Probiotics and health – summing up the evidence with a focus on inflammatory bowel disease

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British Nutrition Foundation

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Probiotics in the headlines

BBC NEWS

Probiotics may ease gut disorders

Mail Online

Why up to half of all probiotics 'don't work'

Mail Online

Miracle bugs: Fancy 'probiotic' yoghurt drinks really ARE good for you, scientists say

TIMES ONLINE

Probiotics, not so friendly after all?

A probiotic drink a day helps women lose weight after giving birth

A probiotic drink or yoghurt a day can help women lose a significant amount of weight after giving birth.
Probiotics Review
AIM:

To review the current evidence on the effect of probiotics on health, focusing on gut related health issues and immune system.
Probiotics Review

• Literature search: 448 original studies and 30 meta-analyses and systematic reviews (only human studies)

• After detailed screening and reviewing, 86 original studies and 15 meta-analyses and systematic reviews included in review

• Review will be published in the December 2009 issue of the *Nutrition Bulletin*
Probiotics Review

TOPICS COVERED

• Inflammatory bowel disease
• Irritable bowel syndrome
• Antibiotic-associated diarrhoea, including *C. difficile*
• Acute diarrhoea
• Constipation
• Immune system (common colds, flu)
• Allergies
• Eczema
Inflammatory bowel disease (IBD)

IBD

Crohn‘s disease (CD)  Ulcerative colitis (UC)
Ulcerative Colitis

- Ulceration and inflammation of inner lining of rectum and colon
- Limited to colon
  - Rectum
  - Rectum and sigmoid colon
  - Up to splenic flexure
  - Up to hepatic flexure
  - Whole colon
- Main symptom: bloody diarrhoea
- Colicky abdominal pain, urgency, tenesmus
Crohn’s disease

- Inflammation that extends to deeper layers of the intestinal wall
- May affect any part of GI-tract
  - Small intestines (ileum)
  - Colon
  - Ileum and colon
  - Upper gastrointestinal

- Symptoms more heterogeneous
- Typically include abdominal pain, diarrhoea, weight loss
- CD may cause different forms of obstruction
Impact of IBD

- Patients find symptoms embarassing and humiliating
- Loss of education, difficulty in gaining employment
- Psychological problems
- Growth failure or retarded sexual development
- Medical treatments can cause secondary health problems
Impact of IBD

- IBD often occurs at young age
- Peak incidence between 10 and 40 years of age
- Potential to cause lifelong illness
- 100-200 per 100,000 suffering from UC
- 50-100 per 100,000 suffering from CD
- Up to 240,000 affected by IBD in the UK
What causes IBD?

- Not fully understood yet – theories very complex
- Genetic predisposition
- Environmental factors (e.g. infection, drugs)
- Emerging evidence of role of gut bacteria in IBD
Evidence

Crohn’s disease
Crohn’s disease

- Double-blind, randomised controlled trial
- *Lactobacillus johnsonii*, LA1 ($10^{10}$ colony-forming units/day)
- Patients with CD scheduled for curative surgery (n=70)
- Primary outcome: endoscopic recurrence at 12 weeks after surgery

Van Gossum et al. 2007, *Inflamm Bowel Dis*
Crohn’s disease

Overall P=0.33

Van Gossum et al. 2007, Inflamm Bowel Dis
Crohn’s disease

- Double-blind, randomised controlled trial
- *Lactobacillus johnsonii*, LA1 (4x10⁹ CFU/day)
- Patients with CD undergone curative surgery (n=90)
- Primary outcome: endoscopic recurrence at 6 months

Marteau et al. 2006, *Gut*
Crohn’s disease

Marteau et al. 2006, Gut

Recurrence: 49 LA1, 64 Placebo, P=0.15
Severe recurrence: 21 LA1, 26 Placebo, P=0.61

n=90
Crohn’s disease

- Double-blind, randomised controlled trial
- *Lactobacillus rhamnosus* GG (LGG, 12x10⁹ CFU/day)
- Patients with CD undergone curative surgery (n=45)
- Primary outcome: endoscopic recurrence at 12 months

Prantera *et al.* 2002, *Gut*
Crohn’s disease

*of those still in clinical remission

Prantera et al. 2002, Gut
Crohn’s disease

- RCT (n=32): *Saccharomyces boulardii* in addition to standard treatment (mesalizine) significantly reduced relapse rate in CD patients compared to standard treatment only (p=0.04) (Guslandi et al. 2000)
Crohn’s disease

SUMMARY

- The studied strains (*L. johnsonii* LA1 and LGG) were not able to reduce recurrence in patients with CD after surgery
- *S. boulardii* in addition to standard treatment may be effective
- More studies are needed to see whether other strains could be effective
Evidence

Ulcerative colitis
Ulcerative colitis

- Double-blind, randomised controlled trial
- *E. coli* Nissle (EcN, 2.5-25x10⁹ viable bacteria/day), vs. mesalazine (gold standard treatment for UC)
- Patients with UC in remission (n=327)
- Primary outcome: patients experiencing relapse during 12 months study period

Kruis et al. 2004, Gut
Ulcerative colitis

Kruis et al. 2004, Gut
Ulcerative colitis

- Double-blind, randomised controlled trial
- *E. coli* Nissle (5x10^{10} viable bacteria/day), vs. mesalazine (gold standard treatment for UC)
- Patients with UC in remission (n=116)
- Primary outcome: patients experiencing relapse during 12 months study period

