ESPEN Congress Leipzig 2013

The ESPEN Guidelines session

Nutrition support in inflammatory bowel diseases

A. Forbes (UK)
Nutrition in IBD
Guidelines for ESPEN

Alastair Forbes
For the ESPEN IBD guidelines
working group
Introduction

Malnutrition
Treatment of malnutrition
Nutrition in aetiology
Nutrition in primary therapy
Existing guidelines

ESPEN Guidelines on Parenteral Nutrition: Gastroenterology
André Van Gossum, Eduard Cabre, Xavier Hébuterne, Palle Jeppesen, Zeljko Krznaric, Bernard Messing, Jeremy Powell-Tuck, Michael Staun, Jeremy Nightingale

2009

ESPEN Guidelines on Enteral Nutrition: Gastroenterology
DGEM: H. Lübke, S. Bischoff, N. Engelmann, P. Thul

2006
Introduction

New methodology for ESPEN guidelines
Disease focus – not technique
Multidisciplinary, multinational approach remains
More structured
Dependent on systematic review when this is possible
Expert opinion when it is not
Nutrition in IBD
Guidelines for ESPEN

Commissioned in April 2012
To be launched in August 2013
Nutrition in IBD
Guidelines for ESPEN

Recruitment of expert writing panel
Retention of key contributors to previous guidelines by mutual consent
Choice of new faces
Choice of chair and deputy
Nutrition in IBD
Guidelines for ESPEN

Intended integrated approach with ECCO ESPGHAN
Positive attitudes but practical obstacles
Much discussion
Panel chosen with representatives
But not joint guidelines
Nutrition in IBD
Guidelines for ESPEN

Chair resigned
Deputy became chair
Nutrition in IBD
Guidelines for ESPEN
Nutrition in IBD
Guidelines for ESPEN

Plan for guidelines in 2 parts
  a) introductory elements - opinion
  b) elements susceptible to systematic review

Team discussions and agreements
PICO listing for systematic review devised and sent off – first version late December refined version mid January
PICO ??

Population
Intervention
Comparison
Outcome
Nutrition in IBD
Guidelines for ESPEN

Jan-Feb writing of introductory elements commenced
Data from systematic review due mid April
For general circulation
Plan for work-in-progress meeting in June
Final guidelines to ESPEN in July
Public launch in August at Congress
Publication in Clin Nutr in Autumn
Nutrition in IBD
Guidelines for ESPEN

But …….
Writing of introductory elements
first drafts essentially complete
Nutrition in IBD
Guidelines for ESPEN

But ......
Writing of introductory elements
first drafts essentially complete
Receipt of systematic analysis ....
Nutrition in IBD
Guidelines for ESPEN

But .......
Writing of introductory elements
  first drafts essentially complete
Receipt of systematic analysis ....
on 25/8/13
Nutrition in IBD
Guidelines for ESPEN
Nutrition in IBD
Guidelines for ESPEN

1a) Malnutrition in adults
1b) in children
2) Diet in aetiology/prevention
3a) Nutrition and nutritional support in patients with IBD
3b) Surgical aspects of nutrition in IBD
3c) When AN is indicated which are the advised routes – oral, enteral tube, parenteral?
3d) When AN is indicated what special steps are needed and what complications may occur
Common sense for ESPEN members

1a) Malnutrition in adults
1b) in children
2) Diet in aetiology/prevention
3a) Nutrition and nutritional support in patients with IBD
3b) Surgical aspects of nutrition in IBD
3c) When AN is indicated which are the advised routes – oral, enteral tube, parenteral?
3d) When AN is indicated what special steps are needed and what complications may occur
Headlines from systematic review

• 1299 papers assessed
• The data almost uniformly poor or absent
• Studies are small and underpowered
• Few strong recommendations possible
• Major need for new and better research
Headlines from systematic review

Grade A recommendations

- Omega-3 supplementation not supported in maintenance of UC
- High fibre diet not supported in maintenance of Crohn’s
- Treatment of iron deficiency anaemia in IBD is valuable (oral or iv)
Progress
Headlines from systematic review

Medium grade evidence

• Probiotics ineffective in maintenance of CD
• Elemental diet ineffective in inducing remission in CD (and no different from polymeric feed)
Headlines from systematic review

Medium grade evidence 2

• Probiotics effective in maintenance of UC
• Probiotics effective in inducing remission in acute UC
  (but only 15% better than placebo)
Headlines from systematic review

No reliable evidence for

• Bowel rest
• Exclusion diets
• Enteral feeding as primary therapy
• Special feeds (includes glutamine)
We have a dream!

And hope it won’t take 50 years!
And hope it won’t take 50 years!

at least for the new guidelines!
Western diet - a cause of Crohn’s?

not a single well-defined entity

general shift away from fruit, vegetables
resistant starch and unrefined cereals
to more saturated fats and carbohydrates
of high glycaemic index
predispose to intestinal inflammation via
phenols and N-nitroso compounds?
Western diet - a cause of Crohn’s?

