Efficacy of probiotics in the treatment of pediatric atopic dermatitis: a meta-analysis of randomized controlled trials

Michail S K, Stolfi A, Johnson T, Onady G M

CRD summary
This review investigated the efficacy of probiotics in the treatment of paediatric atopic dermatitis. The authors concluded that there may be a modest role for probiotics in paediatric atopic dermatitis. This effect was seen in moderately severe rather than mild disease. The authors’ conclusions reflect the results presented and are likely to be reliable.

Authors’ objectives
To investigate the efficacy of probiotics in the treatment of paediatric atopic dermatitis.

Searching
MEDLINE, EMBASE, CINHAHL and The Cochrane Library were searched from inception to January 2008 (no search terms reported). Abstracts presented at major gastrointestinal and allergy meetings were searched.

Study selection
Randomised controlled trials (RCTs) of participants with atopic dermatitis in which a probiotic micro-organism had been consumed and the outcome measure was a Scoring of Atopic Dermatitis Severity Index (SCORAD) score were eligible for inclusion. Studies of the prevention of atopic dermatitis were excluded. The ages of participants in the included studies ranged from one month to 13 years old. Probiotics used varied; the most commonly used was Lactobacillus GG (LGG), alone or in combination. Doses used also varied.

Two reviewers independently selected studies.

Assessment of study quality
Three independent reviewers assessed methodological quality using the Consolidated Standards of Reporting Trials (CONSORT) criteria, which provides a quality score out of 25. Studies that scored 10.5 or less were considered low quality, 11.5 to 16.0 intermediate quality and 16.5 or more high quality. Disagreements were resolved by discussion.

Data extraction
Means and standard deviations of SCORAD scores before and after treatment were obtained from the authors. Three studies compared two different probiotic groups with a control group; for two of these studies the probiotic groups were combined using weighted means. Subsequently, the different probiotic groups were analysed separately in the subgroup analyses of type of probiotic. One crossover trial reported similar results for the first and second intervention period and only data from the first intervention period were reported in the meta-analysis. The number of reviewers who extracted data was not reported.

Methods of synthesis
Means and standard deviations were pooled using fixed-effect and random-effects meta-analyses to produce weighted mean differences (WMD) and 95% confidence intervals (CIs). The random-effects model results were presented as both models produced similar results. Statistical heterogeneity was assessed using the $I^2$ statistic and sensitivity analyses were used to determine the effect of removal of specific studies. Publication bias was examined using a funnel plot and Egger's test. A priori subgroup analyses were performed for: therapy duration of four to six weeks versus eight to 12 weeks; type of probiotic; age (<1 versus 1 to 13 years); severity of atopic disease based on initial SCORAD score (<25 versus >25); and IgE sensitisation status.

Results of the review
Eleven RCTs were included in the review (n=718). Seven studies were high quality and four were intermediate quality.
Probiotic treatment was associated with a statistically significant improvement in SCORAD score compared with control (10 RCTs) (WMD -3.01 points, 95% CI: -5.36 to -0.66, p=0.01). The authors stated that this 3-point difference was of doubtful clinical significance.

There were no significant differences between groups in the subgroup analyses of duration of therapy, types of probiotics used and effects of age. Analysis of the effects of atopic dermatitis severity found that probiotics were more likely to be effective at treating moderately severe atopic dermatitis (p=0.01) compared with mild atopic disease (p=0.65). The effect of probiotics appeared greater in the IgE sensitised group (p=0.07 versus control) than the non-IgE sensitised group (p=0.64), but this was not statistically significant.

There was no evidence of publication bias based on Egger's test and the funnel plot appeared to be asymmetrical. Statistical heterogeneity was not detected.

**Authors' conclusions**
This meta-analysis suggested a modest role for probiotics in paediatric atopic dermatitis. This effect was seen in moderately severe rather than mild disease. Findings should be interpreted with caution as studies were small, modest effects were seen and it appeared that shortly after probiotic therapy was discontinued the effect was comparable with placebo.

**CRD commentary**
The research question was supported by inclusion criteria for participants, intervention, outcomes and study design. Several relevant databases were searched, but it was not reported whether language restrictions were applied so the risk of language bias was unknown. Sources of unpublished studies were searched and although publication bias was indicated the funnel plot results may not be reliable due to the small number of studies. Study selection and validity assessment were performed by at least two reviewers, which reduced the risk of error and bias; similar steps were not reported for data extraction. Validity was assessed using an appropriate tool. Statistical heterogeneity was assessed and it appeared that meta-analysis was appropriate. The authors' conclusions reflect the results presented and are likely to be reliable.

**Implications of the review for practice and research**
**Practice:** The authors stated that caution should be used in prescribing probiotic products in children sensitised to cows milk protein to avoid significant reactions.

**Research:** The authors stated that large-scale studies were necessary to delineate the degree of benefit of probiotics, ascertain the probiotic effect of many placebo treatments, identify other probiotic strains or combinations of strains that could potentially show efficacy and identify dosing of probiotics in different age groups and subsets of patients with atopic dermatitis.

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