Specific nutritional care in children

The role of food in children with functional gastrointestinal disorders

M. Benninga (NL)
The role of food in children with functional gastrointestinal disorders

Marc Benninga
Emma Children’s Hospital / AMC, Amsterdam
In compliance with COI policy, ESPEN requires the following disclosures to the session audience:

<table>
<thead>
<tr>
<th>Disclosure Type</th>
<th>Details</th>
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<tr>
<td>Shareholder</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Grant / Research Support</td>
<td>No relevant conflicts of interest to declare</td>
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<tr>
<td>Consultant</td>
<td>Danone, Novalac, FrieslandCampina, Sensus</td>
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<tr>
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<td>Paid Instructor</td>
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<tr>
<td>Speaker bureau</td>
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<tr>
<td>Other</td>
<td>No relevant conflicts of interest to declare</td>
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</table>
Content of the presentation

• Functional GI-Disorders
• Facts
• Fairytales
The more common and the less threatening a disorder, the more likely it provokes unsubstantiated beliefs, which often relate to items of daily life such as food, physical activity and mood. The beliefs may be firmly fixed and can be almost completely resistant to scientific rebuttal........

Functional Disorders: infants and toddlers

G1. Infant Regurgitation
G2. Infant rumination syndrome
G3. Cyclic vomiting syndrome

G4. Infant colic

G5. Functional diarrhea
G6. Infant dyschezia
G7. Functional constipation

Duration of crying

Brazelton TB. Pediatrics, 1962

Barr RG. Dev Med Child Neurol 1990
Infant colic

For Clinical purposes must include all of the following:

1. An infant who is less than 5 months of age:
2. *Recurrent* prolonged periods of infant irritability, fussing, or crying *reported by parents* that occur without obvious cause and cannot be prevented or resolved by *caregivers*
3. No evidence of infant failure to thrive, fever or ill health
Infant colic

- Major medical and public health issue: common, distressing, costly and significant long-term consequences
- Affecting up to 20% of infants < 3 months
- Detrimental to maternal mental health and family QoL
- The most common proximal risk factor for child abuse
- Infants whose crying persists beyond age 3 months are more likely to have later mental health problems including anxiety, aggression and hyperactivity, sleep disorders, migraine, and allergy

Sung V, et al. JAMA Pediatr 2013
Organic Reasons for Excessive Crying in Infants*

**Central nervous System**
- Congenital abnormalities (Chiari type I)
- Migraine
- Subdural Hematoma

**Infections**
- Meningitis
- Otitis media
- UTI
- UTI

**Gastrointestinal**
- Constipation
- Intolerance to milk protein
- GERD
- Lactose Intolerance
- Rectal Fissures

**Trauma**
- Abuse
- Corneal Abrasion
- Foreign body in eye
- Fractures
- Vascular tourniquet

*Occur in < 5%!!!

Flora and infant Colic

Children with colic may have abnormal stool flora
Impact external factors on intestinal microbiota of infant

Intrauterine contamination

- Translocation from the mother's intestinal microbiota
  - Bifidobacterium, Lactobacillus, Enterococcus

Delivery mode

Cesarean section
- Staphylococcus
- Corynebacterium
- Propionibacterium

Vaginal
- Lactobacillus
- Prevotella
- Sneathia

Familial environment
- Clostridium

Prenatal ➔ Birth ➔ First weeks ➔ First months ➔ Adult-like microbiota

Type of feeding

- Breastfeeding
  - Bifidobacterium

- Formula feeding
  - Enterobacteriaceae

Treatments

- Probiotics-Prebiotics
  - Bifidobacterium
  - Lactobacillus

- Antibiotics
  - Reduction of microbial diversity

Colicky infants compared with control infants

- Slower colonization
- Lower diversity and stability
- ↑ Proteobacteria including species producing gas and inflammation
- ↓ Butyrate-producing species
- ↓ Lactobacilli & Bifidobacteria including species with anti-inflammatory effects

Responders

(50% reduction in crying time from baseline)

These studies suggest the benefit of supplementation with L reuteri in infantile colic

Treating infant colic with the probiotic Lactobacillus reuteri: DBPCRT

- Design: Double blind, placebo controlled randomised trial.
- Setting: Community based sample (primary and secondary level care centres) in Melbourne, Australia.
- Participants: 167 breastfed infants or formula fed infants aged < 3 months meeting Wessel’s criteria for crying or fussing.
  - 85 were randomised to receive probiotic and 82 to receive placebo.
- Interventions Oral daily *L reuteri* (1×10^8 colony forming units) versus placebo for one month.