Rembacken *et al.* 1999, *The Lancet*
Ulcerative colitis

Significant equivalence
P=0.006

Rembacken et al. 1999, *The Lancet*
Ulcerative colitis

- Single-blind, randomised controlled trial
- *B. breve* Yakult, *B. bifidum* Yakult, *L. acidophilus* (10^{10} bacteria/day), or placebo, in addition to standard treatment
- Patients with active UC (n=20)
- Primary outcome: patients with clinical improvement at 12 weeks

Ulcerative colitis


Not sign.
Ulcerative colitis

- Unblinded study: EcN as effective as mesalazine in maintaining remission in children and adolescents (11-18 years) suffering from UC (Henker et al. 2008)

- Unblinded study: no significant difference in relapse rate after 12 months with *L. rhamnosus* GG, mesalazine or mesalazine+*L. rhamnosus* GG (Zocco et al. 2006)

- Venturi *et al.* (1999) studied efficacy of VSL#3 on maintaining remission in UC patients allergic to mesalazine; after 12 months, 15 of 20 patients (75%) were still in remission
Ulcerative colitis

SUMMARY

- Good evidence that *E. coli* Nissle as effective as standard treatment to maintain remission
- Also other strains seem to be effective in patients with UC
- More studies are needed to confirm those findings
Pouchitis
Pouchitis

- ~25-30% of patients with UC require surgery
- Colon removed & replaced by an artificial pouch
- Pouchitis is inflammation of the ileal pouch and most common long-term complication in patients undergoing surgery for UC
- Up to 40-60% suffer from pouchitis after surgery
- Causes not fully understood
- It is assumed that the microflora in the pouch plays a role in the abnormal mucosal immune response
Surgery for UC
Pouchitis

- Double-blind, randomised controlled trial
- VSL#3 ($1.8 \times 10^{12}$ viable bacteria/day), vs. placebo
- Patients with chronic relapsing pouchitis in remission (n=40)
- Primary outcome: patients relapsing within 9 months study period

Gionchetti et al. 2000, Gastroenterology
Pouchitis

**VSL#3**: 1 within 2 months, 1 within 5 months, 1 within 8 months

**Placebo**: 8 within 2 months, 7 within 3 months, 5 within 4 months

Gionchetti *et al*. 2000, *Gastroenterology*
Pouchitis

- Double-blind, randomised controlled trial
- VSL#3 (3.6x10^{12} viable bacteria/day), vs. placebo
- Patients with pouchitis in remission (n=36)
- Primary outcome: patients still in remission after 12 months study period

Mimura et al. 2004, Gut
Pouchitis

Mimura et al. 2004, Gut
Pouchitis

- Double-blind, randomised controlled trial
- VSL#3 \(1.8 \times 10^{12}\) viable bacteria/day, vs. placebo
- Patients having closure of side passage after surgery for UC (n=40)
- Primary outcome: patients with pouchitis during 12 months after restoration of fecal stream

Gionchetti et al. 2003, Gastroenterology
Pouchitis

**VSL#3**: 1 after 9 and 1 after 11 months

**Placebo**: 3 within 3 months, 4 within 6 months, 1 within 9 months

Gionchetti *et al.* 2003, *Gastroenterology*
Pouchitis

- Double-blind, randomised controlled trial
- LGG (2-4x10^{10} CFU/day), or placebo
- Patients having surgery for UC (n=20)
- Primary outcome: comparison of Pouchitis Disease Activity Index (PDAI); improvement: reduction of PDAI ≥3 points

Kuisma et al. 2003, Aliment Pharmacol Ther
# Ulcerative colitis

Kuisma et al. 2003, *Aliment Pharmacol Ther*

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<th>LGG</th>
<th>Placebo</th>
<th>P-value</th>
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<tr>
<td>Pre-treatment</td>
<td>8.0±0.8</td>
<td>8.4±0.7</td>
<td>P = 0.44</td>
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<td>PDAI</td>
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<tr>
<td>Post-treatment</td>
<td>8.0±1.1</td>
<td>8.0±0.7</td>
<td>P = 0.97</td>
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<td>PDAI</td>
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$n=20$
Pouchitis

- Uncontrolled study by Gionchetti et al. (2007): high doses of VSL#3 (36x10^{11} bacteria/day)
- Successful in treating mild active pouchitis after 4 wks of treatment
- Complete remission: ~70%; significantly improved PDAI after 4 wks and 6 mths compared to baseline (p<0.001)

Gionchetti et al. (2007)
Ulcerative colitis

SUMMARY

- Good evidence that VSL#3 is effective in maintaining remission in pouchitis patients and in delaying onset of pouchitis after surgery for UC
- High doses of VSL#3 may be effective in treating pouchitis (more evidence needed)
- More studies required to determine if other strains effective
Summary IBD

- Evidence so far does not suggest that probiotics are effective in patients with CD
- The use of certain probiotic strains decreased relapse rate in patients with UC
- The use of VSL#3 is effective in maintaining remission in pouchitis patients and delaying onset of pouchitis after surgery
Probiotics Review

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• Visit www.wiley.com