The Upper Airway

A Prospective, Randomized, Double-blind, Placebo-Controlled Multi-centre Study on the Efficacy and Safety of Sublingual Immunotherapy (SLIT) in Children With Seasonal Allergic Rhinoconjunctivitis to Grass Pollen


PURPOSE OF THE STUDY. Subcutaneous immunotherapy (SCIT) for seasonal allergic rhinitis is a well-established, effective, and potentially curative therapy. This study evaluated an alternate route for immunotherapy: the oral mucosa and gastrointestinal tract.

STUDY POPULATION. Ninety-seven children, aged 3 to 14 years, with seasonal allergic rhinitis and proven sensitivity to grass pollen were studied.

METHODS. Sensitivity to grass pollen was confirmed by positive skin-prick test, grass pollen-specific immunoglobulin E, and conjunctival provocation test. Patients were enrolled in a prospective, double-blind trial comparing sublingual immunotherapy (SLIT) to placebo. The treatment duration was 32 months. The primary outcome measure was the change in a multiple-symptom/medication score (which measured eye, nasal, and lung symptoms and rescue-medication use) after treatment. Data collected included patient-reported symptom scores and medication use, total and antigen-specific immunoglobulin E, skin-prick test, conjunctival provocation test, nasal provocation test, spirometry, exhaled nitric-oxide concentration, atopic dermatitis score, and eosinophilic cationic protein in nasal lavage fluid.

RESULTS. The multiple-symptom/medication score was significantly reduced by SLIT to 77.3% of the placebo group ($P = .049$). This overall score was affected mainly by a large reduction in rescue-medication usage among those in the treatment group (67% of placebo; $P = .0025$). There was no significant difference in any individual-symptom score.

CONCLUSION. SLIT had a positive effect on rescue-medication usage but no significant effect on symptoms alone.

REVIEWER COMMENTS. SLIT represents an alternative therapy with multiple potential advantages to SCIT, including the elimination of injections and improved safety profile. Several studies in adults and children have found improvement in symptom scores as well as reductions in medication use to the point where this is now being used in clinical practice in place of SCIT in many European countries. Additional studies, including investigation of optimal dosing and the potential to use multiple allergens, are needed to further define the future role of SLIT in the United States.

The Safety of Sublingual-Swallow Immunotherapy: An Analysis of Published Studies


PURPOSE OF THE STUDY. To perform a meta-analysis of all published controlled studies concerning sublingual-swallow immunotherapy (SLIT) to determine rates of adverse events (AEs).

STUDY POPULATION. Subjects were from 25 published studies (primarily European) aged 5 to 60 years (6 studies only enrolled children, 9 only adults, and the remainder a mix of both).

METHODS. A systematic Medline review from 1986 to May 2004 was performed. Twenty-five published double-blind, placebo-controlled studies using SLIT that included efficacy and safety data were analyzed. Twelve studies used a high allergen dose (defined as 50–500 times the standard subcutaneous dose), and 13 used a low allergen dose (defined as 1–50 times the subcutaneous dose). AEs were defined as local or systemic: local included oral itching and/or swelling and gastrointestinal complaints, and systemic reactions included skin reactions and ocular, nasal, and chest symptoms. The rates of AEs were compared between the groups. The allergens used in the studies included mites, grasses, trees, and ragweed (single-allergen treatments).

RESULTS. Combining the studies, there were a total of 445 subjects (405 placebo) in the high-allergen-dose group and 302 subjects (285 placebo) in the low-allergen-dose group. Children accounted for 103 total active-dose subjects. A total of 904 AEs were reported in the 198 553 active-allergen doses given, with 694 local reactions and 210 systemic reactions, with a rate of 0.15 to 0.2 reactions per patient. There were no reports of anaphylaxis. Overall, subjects in the low-allergen-dose group had significantly more local reactions than those in the high-dose group. However, there was no significant difference in the number of patients with AEs between the high- and low-allergen-dose groups when compared as a ratio of the number of SLIT doses received.

CONCLUSIONS. This analysis found that local reactions were common with SLIT but were mild and self-resolved. Systemic reactions occurred rarely and were not dose...
dependent. The authors conclude that SLIT is safe for use in adults and children.

