Pre- and postnatal administration of *Lactobacillus* GG reduced the occurrence of atopic disease in offspring

Kalliomäki M, Salminen S, Arvilommi H, et al. **Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial.** Lancet. 2001 Apr 7;357:1076-9.

QUESTION

In offspring at risk for atopic disease, does oral administration of *Lactobacillus* GG (LGG), given prenatally to mothers and postnatally to their infants, prevent atopic eczema?

DESIGN

Randomized (unclear allocation concealment*), blinded (clinicians, patients, and outcome assessors),* controlled trial with 2-year follow-up.

SETTING

Antenatal clinics in Turku, Finland.

PATIENTS

159 pregnant women who had atopic disease or ≥ 1 first-degree relative (mother, father, or older sibling) or partner with atopic eczema, allergic rhinitis, or asthma. 132 women (83%) and 132 children completed follow-up.

INTERVENTION

Mothers were allocated to LGG (1×10^{10} colony-forming units [Valio Limited, Helsinki, Finland]) (n = 77) or to placebo (microcrystalline cellulose) (n = 82). The capsules were taken daily for 2 to 4 weeks before expected delivery. After delivery, breast-feeding mothers continued to take the capsules, or the children received the contents mixed with water by spoon. The capsules were taken postnatally for 6 months.

MAIN OUTCOME MEASURES

A diagnosis of atopic eczema, the main outcome measure, required pruritis or facial or extensor involvement, or both, and a chronic relapsing course (eczema for ≥ 1 mo at the 24-mo study visit and on ≥ 1 previous visit).

MAIN RESULTS

Atopic eczema occurred in fewer children who had received probiotics than in those who received placebo (P = 0.008) (Table).

CONCLUSION

In offspring at risk for atopic disease, *Lactobacillus* GG given pre- and postnatally reduced the occurrence of atopic eczema up to 2 years of age.

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*See Glossary.

***Lactobacillus* GG vs placebo for prevention of atopic disease in children up to 2 years of age†**

Outcome	*Lactobacillus* GG	Placebo	RRR (95% CI)	NNT (CI)
Atopic eczema	23%	46%	49% (16 to 68)	5 (3 to 16)

†Abbreviations defined in Glossary.

COMMENTARY

The study by Kalliomäki and colleagues found an impressive halving of the risk for atopic eczema at 2 years in those given probiotics—cultures of potentially beneficial bacteria of the healthy gut microflora. 2 questions need to be answered: Are the results valid, and if so, should clinicians modify their practice now?

3 methodologic concerns exist with the study. The first is that the method of concealing allocation to the intervention groups is not clear. Second, despite a high follow-up rate, an intention-to-treat analysis was not carried out. Third, the method used to define atopic eczema was nonspecific (e.g., simple irritant contact dermatitis could have been included) (1), and other validated definitions could have been used. These methodologic concerns are unlikely to invalidate the study, but we do not know for sure unless we have more information or the study findings are replicated.

In terms of changing practice, 2 points are noteworthy. First, the results should not be generalized to those without a positive family history of atopy. The lack of change in atopic markers suggests that a study in nonatopic families might be worthwhile. Second, it remains to be seen whether the initial benefit in the intervention group is a sustained one, as opposed to merely delaying the onset of symptoms as other prevention studies have found (2). Longer-term data are also awaited on asthma, hay fever, and safety risk.

So, would I recommend probiotics to the families with atopic eczema that I care for? Not yet. Although this is an exciting study, history teaches me to be cautious about changing my practice on the basis of 1 moderately sized randomized controlled trial, the results of which are entirely dependent on 1 assessor. Additional studies are needed to confirm the findings, and longer follow-up is needed to see whether the benefits are sustained.

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