

Immunotherapy

Efficacy and Safety of 5–Grass-Pollen Sublingual Immunotherapy Tablets in Pediatric Allergic Rhinoconjunctivitis


PURPOSE OF THE STUDY. To determine the efficacy and safety of a 300-index of reactivity sublingual immunotherapy (SLIT) tablet for children with allergic rhinoconjunctivitis.

STUDY POPULATION. Subjects were 278 children (age: 5–14 years) with seasonal grass pollen-induced allergic rhinoconjunctivitis for ≥2 years. Allergy was confirmed by a timothy grass-specific immunoglobulin E (IgE) level of at least class 2 and a wheal diameter of >3 mm in a skin-prick test containing 5 grass pollens included in the SLIT tablet (orchard, meadow, perennial rye, sweet vernal, and timothy grasses). Patients who were sensitized to other allergens present during the grass pollen season, patients who had previously received immunotherapy for grass pollen allergy, and patients with asthma who were receiving medications other than β2-adrenergic receptor agonists were excluded.

METHODS. This was a randomized, multicenter, double-blind, placebo-controlled trial conducted in 29 centers in 5 European countries. Patients received daily dosing with either the SLIT tablet or placebo beginning 4 months before and continuing throughout the grass pollen season. The primary outcome was efficacy of treatment, as assessed with the Rhinoconjunctivitis Total Symptom Score, an 18-point scale using 6 common rhinoconjunctivitis symptoms (nasal pruritus, nasal congestion, sneezing, rhinorrhea, ocular pruritus, and watery eyes) scored from 0 to 3 on the basis of severity. Daily symptoms and adverse events were recorded 1 month before and throughout the pollen season. Rescue medication use was scored from 1 to 3 on the basis of the use of antihistamines, nasally administered corticosteroids, or orally administered corticosteroids. Serum levels of IgG4 and IgE specific for grass pollen allergens were measured before and at the end of the study.

RESULTS. A total of 278 children received either a SLIT tablet or placebo. The Rhinoconjunctivitis Total Symptom Scores showed benefit corresponding to mean and median improvements across all 6 categories of 28% and 39.3%, respectively, for the SLIT tablet over placebo (P = .01). Significant improvements in rescue medication scores (P = .0064), corresponding to mean and median improvements of 24.1% and 48.7%, respectively, and reductions in symptom scores (P < .038) were seen for the active group, compared with the placebo group. A threefold increase in grass-specific IgG4 levels was seen for the active group, with little change for the placebo group. Changes in grass-specific IgE levels were similar between the groups. Adherence to therapy was similar between the groups (placebo: 95%; active: 94%). A total of 902 treatment-associated adverse events were noted (active: 84.9%; placebo: 82%), with most being mild to moderate in severity. Nine subjects withdrew from the study because of adverse events, including 7 in the treatment group and 2 in the placebo group.

CONCLUSIONS. Study data demonstrate that a grass pollen SLIT tablet is effective and safe in decreasing seasonal symptoms in children with allergic rhinoconjunctivitis.

The Safety of Sublingual Immunotherapy With One or Multiple Pollen Allergens in Children


PURPOSE OF THE STUDY. To evaluate the rate and type of adverse events experienced by children receiving sublingual immunotherapy (SLIT) for pollen allergy with either single or multiple allergen extracts.

STUDY POPULATION. Prospective postmarketing survey of 433 children receiving SLIT for respiratory allergies attributable to pollen.

METHODS. Consecutive children with respiratory allergies attributable to pollens who were receiving SLIT with multiple or single allergens were enrolled. Parents recorded adverse events (eye symptoms, rhinitis/ear itching, asthma, oral itching/swelling, nausea, vomiting, abdominal pain, diarrhea, urticaria, angioedema, and anaphylaxis) on a diary card. The adverse events were graded as mild, moderate, or severe.

RESULTS. Four hundred thirty-three children (male: n = 285; age range: 3–18 years) receiving SLIT were surveyed. Of them, 179 received a single allergen extract and 254 received multiple allergens. The total number of doses given was 40 169 (17 143 with single allergen). Overall, 178 adverse events were reported. Of those, 76 occurred in children receiving a single allergen extract (42.46% of patients; 4.43 of 1000 doses) and 102 in children receiving multiple allergens (40.3% of patients;
CONCLUSIONS. The use of multiple allergens, compared with single allergens, for SLIT does not increase the rate of adverse events in children.

