In infants with ‘colic’/persistent crying, administration of daily *Lactobacillus reuteri* DSM 17938 was associated with reduced crying time at 1, 2 and 3 weeks

**Design:** Single centre randomised controlled trial. **Allocation:** Computer generated random-digit randomisation. **Blinding:** Participants, physicians and statisticians. **Setting:** Tertiary hospital paediatric outpatient department, Turin, Italy, March 2008 to August 2009. **Patients:** Breast-fed infants (n=46) aged 2–16 weeks with persistent crying fulfilling Wessel’s criteria for colic: crying for more than 3 h/day for more than 3 days/week for more than 3 weeks. **Intervention:** A 5 ml oil suspension of *Lactobacillus reuteri* or an identically appearing and tasting placebo oil. **Outcomes:** **Primary:** Reduction in mean daily crying time at day 21 of treatment to less than 3 h/day. **Secondary:** Reduction in daily mean crying time to less than 50% of baseline at 7, 14 and 21 days. **Follow-up period:** 21 days.

**MAIN RESULTS**

By day 21 median crying times were significantly lower in the intervention than in the control group and were 35 (IQR 85) min/day and 90 (IQR 148) min/day, respectively (see table 1). Additionally, by day 21, a significantly greater proportion of infants in the intervention group were responders (50% reduction in crying time since the start; see table 2).

**ABSTRACTED FROM**


**Sources of funding** BioGaia AB Stockholm, Sweden

**Table 1** Continuous outcome measures

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Intervention, median (IQR)</th>
<th>Control, median (IQR)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crying time/day (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 7</td>
<td>95 (85)</td>
<td>185 (149)</td>
<td>0.082</td>
</tr>
<tr>
<td>Day 21</td>
<td>35 (85)</td>
<td>90 (148)</td>
<td>0.022</td>
</tr>
<tr>
<td>Change in faecal <em>Escherichia coli</em> colonizing forming unit counts (days 0 to 21)</td>
<td>-$6.55 \times 10^7$</td>
<td>$+4.3 \times 10^3$</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Table 2** Dichotomous outcome measures

<table>
<thead>
<tr>
<th>Treatment failure</th>
<th><em>Lactobacillus reuteri</em></th>
<th>Placebo</th>
<th>RR (95% CI)</th>
<th>Adjusted RR (95% CI)</th>
<th>Number needed to treat (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to achieve 50% crying time reduction (day 7)</td>
<td>5/25</td>
<td>13/21</td>
<td>0.32 (0.14 to 0.76)</td>
<td>0.41 (0.14 to 0.62)</td>
<td>2 (2 to 7)</td>
</tr>
<tr>
<td>Failure to achieve 50% crying time reduction (day 21)</td>
<td>1/25</td>
<td>6/21</td>
<td>0.14 (0.02 to 1.0)</td>
<td>0.24 (0.03 to 0.46)</td>
<td>4 (2 to 32)</td>
</tr>
</tbody>
</table>

One of paediatrics’ newest agents, ‘colic’ was destined to meet the new universal panacea on the block at some point; probiotics now have several Cochrane paediatric reviews to their name. These include, among others, reports of their purported benefits in infective diarrhoea (insufficient evidence), eczema (no benefit) and preventing preterm labour (insufficient evidence).

This study appears robust and to have been conducted along standard randomised controlled trial lines. On face value, it worked well, with crying times in the intervention group being one half of those in the controls by 1 week of supplementation and one third by 3 weeks. In terms of mechanistic explanation, the accompanying ‘faecology’ underpinned a number of hypothetical microbiological and immunological mechanisms but the study was insufficiently powered to test the association between coliform load and symptom severity.

If you sense my reserve, let me explain. First, the infants ranged in age from 2 weeks to 4 months. This heterogeneity raises the possibility of a variety of causes for their crying. Unfortunately, the sample size is insufficient to allow a subanalysis by age strata. Second, all the babies were breast fed and as the microflora of formula fed infants is inherently different, the generalisability of the intervention comes into question.

Third, the follow-up stopped at 3 weeks when the intervention period ended. We have no idea whether the purported benefits lasted beyond this time.

Fourth, I wonder about the pragmatics of management. Many such babies in the UK, for better or worse, are ‘labelled’ as having gastro-oesophageal reflux (GOR) or milk protein intolerance and treatment is started, often empirically. In this study, only one of 50 babies was excluded for GOR, suggesting that it is considered less readily in Italy than in the UK.

What then are the implications for practice? Perhaps a week’s trial of probiotics in a screaming baby whose parents report neither vomiting nor colitis or eczema is reasonable before venturing down the usual avenues? I don’t pretend to know the answer. The only definite is that all babies slowly get better from ‘whatever-it-is’ that makes them cry (daily crying time halved in the control group over 3 weeks), so parents can be confidently reassured that there is an end in sight.

I’m prepared to believe that a proportion will become ‘happier’ faster with probiotics, although this study doesn’t tell me which ones.

**Dr Nick Brown**

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**REFERENCES**


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