No specific evidence and much recall bias
Case-control questionnaire study from Japan
In Crohn’s patients
  higher prior sugar, sweets, fish and shellfish
  higher intakes of fats and vitamin E
Support from Netherlands and other Japanese studies implicating animal fat
Influence of diet on symptoms

Patients with Crohn's select a sugar-orientated diet with relatively low fibre content. They may also have inflammation-associated, acquired hypolactasia.
Advice to the high-risk individual

be breast-fed
avoid sweets
avoid total and animal fat, n-6 fatty acids
select fruits and vegetables rich in vitamin C
Advice to patients

select diet on which they feel comfortable
advice in line with that to general population
? restrict red and processed meats
? restrict sweets, soft drinks and concentrates
? FODMAP diet
if dairy foods are restricted then add calcium
consider folate and vitamin supplements
I think you’re eating too much fibre now.
Anticipating and preventing malnutrition

weight loss and malnutrition very frequent at presentation
only diarrhoea and abdominal pain more common
additional subtle deficiencies
French remission study

54 patients compared to healthy controls
30% at risk on nutritional risk index
Lower fat mass despite higher energy intake
Lower intake of beta-carotene, thiamine, vitamin C and magnesium
Zinc intake higher but low levels in 65%
Low levels of vitamin C (84%), copper (84%) and niacin (77%)
Vitamin D low in Crohn's

Contributes to bone disease
- 8% have overt vitamin D deficiency (Canada)
- 22% have suboptimal 25-hydroxy vitamin D

Sunlight important in some countries
- 19% vs 50% deficient in summer vs winter in Ireland
Micronutrients in Crohn’s

good argument for indefinite micronutrient supplement
should include zinc, thiamine, ascorbic acid and vitamin D
iron supplements reserved for those found to be deficient
Supportive nutrition in Crohn's
Supportive nutrition in the overtly malnourished

nutritional supplementation still too often overlooked (in UC too)

coincides with maximal inflammatory activity when that is therapeutic focus

ESPEN guidelines give good example of cohesive plan (www.espen.org)

problem of absence of controlled trial data
Supportive nutrition in Crohn's

follow general principles for artificial nutrition

if prominent diarrhoea add sodium and magnesium

may need to add these to enteral feeds

if tube feeding needed gastrostomies are safe
Primary nutritional therapy

reasonable evidence (trials and experience)
first demonstrated with elemental preparation
assumed mechanisms
  reduced food antigens
  avoidance of fibre
  reduced need for digestion of complex nutrients
each called into question
Enteral nutrition vs. steroids for inducing remission in active Crohn’s disease

Nutritional therapy vs. placebo

results from nutritional therapy almost universally markedly better
placebo interventions in active Crohn's very rarely >25%
no study has placebo remission rate >50%
Elemental vs. polymeric feeds

lesser palatability, higher osmolar load and larger volumes
polymeric regimens evaluated
21 patients with active Crohn's randomised to amino acids or whole protein
“equally effective”
Elemental vs. polymeric feeds

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polymeric regimens evaluated

21 patients with active Crohn's randomised to amino acids or whole protein

“equally effective”

numerical advantage to elemental
Paediatric study (Borrelli)

frustratingly unblinded
relatively homogeneous group of
previously untreated children
10 weeks’ exclusive polymeric feeding
(Modulen) or steroids
multiple endpoints
TGF-β enriched polymeric diet vs steroids in active paediatric Crohn’s disease.

Remission at 10 weeks

Steroids (n=18)  

TEN (n=19)

p=NS; but significant on histology.

Borrelli, Clin Gastroenterol Hepatol 2006
Trials of defined formulae

remains a contentious area
absence of placebo-controlled trials
not in major guidelines for adults
reliable data and meta-analyses do exist
differences from placebo in other Crohn's studies compelling
fat content probably important
The fat content of feeds
The fat content of feeds

Japanese study of active Crohn's
Elemental diet (Elental) + LCT to provide low (3g/day) medium (16.5g) or high (30g/day) total fat intake
Only low fat group achieved response rate anticipated (80%)
High fat regimen effective in only 2 of 8
Small numbers
The fat content of feeds

- quantity vs quality
- Japanese study of 3.4g fat per 2000 kcal vs 55.6g per 2000 kcal
- remission rates (67% and 72%) not different, despite changes in lipid profile
Low vs high fat EN in 1 therapy in CD

Remission rate

Low Fat

High Fat

3.4 g/2000 kcal

55.6 g/2000 kcal (40g MCT)

Sakurai T et al. JPEN 2002
# High vs. low fat formula-diets for inducing remission in active Crohn’s disease

