 Fernandez-Banares F et al, 1994
9 Griffiths AM et al, 1995
10 Messori A et al, 1996
11 Zachos M et al, 2007
Primary Therapy: EN vs Steroids in CD Clinical Trials

![Bar chart showing remission rates for different trials comparing EN and Steroids.](chart.png)
Evidence – inducing remission

- In Japan – used first line with good success\textsuperscript{12}
- Overall remission rate with liquid diets ~ 60\% - similar to that found with pharmacological alternatives 5-ASAs/aminosalicylates & substantially higher than placebo response\textsuperscript{13}
- Compliance an issue – remission rate of 85\% with well-supported compliant patients on an elemental diet\textsuperscript{14}

\textsuperscript{12} Matsui T et al, 2005
\textsuperscript{13} Gassull MA et al, 2001
\textsuperscript{14} Teahon K et al, 1990
Evidence - inducing remission

- **Trophic effects** of liquid diet on gut mucosa along with down regulation of inflammatory response\(^{15,16}\)
  - Prolongs remission
  - Paediatric population
  - Used formula with a natural **anti-inflammatory growth factor** (TGF B2 - *Modulin IBD*, Nestle)

\(^{15}\)Fell JM *et al*, 2000
\(^{16}\)Borelli O *et al*, 2006
Evidence - maintaining remission

- Few studies on exclusive liquid diet to maintain remission
- All beneficial \(^{17,18,19}\)
- Cochrane review - may be effective but larger studies needed \(^{20}\)

\(^{17}\)Matsui T \textit{et al}, 2005  
\(^{18}\)Verma S \textit{et al}, 2000  
\(^{19}\)Takagi S \textit{et al}, 2006  
\(^{20}\)Akobeng AK \& Thomas AG, 2007
Evidence – concurrent therapy

- Concurrent dietary treatment can increase medical efficacy\(^{21}\)

- **Used as a bridge** to control symptoms before 2\(^{nd}\) line medications such as 5-ASAs take effect
  - Supported by BSG guidelines & cochrane review\(^{11,22}\)

\(^{21}\)O’ Brien CJ *et al*, 1991

\(^{22}\)Carter MJ *et al*, 2004
Evidence - formulae

- Majority of studies comparing elemental, semi-elemental, and polymeric formulae found equal efficacy \(^8,9,11,18,23\)
  - Most studies in adults have used elemental so difficult to draw concise conclusions\(^11,14,24,25\)
  - One meta-analysis – trend towards greater efficacy with formulas with lower content of long chain triglycerides\(^26\)
  - Further studies required to identify ‘ideal’ formula
  - Polymeric first line in practice – cheaper, more palatable, lower osmolarity

\(^{23}\) Raouf AH et al, 1991
\(^{24}\) O’ Morain CA et al 1984
\(^{25}\) Silk DAA, 1992
\(^{26}\) Middleton SJ et al, 1995
Patient selection
Why nutrition not steroids?

- Risk-benefit of different treatment strategies
  - Efficacy
    - As effective as steroids in inducing remission
    - 60-80% remission rate - greater with better case selection
  - Mucosal healing
    - Certain formulas – anti inflammatory growth factor
  - No undesirable side effects
    - Bone health and growth unaffected
Indications for using nutrition as primary treatment

- TEN may not suit all circumstances
- **Careful case selection** for better efficacy
  - Crohn’s disease
  - Anatomic location of disease
  - Age or disease duration
  - Gap between medical treatments
  - Patient preference - highly motivated
  - Paediatric population
  - During pregnancy
Patient selection

**Indications**
- Active disease of small or large bowel
- Childhood/adolescent
- Steroid resistant
- Steroid poorly tolerated
- Narrowing due to oedema or swelling of mucosa

**Contraindications**
- Quiescent disease
- Disease affecting rectum only
- Patient unable or unwilling to comply
- Bacterial overgrowth
- Presence of fistulae or abscesses
- Presence of tight or multiple strictures

*Source: King TS et al, 1997*
### Case Study

**Female, DOB: 16.08.1983 - Small bowel CD diagnosed Apr 2008**

<table>
<thead>
<tr>
<th>Date</th>
<th>Symptoms and Treatments</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov 2008</td>
<td><strong>C/o Imuran</strong> 150mg OD po + weaning dose prednisolone</td>
<td>63.8kg</td>
</tr>
<tr>
<td>May 2009</td>
<td>Bloating, joint pains, BO x 4/d – formed (baseline).</td>
<td></td>
</tr>
<tr>
<td>Dec 2009</td>
<td>Distressed with bloating, nausea, &amp; anorexia. BO x 4-5/d – formed.</td>
<td>62.9kg</td>
</tr>
<tr>
<td>May 2010</td>
<td>Increased diarrhoea (4-8/d, no blood/mucus), nausea, abdo pain, wt loss.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Reluctant to start steroids – <strong>c/o entocort</strong> 9mg (reducing)</td>
<td>59.3kg</td>
</tr>
</tbody>
</table>
## Case study cond..

<table>
<thead>
<tr>
<th>Date</th>
<th>Details</th>
<th>Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jun 2010 -</td>
<td>No improvement with entocort 6mg OD - Diarrhoea x 4/d, Wt loss, abdo pain &amp; bloating Imp: Active Crohn’s + ? stricture Work up for humira &amp; SIFT Change entocort → prednisolone</td>
<td>58.4kg</td>
</tr>
<tr>
<td>Jul 2010 -</td>
<td>Symptoms improved with prednisolone Humira postponed due to LRTI + antibx</td>
<td>62.5kg</td>
</tr>
<tr>
<td>24th Aug 2010 -</td>
<td>Off steroids, symptoms returning (BO x 4-5/d and nocturnal, fatigue).  SIFT – NAD. C/o humira (with ongoing imuran 150mg)</td>
<td>63.3kg</td>
</tr>
<tr>
<td>15th Sept 2010 -</td>
<td>Diarrhoea +++ and RIF pain Humira ongoing – no symptomatic response (dose 2) c/o budesonide 9mg/d Dietitian referral for exclusive liquid diet</td>
<td>60.3kg</td>
</tr>
</tbody>
</table>
Case study cond..