Daily duration of cry or fuss over study period and at 6 month follow-up

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Age</th>
<th>Intervention</th>
<th>Results</th>
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<tbody>
<tr>
<td>Jackobson</td>
<td>22</td>
<td></td>
<td></td>
<td>whey hydrolysate</td>
<td>Significant decrease in colic</td>
</tr>
<tr>
<td>Savino</td>
<td>214</td>
<td></td>
<td>2 weeks to 3 months</td>
<td>whey hydrolysate for 2 weeks</td>
<td>Not controlled. Decreased colic in 79%</td>
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<tr>
<td>Forsyth</td>
<td>17</td>
<td>17 Cows milk</td>
<td>&lt;8 weeks</td>
<td>Hypo-allergenic formula</td>
<td>Significant improvement</td>
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<tr>
<td>Lucassen</td>
<td>23</td>
<td>20 Cows milk</td>
<td>2 weeks–3 months</td>
<td>whey hydrolysate Vs standard cows milk formula</td>
<td>Significant improvement. 63 less minutes of crying/d</td>
</tr>
<tr>
<td>Savino</td>
<td>96 whey hydrolysate with prebiotics</td>
<td>103 Cows milk + simethicone</td>
<td>2 weeks – 3 months</td>
<td>whey hydrolysate with prebiotics vs cows milk + simethicone</td>
<td>Significant improvement On days 7 and 14; p&lt;.05</td>
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</table>
Studies in which hypo-allergenic formulas have been used have shown them to be effective in the treatment of colic. **Consensus:** Protein milk allergy plays a role in some patients with colic. They may have more allergies. There is an association, but the extent of the association has not been well established.
Functional abdominal pain in children
**Functional Disorders: children and adolescents**

**H1. Functional nausea and vomiting disorders**
- **H1a. Cyclic vomiting syndrome**
- **H1b. Functional nausea and functional vomiting**
- **H1c. Rumination syndrome**
- **H1d. Aerofagia**

**H2. Functional abdominal pain disorders**
- **H2a. Functional dyspepsia**
- **H2b. Irritable bowel syndrome**
- **H2c. Abdominal migraine**
- **H2d. Functional abdominal pain, not otherwise specified**

**H3. Functional defecation disorders**
- **H3.1 Functional constipation**
- **H3.2 Nonretentive fecal incontinence**

Geographic distribution of functional abdominal pain

Abdominal pain

~ 20%

Organic

~ 80%

Functional

Functional dyspepsia
Irritable bowel syndrome
Abdominal migraine
Functional abdominal pain

Blood
Urine
Feces
Radiology

Treatment
Mechanisms Underlying the Irritable Bowel Syndrome (IBS)

Likely mechanism of action of fiber on intestinal transit and hypersensitivity

Eswaran S, Chey WD. Am J Gastroenterol 2013
### Systematic Review of RCTs: Fiber Supplements for Abdominal Pain-Related FGIDs in Childhood

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Favor experimental</th>
<th>Control</th>
<th>Weight %</th>
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<th>RR (M-H, random, 95% CI)</th>
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<td>events</td>
<td>total</td>
<td>events</td>
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<tr>
<td>2.2.1 Crushed crispbread with 66% fiber (ispaghula husk)</td>
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<tr>
<td>Christensen [16], 1982</td>
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<td>20</td>
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<td>16</td>
<td>15.0 (6.8–35.3)</td>
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<tr>
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<td>15.0 (6.8–35.3)</td>
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<td>Total events</td>
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<td>2.2.2 Fiber cookies (corn fiber)</td>
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<td>Feldman et al. [17], 1983</td>
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<td>1.86 (0.89–3.90)</td>
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<td>2.2.3 Glucomannan</td>
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<tr>
<td>Horvath et al. [25], 2011</td>
<td>41</td>
<td>51</td>
<td>20</td>
<td>23</td>
<td>1.21 (0.79–1.83)</td>
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<td>51</td>
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<td>1.21 (0.79–1.83)</td>
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Psyllium Fiber Reduces Abdominal Pain in 103 Children With IBS in a randomized, Double-Blind Trial

At end of study period, percentage of stools that were normal, breath hydrogen or methane production, intestinal permeability, and microbiome composition were similar between groups

20 billion microorganisms in one capsule?

