4.42 of 1000 doses; not significant). A total of 165 episodes (92.5%) were mild and self-resolving, distributed equally in the 2 groups. In 13 cases, the events were judged to be of moderate severity and medical advice was required. Three patients discontinued SLIT, despite the local adverse effects being mild. No emergency treatment was required.

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.

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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