**17\textsuperscript{th} Sept 2010 – Dietetic assessment**

- Reported Wt - **56.9kg**, Ht – 1.68m, BMI = 20.2kg/m\textsuperscript{2} (normal)
- 6.9kg wt loss over 2 years
- Symptoms - BO x 2-3/d formed, abdo cramps, bloating
- Estimated Requirements = 2047kcals, 69-85g protein, 1700-1992mls
  - 10\% Stress Factor & Physical Activity Level 1.4 – aim weight maintenance

**Treatment plan**

- Oral nutrition sipfeeds to reqs – 7 bottles daily (2100kcals, 88g protein, 1400mls)
- Oral fluids (aim ~ 600mls water or weak tea/coffee only)
- Agreed treatment period 2 weeks – 27/09/10 to 11/10/10
- Vit D insufficient (43nmol/l – 4/5/10); other micronutrients normal
  - **Note**: Alb = 54 (CRP 2.8)
- Supplements - Calcichew D3 forte T BD, Centrum T OD, B\textsubscript{12} IM, Omega 3
- Meds - Humira 40mg (~1 month now), imuran 150mg, budesonide 9 mg OD
Daily meal plan

Morning

Afternoon

Evening
<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5th Oct 2010</td>
<td>Humira gradually taking effect (6 wks)</td>
</tr>
<tr>
<td></td>
<td><strong>60.5kg</strong></td>
</tr>
<tr>
<td>12th Oct 2010</td>
<td><strong>Commenced reintroduction diet</strong> now established on medical treatment and weaned off exclusive liquid</td>
</tr>
<tr>
<td>10th Nov 2010</td>
<td>Much improved - formed BO x 1/d Weaned onto normal diet – no intolerances noted Sipfeeds ongoing x1/d + humira 40mg (11wks) &amp; imuran</td>
</tr>
<tr>
<td></td>
<td><strong>63kg, BMI 22.3kg/m2</strong></td>
</tr>
</tbody>
</table>
Guidelines
Consensus – exclusive liquid

- **BSG guidelines 2004** (British Society of Gastroenterology)
  - Liquid diets as primary therapy in active ileal, ileocolonic, or colonic CD & contraindication to or prefer to avoid corticosteroids
  - As adjunctive therapy in ileal, ileocolonic or colonic active fistulating and perianal disease

- **ECCO 2006** (European Crohn’s & Colitis Organisation)
  - Liquid diets only to be used as adjunctive to medical therapy except where patients decline other drug therapy. Do not recommend in corticosteroid refractory or dependent disease.

28 Travis SPL et al, 2006
Consensus – exclusive liquid

- **ESPEN 2006**\(^{29}\) (European Society of Enteral & Parenteral Nutrition)
  - In paediatrics, nutrition therapy as first line
  - In adults, use enteral nutrition as sole therapy for the acute phase mainly when treatment with corticosteroids is not feasible (Grade A)
  - No significant difference in the effect of free amino acid, peptide-based, and whole protein formulae (Grade A)
  - No clear benefits for omega 3, glutamine, TGF-B enriched formulae (Grade A)

\(^{29}\)Lochs *et al*, 2006
Mechanisms of Action?

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

Exclusive liquid diet
Unknowns

- **Mechanism of action?**
  - Theories

- **Which patients benefit most?**
  - More subgroup analysis needed

- **Optimal length of treatment?**
  - Min 10 days
  - Unlikely to respond if still symptomatic in 2\textsuperscript{nd} week \textsuperscript{27}

- **How best to reintroduce food when in remission**
  - Various reintroduction diets – not evidence based
Parenteral nutrition

- **ESPEN PN guidelines 2009**
  - PN should **not** be used as primary treatment of inflammatory luminal Crohn’s Disease. Bowel rest has not been proven to be more efficacious than nutrition per se (Grade A)
  - The most common indication is the presence of short bowel syndrome (Grade B)
  - Indicated for those who are malnourished, have inadequate or unsafe oral intake, or a non functionning, inaccessible or perforated gut. Specific indications – obstruction, high intestinal or fistulae output (Grade B)
    - Supported by BSG guidelines 2004 - ‘Enteral nutrition is preferred (Grade C)’

\(^{30}\)Van Gossum A *et al*, 2009
Future

- **Nutrigenomics**
  - Interplay between genes and diet
  - ? more targeted & individualised treatment

- **Role of specific nutrients**
  - Probiotics & prebiotics, omega 3 fatty acids, polyphenols
  - Emerging evidence but roles yet to be elucidated
Solutions

- Can nutrition be used to treat active IBD?
  - Yes – Crohn’s disease only
    - First line in paediatrics
    - Better efficacy in certain adult cases

- What are the important nutritional issues?
  - Identifying risk of malnutrition
    - Consider disease phase & location/surgical history
  - Setting goals of nutritional intervention
    - Adjunct, primary or concurrent?
Conclusions

• Nutrition status varies according to disease phase and malnutrition is not always overt

• Nutrition is a viable treatment option for certain subgroups with Crohn’s disease

• A combination of diet and medical treatments may enhance outcome

• Require more clinical trials
References

3. Nic Suibhne et al, 2009
References

References


References

Thank-you