NOT BAD

fb.com/optibacprobiotics
Altered microbiota in IBS

Permeability
Motility
Immune activity
Gut-brain-axis

Öhman L et al, Nat Rev Gastroenterol Hepatol 2015
Can we modulate the microbiome to change stool consistency?
IBS vs. healthy children

Saulnier DM, et al, Gastroenterology 2011
Effect of Lactobacillus GG on responder rates (defined as no pain or a decrease in pain intensity)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
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<td>Francavilla 2010</td>
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<td>Gawronska 2007</td>
<td>38</td>
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<td>Irritable bowel syndrome</td>
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<td>Bausserman 2005</td>
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<td>33</td>
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<td>82</td>
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<td>Test for overall effect: $Z = 3.56$ (P = 0.0004)</td>
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<td>Functional abdominal pain</td>
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<tr>
<td>Francavilla 2010</td>
<td>12</td>
<td>25</td>
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<td>Test for overall effect: $Z = 0.43$ (P = 0.67)</td>
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<tr>
<td>Test for overall effect: $Z = 0.45$ (P = 0.66)</td>
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</table>

Lactobacillus reuteri DSM 17938 for the Management of Functional Abdominal Pain: A RDBPCT

- L reuteri DSM 17938, stimulates gastrointestinal motility and reduction of pain perception
- 101 children, aged 6-15 years, Rome III criteria for FAP
- Randomly assigned to receive either L reuteri DSM 17938 or placebo (tablets) for 4 weeks, with further follow-up of additional 4 weeks

Lactobacillus reuteri DSM 17938 for the Management of Functional Abdominal Pain in Childhood: A RDBPCT

A Mixture of 3 Bifidobacteria in Children With IBS and FD

Giannetti E, et al. JPGN 2016
FODMAP

- **F**ermentable
- **O**ligosaccharides (fructans, (FOS and GOS))
- **D**isaccharides (lactose)
- **M**onosaccharides (fructose)
- **A**nd
- **P**olyols (sugar alcohols)
  - artificial sweeteners sorbitol, mannitol, maltitol
Low FODMAP diet for Irritable Bowel Syndrome

The research team at Monash University have developed a diet to control gastrointestinal symptoms associated with IBS/FODMAPs. The team has focused on a group of carbohydrates they have named FODMAPs (Fermentable Oligo-, Di-, Mono-saccharides and Polyols). FODMAPs can be poorly absorbed in the small intestine. Mal-absorbed carbohydrates are fermented by gut bacteria, resulting in symptoms. The Monash University Low FODMAP diet

The Monash University Low FODMAP diet app

The Monash University department of Gastroenterology/research team has created a smartphone application which provides accurate information about foods that trigger the symptoms to help users manage their symptoms. See More about the Low FODMAP App

http://www.med.monash.edu/cecs/gastro/fodmap/
Gastrointestinal symptoms during different diets

RCT: gut microbiome biomarkers are associated with clinical response to a low FODMAP diet in children with IBS

- Less abdominal pain occurred during the low FODMAP diet vs. TACD [1.1 episodes/day vs. 1.7  \( P < 0.05 \)]
- Compared to baseline (1.4 ± 0.2), children had fewer daily abdominal pain episodes during the low FODMAP diet (\( P < 0.01 \)) more episodes during the TACD (\( P < 0.01 \))
Systematic review: quality of trials on the symptomatic effects of the low FODMAP diet for IBS

- 9 RCTs, including 542 patients
- Intervention period 2ds-6wks, 1 trial included a 6-month FU
- Domains with a high risk of bias identified for all trials
- Only one trial double-blinded

Conclusions:
- RCTs on low FODMAP diet characterized by high risk of bias
- Diet not studied in a randomized, controlled setting for > 6wks
- Trials examining effect of important reintroduction period are lacking
- Risk that symptomatic effects reported in trials are driven primarily by placebo response

I think Donald Trump needs a laxative not only is he full of shit, he always looks like he is severally constipated.
Functional constipation

Must include one month of at least two of the following in infants up to 4 years of age:

1. Two or fewer defecations per week
2. History of excessive stool retention
3. History of painful or hard bowel movements
4. History of large diameter stools which may obstruct the toilet
5. Presence of a large fecal mass in the rectum

In toilet trained children the following additional criteria may be used:

6. At least 1 episode/week of incontinence after the acquisition of toileting skills
7. History of large diameter stools which may obstruct the toilet
Mechanisms of Constipation

Behavior

Abuse

Nerves, muscles, ICCs

Sensation

Stress

Food

Genetics

Microbiome
fabeltjes krant
BOR DE WOLF HEELHUIDS OP HET DROGE
Chocolate

• Roasted cacao beans, which contain about 50% cocoa butter

  - Cocoa contains a host of known chemicals, including caffeine, theobromine, serotonin and its precursor tryptophane, and phenylethylamine