REVIEWER COMMENTS. SLIT has been widely used in Europe in recent years, has been found to be efficacious by other studies, and has a good safety profile (supported by the meta-analysis). Another article in this same journal (Clin Exp Allergy, 2005;35:560–564) found SLIT to be safe in children younger than 5 years. SLIT is being studied in the United States as well and may be an option in the near future for treatment of allergic rhinitis.

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Mary Beth Bollinger, DO
Baltimore, MD

The Efficacy and Safety of Heat-Killed Lactobacillus paracasei for Treatment of Perennial Allergic Rhinitis Induced by House-Dust Mite


PURPOSE OF THE STUDY. Live Lactobacillus paracasei 33 (LP33) may effectively improve the quality of life for patients with perennial allergic rhinitis. It has been demonstrated that heat-killed lactic acid bacteria suppress specific immunoglobulin E synthesis and stimulate interleukin-12 production in animals. The aim of this study, therefore, was to evaluate the efficacy of heat-killed LP33 in the treatment of allergic rhinitis induced by house-dust mite in human subjects.

STUDY POPULATION. A total of 90 patients older than 5 years with perennial allergic rhinitis characterized by intermittent or continuous nasal symptoms for ≥1 year were enrolled in a randomized, double-blind, placebo-controlled trial and assigned to 3 treatment groups.

METHODS. Patients in groups A and B received 2 capsules per day of live or heat-killed lactic acid bacteria (5 × 10⁹ colony-forming units per capsule), respectively, over a period of 30 days, whereas those in group C received placebo capsules. A modified questionnaire on pediatric rhinoconjunctivitis-related quality of life was administered to all subjects or their parents during each clinical visit.

RESULTS. The overall quality-of-life score decreased for groups A and B compared with the placebo group in terms of both frequency (9.47 ± 2.89, 6.30 ± 2.19, and −3.47 ± 1.53, respectively; P < .0001) and level of bother (5.91 ± 3.21, 6.04 ± 2.44, and −2.80 ± 1.64, respectively; P = .004) after the 30-day treatment. The efficacy of the heat-killed LP33 was not inferior to the live variant. No obvious adverse effects were reported for either active-treatment group during the study period.

CONCLUSIONS. The results suggest that heat-killed LP33 can effectively improve the overall quality of life for patients with allergic rhinitis and that it may be efficacious as an alternative treatment.

REVIEWER COMMENTS. The hygiene hypothesis suggests that lack of early exposure to microorganisms is a factor in the recent rise in allergic disorders. Studies have shown the certain gut flora, including Lactobacillus, may have immunomodulatory effects that may be beneficial in regulating allergic responses. Concerns over safety of administering live bacteria as a therapeutic agent led Peng and Hsu to investigate the effectiveness of heat-killed lactobacillus in the treatment of allergic rhinitis. The authors demonstrate that the heat-killed version is effective in improving the quality of life of patients suffering from allergic rhinitis.

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Julie Wang, MD
New York, NY

Surgical Management of Chronic Sinusitis in Children

Ramadan HH. Laryngoscope. 2004;114:2103–2109

PURPOSE OF THE STUDY. To compare the outcomes of children treated for refractory chronic sinusitis with adenoidectomy, endoscopic sinus surgery (ESS), or adenoidectomy with ESS.

STUDY POPULATION. Children, 2 to 13 years old, with sinusitis that persisted after 6 months of medical treatment (eg, antibiotics, nasal steroids, decongestants, reflux medications). These children had surgery (adenoidectomy, ESS, or both) over the 10-year study period.

METHODS. This was a nonrandomized study in which children were followed prospectively every 3 months after the surgical approaches. Each child was evaluated preoperatively for allergy, immunodeficiency, and cystic fibrosis and had a sinus computed tomography (CT) scan to assess disease severity. Parents filled out a questionnaire to assess improvement every 6 months for 1 year. Improvement based on questionnaire reports and need for more surgery were the principal outcome measures.

RESULTS. A total of 222 children had surgery for sinusitis during the study period (11% of children referred for evaluation of sinusitis), and 183 had adequate follow-up. The 3 surgical groups were similar with regard to gender, asthma, allergy, smoke exposure, and day care attendance. The children who had adenoidectomy alone were younger and had less severe sinus disease on CT scan than those in the other groups. Children who had adenoidectomy/ESS showed the greatest rate of improvement (87%) and lowest need for more surgery.
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Mary Beth Bollinger

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