

Sublingual immunotherapy in southern Africa: Lessons learned

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Sublingual immunotherapy (SLIT) is recommended in South Africa for the treatment of allergic rhinitis (with or without asthma) to house dust mites or grass pollens. Recent local studies have confirmed efficacy and safety but have also shown heterogeneity in clinical responses to the European SLIT vaccines used in the region. It has been found that regular follow-up with standardized rhinitis quality-of-life questionnaires improves compliance and encourages the patients to complete the 3-year SLIT course. Patients who discontinue usually do so in the first year because of logistic and financial reasons rather than adverse side effects. Further studies are in progress at the Allergy Diagnostic & Clinical Research Unit to identify immunologic markers of the SLIT responder phenotype. (J Allergy Clin Immunol 2013;■■■:■■■-■■■.)

Key words: Sublingual immunotherapy, heterogeneity of response, quality of life, follow-up

In our new mini-series, "Allergy and clinical immunology around the world," we ask experts from different parts of the world to tell us about issues that are of particular interest in their regions, reflecting either distinctive diseases or unique approaches to common problems.

Allergen sublingual immunotherapy (SLIT) has been a treatment option for patients with grass pollen and house dust mite allergy in South Africa for nearly 15 years. The main indication has been for persistent allergic rhinitis. Although accompanying mild asthma has not been a contraindication, we have not specifically evaluated the efficacy of SLIT in our asthmatic patients.

The vaccines used in South Africa are mainly a 50/50 Bermuda/rye (*Cynodon dactylon*/Lolium perenne) grass pollen mix and *Dermatophagoides pteronyssinus*/*Dermatophagoides farinae* mix for mite allergies. Occasionally, cat and dog vaccines are prescribed. SLIT vaccines used are all imported from Europe, and patients generally receive SLIT after approval by the Medicine Control Council. No allergen extracts or vaccines are produced

Abbreviation used

SLIT: Sublingual immunotherapy

in South Africa. In view of the long grass pollen seasons (up to 8 months in some parts of South Africa), most "seasonal rhinitis" is now classified as persistent rhinitis. SLIT is not generally provided for acute intermittent rhinitis, as defined by Allergic Rhinitis and Its Impact on Asthma guidelines.

More than 80% of patients with allergies in southern Africa are polysensitive. The recommendation by the Allergy Society of South Africa handbook¹ is to only use SLIT for monosensitive patients using standardized vaccines for 3 years. A small local study in South Africa² has confirmed that SLIT has a beneficial effect on quality of life when administered for 2 or more years. Immunotherapy is largely practiced by specialists and family practitioners who have been trained in the practice of immunotherapy. In South Africa family practitioners are required to spend at least 5 hours of training in immunotherapy to be eligible to write the College of Medicine of South African Diploma in Allergology examination.³ Training in immunotherapy and skin prick testing is also regularly offered in workshops offered each year at the Annual Congress of the Allergy Society of South Africa. Local suppliers of the SLIT vaccines encourage doctors to undergo training in academic hospitals or local congresses, but there is no legal requirement to undergo such training.

More than 80% of SLIT practiced in South Africa is administered by family practitioners or pediatricians who in most cases have received training through meetings of the Allergy Society of South Africa. Any registered practitioner is eligible to join the Allergy Society of South Africa. There are approximately 50 doctors in South Africa who have had postgraduate training in allergology and 7 registered subspecialists in allergology as of 2012. In a 2-year study of 60 adults using a *D pteronyssinus* vaccine,⁴ a strong association between a good response ($\geq 60\%$ improvement) in quality-of-life scores was found when compared with a separate symptom score index (blocked nose, rhinorrhea, itchy throat, and itchy eyes or palate), resulting in an odds ratio of 15 ($P < .0001$) overall. In this study a heterogeneity of clinical response to sublingual vaccines was noted in the study group, with 56% of subjects improving by greater than 60% in total symptom scores, whereas 20% did not improve with the vaccine ($< 30\%$ improvement). This heterogeneity of response is the subject of current studies investigating compliance, T-cell immune responses accompanying good or poor responses, and selection of patients for SLIT.

A review of 100 patients receiving SLIT by McArthur et al⁵ addressed the difficulties in implementing and sustaining a SLIT program in an academic allergy clinic. In this study, a

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retrospective investigation using medical records review and a telephone survey, a 2-year follow-up study was conducted on 100 SLIT-treated patients. Forty-seven percent were older than 21 years, 19% were 13 to 20 years of age, and 33% were less than 12 years of age. Sixty-two percent were receiving SLIT with house dust mite antigens, 33% with grass pollen antigens, and 5% with cat or dog antigens. Twenty-nine had concomitant mild asthma, and 3 had concomitant eczema. At the time of assessment, 16% had completed a 3-year course of SLIT, 27% were currently receiving SLIT, but 29% had terminated prematurely. Of those who terminated, approximately one third were lost to follow-up, but the remaining two thirds were contacted. Seventy-five percent of the patients who completed at least 3 years of SLIT were satisfied with the outcome compared with 54% of those who self-terminated treatment. Reasons for terminating treatment included affordability of the vaccine and practical difficulties with ordering the vaccine because it is unregistered in South Africa.

On the basis of the South African experience, patients are most likely to discontinue SLIT during the first year of treatment, regardless of the reason for terminating therapy. Regular scheduled follow-up by the treating clinician improves outcomes by improving compliance. Visits are scheduled with treated subjects every 3 to 4 months to discuss vaccine tolerance, to modify medications, and to assess quality of life. In our experience a

routine, 6-month quality-of-life questionnaire completed by treated patients increases compliance with and likelihood of completion of a SLIT course. The value of regular follow-up and encouragement is demonstrated by the South African clinical trial experience in which more than 80% of treated subjects are compliant during 2 years of treatment. Such data reinforce the practical applicability and clinical value of SLIT.

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