



**Allergy Update:
Is Oral Allergy Desensitization Ready For 'Prime Time'?**

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Subcutaneous Immunotherapy (SCIT) desensitization (“allergy shots”) has been recognized as an efficacious therapy for allergic rhinitis, allergic asthma and stinging insect allergy for many decades. Double-blind placebo-controlled studies and meta-analyses in peer reviewed journals have corroborated its efficacy. The Cochrane Collaboration, an independent evidence-based systematic review, has re-confirmed the efficacy of SCIT in both asthma (2003) and seasonal allergic rhinitis (2006) ⁽¹⁾.

Although subcutaneous immunotherapy (SCIT) is a valuable tool in the allergist’s treatment regimen, it has several limitations. Some patients are hesitant to receive the series of subcutaneous injection over several years to achieve and maintain desensitization. Other patients have logistic difficulties with the requirement for physician office based administration of injections. Finally, the risk of anaphylaxis may dissuade practitioners and patients alike from embarking on a course of injection therapy.

Sublingual Immunotherapy (SLIT), is a relatively new method of desensitization that has been studied in Europe over the past twenty years. Allergy extract is administered orally either in drops (swallowed or spit out after administration) or tablets. Unlike very low dose homeopathic allergy drops which have been shown to be ineffective due to inadequate allergen exposure necessary to promote immune tolerance, SLIT has been shown to be efficacious in the vast majority of studies. SLIT has been effective because allergen doses are much higher than the homeopathic doses previously studied. Although the studies of SLIT published thus far are encouraging from a safety and efficacy standpoint, adoption as a scientifically recognized and health insurance covered procedure in the United States has not yet been achieved. The use of SLIT is not yet approved by the FDA for treatment of allergic diseases. This newsletter focuses on the encouraging clinical aspects of SLIT as well as the potential drawbacks and suggests that caution still be exercised in its clinical adoption.

Efficacy

Sublingual Immunotherapy (SLIT) has been documented in European clinical trials to be effective in both adults and children, although the data is much more robust in adults. In 2001, the World Health Organization examined 10 double blind placebo controlled studies and concluded that SLIT was an effective treatment modality for allergic rhinitis triggered by several pollens and dust mite ⁽²⁾. Four recent meta-analyses published in 2005-2006 concluded that SLIT is effective for treatment of allergic rhinitis in adults but not in children ⁽³⁻⁶⁾. Although no head to head studies have been done comparing SLIT and SCIT, the impression of experts in allergy immunotherapy suggest that SCIT may offer more potential efficacy than SLIT. The clinical data for the use of SLIT in allergic asthma is positive but less compelling than that for its use in allergic rhinitis. A preliminary study for the use of SLIT in food allergy has also been encouraging. One recent study of hazelnut allergy in children showed that 2-4 months of SLIT increased the threshold dosage of allergen tolerated ⁽⁷⁾. If corroborated by future studies, SLIT may allow individuals with food allergy an added measure of safety for inadvertent ingestion

of an offending allergen. It is unknown if absolute tolerance for a food allergen can be achieved with SLIT.

Unresolved Issues

Several issues remain to be resolved before SLIT is ready to be adopted by the practicing allergist in the United States.

a) The dose of allergen administered by SLIT needs to be clearly ascertained. Most SLIT studies have found that an allergen dose of 50-100 times higher than that used with SCIT must be used to be effective. It is not yet known if this is due to digestive inactivation of the relevant allergens or due to decreased immune presentation of the allergen. Furthermore, the schedule of SLIT administration varies from several times a day to weekly in the various studies. Therefore, both the required allergen dose and the administration interval need to be more clearly defined so that treatment parameters can be established in clinical practice (as they are for SCIT).

b) Efficacy of SLIT for individuals with multiple allergic sensitivities also needs to be established. European studies have almost without exception evaluated SLIT for single allergen desensitization (such as grass or mite). Most allergic individuals have multiple relevant allergic sensitivities. SCIT has a track record of efficacy in patients with multiple sensitivities. SLIT needs to be examined in these patients before it is widely utilized.

c) Although studies in Europe suggest a wide margin of safety in SLIT, this issue needs to be critically assessed in the United States. It is reassuring that a recent 20-year analysis of clinical trials of SLIT in Europe showed no severe cases of anaphylaxis or fatalities⁽⁸⁾. Safety data is also reassuring in children less than 5 years old. The main side effects in SLIT have been oral itching and mild swelling, and occasional abdominal pain and diarrhea. Increased rhinitis, wheezing, and urticaria have very infrequently been encountered. Recently, however, two cases of anaphylaxis have been identified in SLIT Trials suggesting that, although very uncommon, anaphylaxis is still a concern⁽⁹⁻¹⁰⁾.

Summary

Sublingual Immunotherapy (SLIT) is a promising new mode of allergen desensitization for allergic rhinitis, asthma, and potentially for food allergy. Although studies performed principally in Europe show SLIT to be effective for treatment of allergic rhinitis and asthma generally, concerns regarding dosing algorithms, treatment of individuals with multiple allergic sensitivities, and safety of at home administration remain unresolved.

Currently, two United States pharmaceutical companies are investigating the efficacy and safety of SLIT in clinical trials. The FDA will have a chance in the next few years to assess this data and determine suitability for administration in the United States. Watch and wait appears to be the appropriate course for the allergist to take regarding SLIT. Until more data is available in the United States, subcutaneous immunotherapy ("allergy shots") remains available as a proven efficacious treatment for allergic rhinitis and asthma. Avoidance of foods causing anaphylaxis remains the only safe approach to prevent symptoms from food allergy. Stay tuned, SLIT will continue to be critically examined over the next few years.

References:

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