Meta-analysis of clinical trials of probiotics for prevention and treatment of pediatric atopic dermatitis

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CRD summary
This review, which investigated the effectiveness of probiotics for paediatric atopic dermatitis, concluded that current evidence is more convincing for prevention rather than treatment. The review had key methodological flaws and the authors' conclusions should be interpreted with caution.

Authors' objectives
To summarize and interpret clinical trial findings on the efficacy of probiotics for paediatric atopic dermatitis (PAD) and to define key trial features correlating with high methodologic quality. This abstract will focus mainly on the study of efficacy.

Searching
The PubMed and Cochrane Library databases were searched to July 2007. Search terms were reported. Reference lists of reviews and relevant publications were also checked. Unpublished trials and abstracts were excluded.

Study selection
It appeared that clinical studies of probiotics for PAD were eligible for inclusion in the review. Around two-thirds of the studies evaluated probiotics as a treatment with the rest looking at prevention. The majority of trials used Lactobacillus rhamnosus as probiotic. Probiotics were administered prenatally and/or postnatally. The ages of included participants ranged from newborn to 13 years. Comparator groups received identical placebo pills or powders. PAD severity was commonly assessed using the Scoring Atopic Dermatitis (SCORAD) system.

The authors did not state how the studies were selected for the review or how many reviewers performed the selection.

Assessment of study quality
Studies were evaluated using the Cho & Bero Methodological Quality (MQ) and Clinical Relevance (CR) scales, which assess criteria such as randomisation, blinding, representativeness, and statistical analyses. Studies were also evaluated using Jadad and Delphi scales.

Two reviewers assessed study quality with disagreements resolved by a third reviewer.

Data extraction
Outcome data were extracted and relative risk ratios (RRs) or weighted mean differences (WMDs) with 95% confidence intervals (CIs) were calculated. Trial investigators were contacted and additional information obtained when necessary.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
Double-blind randomised controlled trials (RCTs) which reported SCORAD as means were eligible for the meta-analysis, which pooled RRs or WMDs using both a fixed-effect and a random-effects model. The studies were weighted but the method of weighting was not stated. Heterogeneity was assessed using the $\chi^2$ and $I^2$ statistics.

Results of the review
Twenty-one studies were included in the review (n=2,134). There were 19 randomized controlled trials (RCTs)
(n=1,898), one observational study (n=9) and one questionnaire-based retrospective study (n=227). The mean raw MQ score was 0.91 for the primary prevention studies and 0.81 for the secondary studies. It was reported that the prevention studies were of the highest quality.

Prevention trials (six trials): Probiotics significantly reduced the incidence of PAD two years after intervention, when compared to placebo, RR 0.66 (95% CI: 0.49, 0.89). Details of heterogeneity were not provided for this random-effects analysis, but the $I^2$ value was 55% for the fixed-effect analysis. Exclusion of the one prevention trial which administered probiotics only postnataally resulted in a fixed effect $I^2$ of 0%.

Treatment trials (four trials): There were no statistically significant changes in either intra- or inter-group SCORAD scores. In trial subgroup analyses, four trials detected significant therapeutic effect in sensitised (immunoglobulin E status) patients.

**Authors' conclusions**

Current evidence is more convincing for probiotics' efficacy in prevention than treatment of PAD.

**CRD commentary**

The review question and inclusion criteria were not explicit, since studies other than trials appeared to be eligible. More detail was provided on eligibility for meta-analysis than for eligibility for inclusion in the review. Attempts to identify relevant studies were undertaken by searching electronic databases and checking references, although the authors may have missed relevant trials by restricting the review to only published trials. It was unclear whether studies not published in English were eligible. Suitable methods were used to minimise the risks of reviewer error and bias for the process of assessing study quality but the authors did not report on the methods used to select studies for inclusion or extract the data. Although a detailed analysis was conducted on the relative merits of the various quality assessment scales, the absolute individual trial scores were not presented, making interpretation of the results of the review more difficult. Appropriate methods were used to pool results. Although heterogeneity was assessed, the possible causes were not adequately investigated for the treatment studies. Only a brief narrative synthesis was conducted for the 11 studies not eligible for meta-analysis. This review had key methodological flaws, therefore the authors' conclusions should be interpreted with caution.

**Implications of the review for practice and research**

**Practice:** The authors stated that a prenatal and postnatal regimen of probiotics is an effective option for pregnant women with risk factors for atopic disease to help prevent persistent PAD in their children.

**Research:** The authors stated that further studies of probiotics for PAD treatment were needed, and that clinical trials should verify the quality of the probiotics used and explicitly state that the products fulfill criteria set by European Union-funded research groups.

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