REVIEWERS COMMENTS. Although it is not commercially available in the United States, SLIT for pollen allergy has gained widespread acceptance in Europe, and evidence supporting its safety and efficacy is accumulating. The promise of SLIT is that it might provide a safer and more-convenient alternative to subcutaneous immunotherapy while maintaining efficacy. Much of the literature supporting its use has involved single allergen extracts, and recent case reports described anaphylaxis with multiple-allergen SLIT. This study, which did not evaluate efficacy, addressed the question of whether the use of multiple allergen extracts for SLIT is safe in children. In this study, the authors did not find any serious adverse events in children using either single or multiple allergen extracts. Their survey involved a limited number of patients and, although SLIT seems to be safe for children, the possibility of anaphylaxis with pollen SLIT cannot be excluded on the basis of these results.

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Safety and Immunogenicity of a Cluster Specific Immunotherapy in Children With Bronchial Asthma and Mite Allergy
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PURPOSE OF THE STUDY. The authors evaluated whether cluster specific immunotherapy (SIT), which involves rapid allergen desensitization over a shorter time, compared with standard SIT, could safely and effectively desensitize children with allergic asthma attributable to house dust mites.

STUDY POPULATION. Children with asthma (N = 34; age: 6–18 years) with evidence of house dust mite allergies were randomly assigned to receive either cluster or standard SIT.

METHODS. Twelve individuals received standard SIT, which allowed for maintenance doses to be reached after 14 weeks of injections. The rest received multiple increasing doses per treatment day, to reach maintenance doses in 6 weeks according to the cluster SIT schedule. Immunotolerance was measured with specific immunoglobulin G (IgG) and IgG₄ levels for house dust mite, antibody-blocking properties on basophil activities, and T-cell subset transcription factors (Foxp3, T-bet, and GATA-3) at weeks 1, 8, and 16.

RESULTS. Initially, cluster SIT involved 3 injections at increasing doses per treatment day up to week 4, but 5 subjects developed systemic adverse effects (mainly coughing); therefore, at week 4, the regimen was changed to 2 injections per treatment day. With that, the authors found no significant differences in local (54.2% vs 53%) and systemic (3.5% vs 4.6%) adverse effects between the cluster and standard SIT groups. The most common local adverse effects were redness and swelling <5 cm in diameter. Systemic reactions were all respiratory (cough and dyspnea), and no anaphylaxis occurred. In the cluster SIT group, serum levels of specific IgG for dust mites (P < .001) and specific IgG₄ for dust mites (P < .001) significantly increased after 8 weeks, whereas such changes required 12 weeks in the group receiving standard SIT. In vitro basophil stimulation showed a significant decrease in cysteinyl leukotriene release in the cluster SIT group at 8 weeks; this was not reached in the standard SIT group until the 16-week time point. CD63 expression in both groups was decreased at 8 weeks. There were no significant differences in expression of Foxp3, T-bet, or GATA-3 between the 2 groups.

CONCLUSIONS. Cluster SIT was safe and showed more-rapid induction of specific immunotolerance in children, compared with conventional SIT.

REVIEWER COMMENTS. Building immunotolerance to allergens through immunotherapy (more commonly known as allergy shots) is effective but can be very time-consuming. The ideal schedule would be fast and efficacious, with minimal risk of adverse effects. The authors indicate that cluster dust mite SIT is a safe alternative for children, and they note that markers such as increased levels of specific IgG suggest that immunotolerance is being achieved. This is promising news for patients who are reluctant to undergo extensive, prolonged, immunotherapy protocols but need an alternative therapeutic option because of complications such as allergic asthma and/or poor responses to allergy medications. However, cluster SIT is not without adverse effects, and immunotherapy should always be conducted under the care of qualified physicians. Future studies should investigate the effectiveness of cluster SIT in managing allergy and asthma symptoms, as well as the possibility for step-down asthma therapy.

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