PROBIOTICS FOR TREATMENT OF CHRONIC CONSTIPATION IN CHILDREN: A COCHRANE SYSTEMATIC REVIEW

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Abstract

**TITLE:** Probiotics for the management of functional abdominal pain in children: A Cochrane systematic review

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**ABSTRACT BODY:**

Abstract Body: Background

Functional abdominal pain is pain located in the abdomen that cannot be explained by visible or detectable abnormalities. It is hypothesised that the use of probiotics might alter the growth of bacteria in the bowel, promote normal gut physiology and reduce functional symptoms. Given the recent growth in published studies in this area it is necessary to produce a new and focussed synthesis of this evidence by deploying a robust methodology to ensure that there can be a contemporaneous impact on clinical practice.

Methods

The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL and Cochrane Inflammatory Bowel Disease & Functional Bowel Disorders Group Specialised Trial Register were searched (Inception – July 2015). Manufacturers of probiotics were contacted to identify unpublished trials. References of trials were also searched. Abstracts were considered for inclusion if full details to judge inclusion were offered or available from the authors. Randomised controlled trials (RCTs) that compared probiotics against placebo or any other intervention were eligible for inclusion. Data extraction and assessment of methodological quality of included studies were independently performed by two authors. Analysis was completed in accordance with the intention to treat approach.

Results

The search yielded 1672 results and nine placebo controlled studies (n = 701) met the inclusion criteria, two as abstracts and seven as published studies. Three studied Lactobacillus GG, three lactobacillus reuteri, one VSL\#3, one bacillus coagulans and one bifidobacteria. The studies ranged in length from 4 to 16 weeks. The risk of bias was low for randomisation for seven trials and moderate for two trials. Allocation concealment was low in two studies and unclear in the others. All studies were double blinded, but only four gave details of how this was achieved. The risk of bias was low or unclear in all studies for incomplete outcome data and selective reporting. Meta-analysis of seven studies (n=541) found a statistical significant reduction in the severity of pain using probiotics compared to placebo (MD -0.32; 95% CI -0.38 to -0.25). Meta-analysis of four studies (n=440) found a statistical significant difference in patients reaching treatment success favouring probiotics compared to placebo (OR 1.80; 95% CI 1.20 to 2.69). Meta-analysis of five studies (n=385) found no statistical significant difference in adverse events between probiotics and placebo (OR 0.00; 95% CI -0.07 to 0.06).

Conclusions

The evidence from the published suggests superior efficacy of probiotics for functional abdominal pain in children when compared with placebo. There is no difference in adverse events, suggesting safety. The evidence base is of moderate quality and relatively small. Further research to investigate the long term impact of probiotic therapy is suggested.
(no table selected)
Figure 1: Forest plot of severity of pain, Probiotics vs Placebo

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Probiotics Mean</th>
<th>SD</th>
<th>Total</th>
<th>Placebo Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
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</thead>
<tbody>
<tr>
<td>BAUSEMEYER 2005</td>
<td>1.5</td>
<td>0.5</td>
<td>26</td>
<td>1.8</td>
<td>0.7</td>
<td>25</td>
<td>-0.30 [-1.64, 0.94]</td>
<td></td>
<td>-0.30 [-1.64, 0.94]</td>
<td></td>
</tr>
<tr>
<td>Francavilla 2010 1</td>
<td>1.9</td>
<td>0.3</td>
<td>42</td>
<td>3.3</td>
<td>1.5</td>
<td>38</td>
<td>-1.59 [-1.98, -1.19]</td>
<td></td>
<td>-1.59 [-1.98, -1.19]</td>
<td></td>
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<tr>
<td>Francavilla 2010 2</td>
<td>2.2</td>
<td>1.2</td>
<td>25</td>
<td>3.3</td>
<td>1.7</td>
<td>31</td>
<td>-1.12 [-1.56, -0.68]</td>
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<td>-1.12 [-1.56, -0.68]</td>
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<tr>
<td>GAYA 2006</td>
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<td>1.8</td>
<td>42</td>
<td>2.9</td>
<td>1.5</td>
<td>42</td>
<td>-0.64 [0.13, 0.33]</td>
<td></td>
<td>-0.64 [0.13, 0.33]</td>
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<tr>
<td>Jansske 2015</td>
<td>0.38</td>
<td>0.11</td>
<td>26</td>
<td>0.65</td>
<td>0.14</td>
<td>29</td>
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<td></td>
<td>-0.29 [0.38, -0.22]</td>
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<tr>
<td>Kanaar 2015</td>
<td>2.1</td>
<td>1.4</td>
<td>59</td>
<td>1.8</td>
<td>1.4</td>
<td>56</td>
<td>0.30 [0.21, 0.41]</td>
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<td>0.30 [0.21, 0.41]</td>
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<tr>
<td>YEGAN 2014</td>
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<td>2.1</td>
<td>58</td>
<td>5.2</td>
<td>2.1</td>
<td>51</td>
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<td>-2.09 [3.03, -1.15]</td>
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<tr>
<td>Total (95% CI)</td>
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<td>0.7</td>
<td>209</td>
<td>2.72</td>
<td>0.00</td>
<td>272</td>
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<td>-0.72 [-1.19, -0.25]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: T² = 5.11; CH² = 14.75; df = 6 (P = 0.0061); I² = 65%
Forest plot of Adverse events, Probiotics vs Placebo
Disclosure Status

The following authors have completed their 2016 DDW disclosure:: Morris Gordon: Disclosure completed | Joe Stone: No Answer. | Adrian Thomas: No Answer. | Anthony Akobeng: No Answer.