• Concentration of the mentioned substances seems too low to exert neuropharmacological effects

Bananas

- Contain large amounts of serotonin
- No experimental data to suggest an effect of bananas on colonic function

RCT: plums (prunes) vs. psyllium for constipation

The laxative effects a combination:

• sorbitol (14.7g/100g)
• dietary fiber (6g/100g)
• polyphenols (184 mg/100g)
• exact mechanism has not been established

Effects of kivia powder in patients with constipation: a randomized, double-blind, placebo-controlled study

• Kivia powder containing Zyactinase™ is a freeze-dried powder from kiwifruit (Actinidia deliciosa var. Deliciosa) containing the enzyme actinidin, plant polyphenols, dietary fiber, carbohydrates, and oligosaccharides.
Comparison of Kivia powder and placebo in defecation characteristics

Udani JK, Bloom DW. Nutr J 2013
Increasing Oral Fluids in Chronic Constipation in Children

- 108 children with constipation
  - Control group
  - Increased water intake group (increase water intake by 50% on the basis of total measured oral liquid intake during the 1st week)
  - Increased hyperosmolar liquid group (supplemental liquid in the form of Kool-Aid, juice, soda pop, or other liquids known to contain more than 600 mOsm/L).
- The Stool Consistency Continuum
- Constipation Assessment Scale score of 8 or greater

## Results

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 2</th>
<th>Week 3</th>
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<tbody>
<tr>
<td><strong>Stool frequency</strong></td>
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<tr>
<td>Control</td>
<td>3.45</td>
<td>4.05</td>
<td>3.40</td>
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<tr>
<td>H₂O</td>
<td>3.52</td>
<td>3.57</td>
<td>3.70</td>
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<td>HiOsm</td>
<td>3.75</td>
<td>4.31</td>
<td>3.44</td>
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<td><strong>Stool Consistency</strong></td>
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<tr>
<td>Control</td>
<td>6.30</td>
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<td>6.30</td>
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<td>H₂O</td>
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<td>0.74</td>
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</table>

CONSTITIPATED?
Forget Laxatives.

Take FIBRECOL™
Effect of Glucomannan in the treatment of childhood constipation

- Baseline
- 4 weeks later

_**p = NS**_

Rate of success

Gluco Placebo

Success %

P=NS

56% 58%

95% CI 38%-72%
95% CI 41%-74%

Effectiveness of using a behavioral intervention to improve dietary fiber intake in 43 children with constipation

Effectiveness of using a behavioral intervention to improve dietary fiber intake in 43 children with constipation

Effectiveness of using a behavioral intervention to improve dietary fiber intake in 43 children with constipation
No significant benefit was demonstrated in terms of a reduction in laxative use or increased stool frequency associated with additional fiber intake!!!!!
Constipation
Rationale for the use of probiotics

• Differences in the intestinal microbiota in healthy and constipated subjects
  • ↓ bifidobacteria
  • ↑ non-pathogenic *E coli*, bacteroides
  • ↑ total number of microorganisms
• Improved transit time
  • Several studies involving *B. animalis* DN 173 010

### Probiotics for functional constipation
**RCTs in children - summary**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Probiotic</th>
<th>Constipation</th>
<th>N</th>
<th>Effect</th>
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<tbody>
<tr>
<td>Banaszkiewicz &amp; Szajewska 2005</td>
<td>LGG</td>
<td>&lt;3 BM per wk for at least 12 wk</td>
<td>60</td>
<td>NS</td>
</tr>
<tr>
<td>Bu et al. 2007</td>
<td>L casei rhamnosus Lcr35</td>
<td>&lt;3 BM per wk for &gt;2 mo</td>
<td>27</td>
<td>√ (?)</td>
</tr>
<tr>
<td>Coccorullo et al. 2010</td>
<td>L reuteri DSM 17938</td>
<td>Rome III criteria</td>
<td>44</td>
<td>√</td>
</tr>
<tr>
<td>Tabbers et al. 2011</td>
<td>B lactis DN 173010</td>
<td>Rome III criteria</td>
<td>160</td>
<td>NS</td>
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<tr>
<td>Guerra et al. 2011</td>
<td>B longum</td>
<td>Rome III criteria</td>
<td>59</td>
<td>√</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>350</td>
<td></td>
</tr>
</tbody>
</table>
Summary and conclusions

• Don’t believe in fairytales

• FGIDs in infants and children are common

• Role of fibers, pre- and probiotics have to be established in FGIDs

• Role of low FODMAP diet is promising