increased in all SLIT regimens compared with controls. These results were statistically significant compared with controls in all but CD4+ IL-4–producing cells, and the results were similar across all treatment arms. All SLIT regimens resulted in an increase in Amb1-specific IgG4, and this increase was most impressive in the prolonged-SLIT treatment arm.

CONCLUSIONS. Although all SLIT regimens resulted in an improvement in clinical efficacy, prolonged SLIT was the most effective. The reduction in IL-4 and increase in IL-10 production is consistent with observations from subcutaneous immunotherapy studies and provides insight into the mechanism of SLIT. These cytokine changes might serve as an objective marker of efficacy of SLIT for patients on treatment.

REVIEWER COMMENTS. Further evaluation of SLIT is of particular importance in the pediatric population because of its less invasive method of administration compared with injection immunotherapy and its improved safety profile. However, more studies are needed before the therapy makes it to US practice.

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Efficacy and Safety of Timothy Grass Allergy Immunotherapy Tablets in North American Children and Adolescents

PURPOSE OF THE STUDY. To investigate the efficacy and safety of timothy grass allergen immunotherapy (AIT) treatment using sublingual tablets in children and adolescents with grass pollen–induced allergic rhinoconjunctivitis (ARC).

STUDY POPULATION. Three hundred forty-five subjects, aged 5 to 17 years, with a clinical history of physician-diagnosed grass pollen–induced ARC with or without asthma were studied.

METHODS. This was a double-blind, randomized, placebo-controlled, parallel-group, multicenter, phase III study. Subjects were randomly assigned (1:1) to once-daily sublingual grass AIT treatment (2800 bioequivalent allergen units; 15 μg of PhlP5) or placebo. Treatment began ~16 weeks before the grass pollen season (GPS) and continued through the entire GPS for a total treatment period of 23 weeks. The total combined score was a summation of the daily symptom score and daily medication score, which were predefined. Immune parameters were measured over time. Safety was measured on the basis of reported adverse events.

RESULTS. The mean total combined scores for the entire GPS were significantly less in the grass-AIT group than in the placebo group by 26% (P = .001). The mean daily symptom score was significantly less in the grass-AIT group than the placebo group by 25% (P = .005). The improvements in scores for ocular and nasal symptoms were 28% and 23%, respectively, were noted in the AIT group (P = .003). The median daily medication score was significantly reduced in the grass-AIT group by 81% (P = .006). There was a significant improvement in quality of life in the AIT group that was greatest at the peak of the season (38%) when compared with the entire season (18%). Treatment with grass AIT did not significantly reduce asthma symptom scores. Levels of PhlP5–specific immunoglobulin G4 (IgG4)- and IgE-blocking factors were similar between the 2 groups at baseline and increased over time in the grass-AIT group (P < .001). Grass AIT was generally well tolerated, but 82% experienced some adverse events, primarily oral and throat pruritus and/or irritation. One subject in the AIT group received epinephrine for dose-related angioedema, dysphagia, and cough.

CONCLUSIONS. Allergen immunotherapy using sublingual grass pollen tablets is effective in the treatment of grass pollen–induced ARC with anticipated and acceptable adverse effects.

REVIEWER COMMENTS. This is the first North American study to show effective symptom control and an acceptable safety profile in children and adolescents with grass pollen–induced ARC by using a sublingual tablet for dose delivery. There was no increase in the outcome of asthma attacks, and there was improvement in quality of life at the peak of the allergy season. These results show promise for future therapy targeting children and adolescents for immunotherapy using an effective, safe, and easy-to-deliver alternative to traditional subcutaneous injection immunotherapy.

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Prevention of Allergy in Infants of Allergic Mothers by Probiotic Escherichia coli

PURPOSE OF THE STUDY. To study the effect of after-birth oral colonization by a probiotic Escherichia coli strain in infants of allergic mothers to reduce occurrence of allergy later in life.
STUDY POPULATION. There were 158 term breastfed infants followed from birth, 113 of whom were born to allergic mothers. Allergic mothers selected for the study met criteria that included clinical manifestation of allergy for more than 24 months, positive allergy-test results, and response to allergy treatment.