<table>
<thead>
<tr>
<th>Study</th>
<th>Low-fat content n/N</th>
<th>High fat content n/N</th>
<th>Odds ratio (fixed effects) 95% CI</th>
<th>Weight %</th>
<th>Odds ratio (fixed effects) 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Giaffer 1990</td>
<td>12/18</td>
<td>5/14</td>
<td>5.40 [1.12, 26.05]</td>
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<td>Middleton 1995</td>
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<td>5/7</td>
<td>0.16 [0.02, 1.63]</td>
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<tr>
<td>Raouf 1991</td>
<td>9/13</td>
<td>8/11</td>
<td>0.84 [0.14, 4.97]</td>
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<tr>
<td>Rigaud 1991</td>
<td>10/15</td>
<td>11/15</td>
<td>0.73 [0.15, 3.49]</td>
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<tr>
<td>Royall 1994</td>
<td>16/19</td>
<td>15/21</td>
<td>2.13 [0.45, 10.10]</td>
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<td>Sakurai 2002</td>
<td>12/18</td>
<td>13/18</td>
<td>0.77 [0.19, 3.19]</td>
<td>20.1</td>
<td></td>
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</table>

>20 vs <20 g/1000 kcal

High vs very low fat formula-diets for inducing remission in active Crohn’s

>20 vs <3 g/1000 kcal

**Very low-fat content**

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<tr>
<th>Study</th>
<th>Very low fat n/N</th>
<th>High fat content n/N</th>
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<td>A: Rigaud 1991</td>
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<td>0.73 [0.15, 3.49 ]</td>
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<td>A: Royall 1994</td>
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<td>A: Sakurai 2002</td>
<td>12 /18</td>
<td>13 /18</td>
<td>0.77 [0.18, 3.18 ]</td>
<td>37.4</td>
<td></td>
</tr>
</tbody>
</table>

Barcelona European study

exclusive enteral regimen containing 35g lipid per 1000kcal

• either oleate predominant formula
  – 79% oleate, 6.5% linoleate

• or high linoleate
  – 45% linoleate, 28% oleate
Barcelona European study

clear numerical advantage to those on linoleate feed
52% full remission vs 20%
significant if >1 week’s compliance
63% v 27%; p<0.01
Oral n-3 PUFA in quiescent CD relapse at 12m

Belluzzi et al, NEJM, 1996
n-3 fatty acid capsules vs placebo as maintenance in inactive Crohn’s

But the “placebo” was MCT!

Feagan, JAMA 2008
Crohn’s and Lipids

Animal and ex vivo experiments
Crohn’s and Lipids

TNBS rat model
Animals fed:
Elemental 028 (in clinical use)
Emsogen (n-6 rich, MCT rich)
Control feeds

Papada E, et al, submitted
Crohn’s and Lipids

![Graph showing IL-6 levels in different conditions: CONTROL+BD, TNBS+BD, TNBS+ED1, TNBS+ED2.](Image)
Crohn’s and Lipids

![Graph showing IL-10 levels in different conditions](image)
Crohn’s and Lipids

TNBS model is in wrong order and more like ulcerative colitis than Crohn’s?
But data consistent with Barcelona clinical study (not Mediterranean-style feed)
Crohn’s and Lipids

Human model
Surgical resection samples
Fat of different tissue origins
Incubation with Elemental or Emsogen
24 hour study period
Control samples (not shown) ≈ UC
Unpublished data (Broadhurst J, et al)
Crohn’s and Lipids
Crohn’s and Lipids

Discrepancies drive next steps
Aetiopathogenesis vs therapy
New doctoral fellow
True TPN as primary therapy for IBD (1-3m followed to >2y)

<table>
<thead>
<tr>
<th>Studies</th>
<th>n</th>
<th>initial remission</th>
<th>long-term remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 in CD</td>
<td>170</td>
<td>81%</td>
<td>23%</td>
</tr>
<tr>
<td>4 in UC</td>
<td>60</td>
<td>37%</td>
<td>12%</td>
</tr>
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</table>
IVN as therapy for Crohn's

? benefit in selected failing patients
No clear advantage unless
short bowel syndrome
severe peri-operative malnutrition
Like Veterans’ study
Non-exclusive/supplementary feeds

Some supportive evidence
Hull, Japan and paediatrics
Possibly simply from improved nutrition
Immune modulating feeds

Healthy scepticism
No unequivocal data
Even for glutamine
remission 44.4% vs 55.5% in controls
Conclusions 1

Probable that Western diet has contributed to increased incidence of Crohn’s
Specific dietary elements yet to be identified
Lower intakes of fruit & vegetables and increased dietary sugar consistently found
Conclusions 2

Malnutrition is common
Should always be sought and treated
Defined nutrition almost certainly effective in Crohn's (mechanisms unclear)
In most cases polymeric regimens may be used
Nutriceuticals and IVN not normally indicated
ESPN Congress on
Clinical Nutrition & Metabolism

LEIPZIG, GERMANY
31 August - 3 September 2013

www.espen.org