

Is Sublingual Immunotherapy an Effective Therapy for Allergic Rhinitis?

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BACKGROUND

Allergic rhinitis is an immunoglobulin E-mediated inflammation of the nasal mucosa following allergen exposure. It affects approximately 20% to 40% of the US population and has a dramatic health impact. Traditional treatments include topical and oral antihistamines, intranasal steroids, and antileukotrienes. In cases of severe allergic rhinitis where standard medications cannot control disease symptoms, allergen-specific immunotherapy offers an effective alternative. Although highly efficacious, injection allergen immunotherapy has drawbacks including local and systemic reactions that require specialized centers for administration. Sublingual immunotherapy (SLIT), which has been used as an alternative treatment for over a century, has increasingly strong evidence for allergic rhinitis and is more easily self-administered.

LITERATURE REVIEW

In a meta-analysis and systematic review by Radulovic et al. (level 1a),¹ 49 randomized, double-blind, placebo-controlled clinical trials were evaluated that were suitable for meta-analysis for SLIT for the treatment of allergic rhinitis. In evaluating overall symptom scores after SLIT treatment compared to control, there was an improvement in standard mean difference (SMD) of -0.49 (95% confidence interval [CI]: -0.64 to -0.34). The SMD for medication score improvement after SLIT was -0.32 (95% CI: -0.43 to -0.21), which indicates decreased usage of other allergic rhinitis medications. There was significant heterogeneity in the studies. This review also analyzed and compared subgroups receiving SLIT versus placebo, including adults versus children, and found both groups had an

improvement in SMD in symptom score. Moreover, SLIT had a greater effect with perennial allergens (predominantly house dust mites) compared to seasonal allergens. A trend was demonstrated toward a greater magnitude of symptom score reduction if SLIT was administered for a duration greater than 12 months. All doses and preparations of SLIT medication were found to be equally effective.

In an international randomized, double-blind, placebo-controlled trial (level 1b), Durham et al. evaluated 238 patients with a history of moderate-to-severe grass pollen-induced allergic rhinoconjunctivitis inadequately controlled by symptomatic medications over a 5-year period.² Patient groups received either a daily treatment of grass pollen SLIT or placebo for 3 years and were followed for 2 years after treatment. An improvement in daily symptom score by 25% to 36% was found, as well as a decrease in daily medication score by 20% to 45% during all 5 years of grass pollen seasons. The effect was similar during the three treatment seasons and the two follow-up seasons. There were no treatment-related serious adverse events during the study. However, minor reactions in the treatment group included pruritus (44%), mouth edema (19%), and throat irritation (13%).

Durham et al. performed a pooled analysis of 34 randomized, double-blind, placebo-controlled trials (level 1a) to indirectly compare the treatment effect of SLIT versus pharmacotherapy for both seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR).³ In the grass and ragweed SAR SLIT trials, an overall improvement in the total nasal symptoms score (TNSS) of 16% and 17%, respectively, was found compared to placebo. In comparison, patients receiving montelukast, desloratadine, or mometasone had an increase of 5%, 8%, and 22% in TNSS compared to placebo, respectively, for SAR. In the house dust mites SLIT trials for perennial allergic rhinitis, they found an overall improvement of 16% compared to placebo. In comparison, patients receiving montelukast, desloratadine, or mometasone had an increase in TNSS of 4%, 5%, and 11% compared to placebo, respectively. The authors concluded that although comparisons were limited by study design, heterogeneity, and the use of rescue medications in the SLIT trials, SLIT was more effective than the traditional

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pharmacotherapies in reduction of total nasal symptom score for PAR. For SAR, SLIT was more effective than montelukast and desloratadine but almost as effective as intranasal mometasone. In patients who are not getting adequate benefit from traditional pharmacotherapies, SLIT offers an effective alternative.

Lin et al. performed a comparative effectiveness review (level 1b) evaluating 74 randomized controlled trials (RCTs) for the efficacy and safety of subcutaneous immunotherapy (SCIT), 60 RCTs for the efficacy and safety of SLIT, and eight studies that compared the two modes of therapy.⁴ Strong-to-moderate evidence was found for the use of SCIT or SLIT in the reduction of rhinitis symptoms and reduction of medication use. When comparing SCIT versus SLIT, six studies with 412 patients were evaluated, demonstrating moderate evidence that SCIT is more effective than SLIT in reducing allergic nasal and/or eye symptoms. However, there was no uniformity in reporting of these scores, and none of the scales were validated. When evaluating change in medication use specifically (five RCTs, $n = 219$), the authors reported that there may not be a difference between SLIT and SCIT. Patients experienced local reactions in the SLIT (7%–56%) and in the SCIT (6%–18%) treatment groups. Most systemic reactions in the SLIT group included gastrointestinal symptoms of nausea and diarrhea and in the SCIT group included worsening rhinitis and asthma. Due to significant heterogeneity, it could not be concluded that SCIT was safer than SLIT.

Nelson et al. performed a meta-analysis comparing the efficacy of commercially available SLIT tablets with SCIT and SLIT drops specifically for seasonal grass pollen allergies.⁵ Thirty-seven double-blinded RCTs with a total of 7,759 patients were included in this study (level 1a). Using indirect analysis with a random effects model, both SLIT tablets and SCIT improved symptom and medication scores compared to placebo. When comparing the SMD indirectly, there was no significant difference between SLIT tablets and SCIT for symptom (0.0145 [95% CI: -0.19–0.23]) or medication scores (0.133 [95% CI: -0.31 to 0.57]). No difference in SMD was found

between SLIT tablets and liquid drops. This study provides indirect evidence that SLIT tablets and SCIT for the treatment of seasonal grass pollen allergies have similar efficacy.

BEST PRACTICE

SLIT is an effective treatment option in adults and children with severe allergic rhinitis symptoms not responsive to traditional pharmacotherapy. SLIT can reduce allergic rhinitis symptoms and decrease the antiallergic medication usage in both seasonal and perennial allergic rhinitis. It has the advantage of being easily self-administered compared to SCIT. Treatment should be given for at least 12 months, and benefits can be seen even 2 years after stopping therapy. The medication is overall well tolerated by patients with no reports of severe systemic reactions, anaphylaxis, or epinephrine use.

LEVEL OF EVIDENCE

Three meta-analyses of randomized controlled trials (level 1a), one systematic review (level 1b), and one RCT (level 1b) were evaluated in this review.

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