TRANSMFORMING GROWTH FACTOR-β IN HUMAN MILK IS ASSOCIATED WITH WHEEZE IN INFANCY


**Purpose of the Study.** To determine whether the cytokines in breast milk could account for some of the apparent protective effects of breastfeeding against wheeze in the first 1 year of life.

**Study Population.** Mothers and their infants participating in the Infant Immune Study in Tucson, Arizona, were studied.

**Methods.** Data on breastfeeding and infant wheeze, from birth to 1 year, were collected prospectively from 243 mothers. Breast milk samples obtained at a mean postpartum age of 11 days were assayed, with enzyme-linked immunosorbent assays, for concentrations of transforming growth factor-β (TGF-β1), interleukin-10, tumor necrosis factor-α, and the soluble form of CD14. The dose of each cytokine was assessed for a relationship with wheeze, in bivariate and logistic regression analyses.

**Results.** Greater duration of breastfeeding was signifi- cantly associated with decreased prevalence of wheeze (P = .039). There was wide variability in the levels of each cytokine in milk, as well as variability among women in the amount of each cytokine produced. There was a signifi- cant inverse association between the dose of TGF-β1 received through milk and the incidence of wheeze (P = .017); the relationship was linear (P = .006). None of the other cytokines showed a linear relationship with wheeze. In multivariate analyses, the risk of wheeze was signifi- cantly decreased (odds ratio: 0.22; 95% confidence interval: 0.05–0.89; P = .034) with increasing TGF-β1 dose (long breastfeeding and medium/high TGF-β1 level, compared with short breastfeeding and low TGF-β level).

**Conclusions.** This analysis shows that the dose of TGF-β1 received from milk has a significant relationship with infant wheeze, which might account for at least some of the protective effects of breastfeeding against wheeze.

**Reviewer’s Comments.** It was previously shown that longer duration of breastfeeding was associated with reduced wheeze in both developing and industrialized countries, but it was unclear which components of breast milk conferred this protective effect. Cytokines secreted in hu- man milk might play important roles in newborn health and in the development of infant immune responses. TGF-β1 has a potent immunosuppressive effect in the gut and acts with interleukin-10 to promote specific immuno- globulin A production, which might reduce susceptibility to both enteric and respiratory infections. A second mech- anism might involve effects on infant lung development, because TGF-β1 appears to regulate the signaling mech- anisms of proliferation and differentiation of lung cells in mice. More importantly, a single human study found a correlation between breastfeeding and lung function among 124 infants who underwent pulmonary function testing before 6 months of age.

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EFFECT OF PROBIOTIC LACTOBACILLUS STRAINS IN CHILDREN WITH ATOPIC DERMATITIS


**Purpose of the Study.** To evaluate the clinical and anti-inflammatorv effects of probiotic supplementation among children with atopic dermatitis (AD).

**Study Population.** Subjects were 43 children (1–13 years of age) in Denmark with known AD.

**Methods.** A randomized, double-blind, crossover de- sign placed patients into 2 treatment groups, group A (placebo followed by probiotics) and group B (probiotics followed by placebo). Dosing was twice daily for 6 weeks, with a 6-week washout period between treatment arms. The probiotics used included *Lactobacillus rhamnosus* 19070-2 and *Lactobacillus reuteri* DSM 12246, strains previ- ously shown to adhere to intestinal mucosa. The placebo was skim milk powder and dextrose. Patients were evalu- ated 2 weeks before study onset, with the scoring AD (SCORAD) system (consisting of itch score, intensity, and extent of eczema) and measurement of serum immuno- globulin E levels. Skin prick test results and serum immuno- globulin E levels were used to divide patients into allerg- ic and nonallergic groups. At weeks 0, 6, 12, and 18, SCORAD indices, serum eosinophilic cationic protein levels, and cytokine (interleukin-2, interleukin-4, interleukin-10, and interferon-γ) levels were measured. Subjective evaluations of the status of AD were obtained from pa- tients/parents at 6, 12, and 18 weeks. Patients continued to receive topical corticosteroids, with the quantity of medica- tion being recorded at each visit.

**Results.** The SCORAD indices at study onset were 18 to 64 (scale: 0–80), indicating moderate to severe AD in the study groups. Thirty-nine patients completed subjective evaluations, with 22 (56%) indicating improvement after active therapy, compared with 6 (15%) after placebo. In the total study group (n = 43), a 24.7% reduction in the extent of eczema after active treatment was seen (P = .02), whereas itch scores and intensity only trended toward lower values. The overall SCORAD index improved slightly during active treatment (from a score of 35.6 to 31.6, P = .06), but no improvement was seen with placebo. For patients whose subjective evaluations indicated im- provement during active treatment, the total SCORAD index was significantly improved, compared with placebo (P < .0001). Serum eosinophilic cationic protein levels de- creased during active treatment, compared with placebo (P = .03). Cytokine levels did not change during any treatment. In the allergic group (n = 27), the total SCORAD index and the extent of disease score both decreased (P = .04 and P = .008, respectively). Topical corticosteroid use was similar for all patients.

**Conclusions.** The use of probiotic *Lactobacillus* strains produced improvement in moderate to severe eczema, with respect to both subjective evaluations and extent of eczema. Results were more pronounced in the allergic group.

**Reviewers’ Comments.** This study supports current evi- dence that intestinal inflammation and subsequent dys- function of the intestinal mucosa occur in AD and that probi- otics may work to reduce intestinal inflammation. The results indicate another therapy for the treatment of AD. The long-term effectiveness of probiotic use for treatment of AD remains to be addressed.

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THE EFFECT OF HYDROLYZED COW’S MILK FORMULA FOR ALLERGY PREVENTION IN THE FIRST YEAR OF LIFE: THE GERMAN INFANT NUTRITIONAL INTERVENTION STUDY, A RANDOMIZED, DOUBLE-BLIND TRIAL


**Purpose of the Study.** To evaluate the clinical and anti- inflammatory effects of probiotic supplementation among children with atopic dermatitis (AD).
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