METHODS. The infants were divided into groups of colonized infants of allergic mothers (56), control infants of allergic mothers (57), and control infants of healthy mothers (45). Infants of allergic mothers were randomly assigned to 1 of the first 2 groups. Incidence rates of bacterial pathogens in stool and levels of anti–E coli immunoglobulins and serum cytokines were determined, and secretory immunoglobulin A was monitored in stool filtrates and maternal milk. Clinical evaluation of infants aged 4 days, 3 and 6 months, and 1, 2, 3, and 5 years was carried out, and clinical symptoms of allergy were monitored. One milliliter of the probiotic E coli strain (0.8 × 10⁹ lyophilized E coli, serotype O83:K24:H31) was administered orally to infants of allergic mothers within 48 hours after birth and subsequently 3 times per week over a period of 4 weeks. Control infants of allergic and healthy mothers were monitored in these intervals as well.

RESULTS. The E coli strain was not found in stool samples before its administration. At the 5-year conclusion of the study, allergy symptoms were found in 14 of 45 (31%) infants of control allergic mothers, 7 of 42 (16%) infants of healthy mothers, and 2 of 46 (4%) infants of allergic mothers who were colonized at birth with probiotic E coli. The incidence of allergy at 5 years was significantly lower in the colonized infants of allergic mothers compared with the infants of control allergic mothers (P < .001). The incidence reduction in the colonized group compared with that in the infants of healthy mothers was not significant. Allergic phenotype and higher interleukin 4 and 13 and lower interferon gamma transforming growth factor beta levels dominated in the allergic group, but the values observed were not quantitatively different.

CONCLUSIONS. After birth, targeted colonization of the intestine by a probiotic E coli strain might be an effective means of allergy prevention for infants of allergic mothers.

REVIEWER COMMENTS. As allergic diseases continue to increase in prevalence around the world, primary prevention of allergic disease has been elusive. Although previous studies have found that probiotics might be an effective intervention for eczema, there is little evidence to show that probiotics are beneficial for preventing other allergic diseases. With a significant reduction in clinical signs of overall allergies in the group treated with probiotics, the results of this study raise an interesting therapeutic option, although when examining the types of allergies that these children had, the effect seems to have been primarily for skin-related allergic disease. Further studies will need to evaluate the true effectiveness of these probiotics in allergy prevention.

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Probiotics in Pregnant Women to Prevent Allergic Disease: A Randomized, Double-Blind Trial

PURPOSE OF THE STUDY. To determine if probiotics given to pregnant and nursing women in a nonselected population could prevent allergic disease in the first 2 years of life.

STUDY POPULATION. There were 278 children (138 on probiotics, 140 on placebo) from a population of 415 women in Trondheim, Norway.

METHODS. This was a randomized, double-blind, placebo-controlled study. Women were given 250 mL of probiotic milk or placebo milk per day from 36 weeks’ gestation to 3 months after delivery while breastfeeding. The probiotic milk contained Lactobacillus rhamnosus, Lactobacillus acidophilus La-5, and Bifidobacterium animalis subsp lactis Bb-12. At 2 years, all children were assessed for atopic dermatitis (AD), asthma, allergic rhinoconjunctivitis, and atop dermatitis (positive skin-prick test result or elevated specific immunoglobulin E [IgE] level). The intention-to-treat analysis was enabled by multiple imputations, and the complete-case analysis included all subjects who completed end-point exams.

RESULTS. Using intention-to-treat analysis, the odds ratio (OR) for the cumulative incidence of AD was 0.51 for those in the probiotic group compared with those in the placebo group (95% confidence interval [CI]: 0.30–0.87; P = .013). The effect was stronger for non–IgE-associated AD (OR: 0.43 [95% CI: 0.23–0.81]; P = .009). There was no effect on IgE-associated AD (OR: 0.90 [95% CI: 0.37–2.17]; P = .812). No significant effect was found for asthma, allergic rhinoconjunctivitis, or atop dermatitis. In complete-case analysis, there was a significant difference in the cumulative incidence of AD between the probiotic and placebo groups (log rank, P = .022), and the relative risk was 0.61 (95% CI: 0.41–0.91; number needed to treat to benefit: 8). The hazard ratio was 0.58 (95% CI: 0.36–0.93) in the probiotic group compared with that in the placebo group (P = .024). There was a significantly (P = .044) reduced risk of having moderate AD compared with the placebo group.
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