

# Sublingual immunotherapy (SLIT) in a standard American allergy practice

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## Abstract

### INTRODUCTION

Subcutaneous Immunotherapy (SCIT) has been used in the United States with little modification for almost 100 years. It has been proven effective in the treatment of allergic disease not responsive to pharmacotherapy and appears to prevent the emergence of asthma in the pediatric population affected with allergic rhinitis. It is also effective in the treatment of Hymenoptera venom allergy, and drug allergy. The standard protocol for the treatment of all allergic disease requires injections twice a week for up to 6 months with maintenance biweekly or monthly shots lasting 3 to 5 years. Rush schedules are also possible though they appear to carry higher risks to patients.

Though SCIT remains the standard treatment, socio economic dynamics of current American society are contributing to a decline in adherence to treatment protocol. With five percent of all employed Americans holding multiple jobs and the majority of American families today earning double incomes, time requirements of SCIT protocol may not be feasible. In addition, suburban sprawl has increased commute time to over 1 hour and single parent families are on the increase. Out of pocket expenses in the form of co-payments may also create another stress in some families.

Local, generalized, near fatal and fatal reactions are well documented in association with SCIT. Despite such obstacles, however, SCIT remains the standard treatment used by American allergists in the treatment of allergic rhinitis, asthma, and Hymenoptera hypersensitivities.

Over the last 2 decades, European researchers have explored alternative modes to standard immunotherapy treatment<sup>(1,2)</sup>. Sublingual immunotherapy (SLIT) emerged as the more

effective, safe and convenient of all treatments explored. Recently, it has been validated as an effective form of treatment in Europe<sup>(2)</sup>.

For the past 2 years, we have explored the usefulness and effectiveness of SLIT in a standard American allergy practice and we present our experience in this article.

### MATERIALS AND METHODS

Seventy five multi-sensitive patients, 22 male, 53 female and an average age of 37.5 years, who were affected with perennial allergic rhinitis received SLIT treatment as SCIT was not possible. All patients underwent standard epicutaneous and intra-dermal skin testing to determine specific allergen sensitivities, diagnostic and therapeutic. Extracts were obtained from Greer laboratories and ALK laboratories. Individual treatment sets were prepared in a comparable fashion, dosage, and proportions used in the preparation standard individual injectable immunotherapy sets in our clinic, following guidelines set by Nelson<sup>(3)</sup>. Adherence to treatment was determined by the completion of sequential vial sets of SLIT treatment. In the SCIT treatment group, adherence was determined retrospectively in a population of 100 consecutive patients that started SCIT protocols. Quality of life was measured using the self administered Rhinoconjunctivitis quality of life questionnaire, validated by Juniper<sup>(4)</sup>, and consisting of the following domains: activities, sleep, nose/eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotional. Questionnaires were given at baseline and post immunotherapy treatment, occurring after 3 months of protocol onset. Time effects were analyzed using repeated measures ANOVA..

**DOSAGE**

The dosage delivered by sublingual drops was increased daily with changing vials on a weekly basis. Provided that no adverse events were observed, the total cumulative dosage of SLIT was calculated by volume (1ml=30 drops.) Patients receiving SLIT treatment were given 10 to 15 times the dosage at maintenance levels compared to those patients receiving the standard SCIT treatment. (Table 1.)

**Figure 1**

Table 1: Maintenance Monthly Dosages of SLIT vs. SCIT Treatment

	SCIT 1:10	SLIT 1:1	SLIT 2:1
	Vial # 5(maint)units/ml	Vial # 8(maint) units/ml	Vial #7 (maint)units/ml
Volume (Stock)	N/A	0.5-1.0	0.5-1.0
Rye Grass(PNU)	2,500	25,000-50,000	18,888-33,000
Timothy Grass(PNU)	2,500	25,000-50,000	18,888-33,000
Bahia Grass(PNU)	500	2,5000-5,000	1,888-3,333
Ragweed(PNU)	11.8	59-118	39.3-78.7
D. Pteronyssinus(Ath)	250	1,250-2,500	833.3-1,666
D. Farinea(AU)	750	3,750-7,500	2,500-5,000
Cat(BAU)	750	3,750-7,500	2,500-5,000

**RESULTS**

**QUALITY OF LIFE**

Seventy five multi-sensitive patients, 22 male, 53 female, average age 37.54 years competed quality of life questionnaires at baseline and post immunotherapy. After completing 3 months of SLIT therapy, highly significant and statistical changes(time effects) were observed in all domains of quality of life survey. (Table 2.)

**Figure 2**

Table 2: Rhinoconjunctivitis Quality of Life Questionnaire Baseline and Post Treatment in 75 patients Treated with SLIT

	Mean Pre	Mean Post	p-value		
Mean Activity	2.84	+ 1.84	1.34	+ 1.24	<0.0001
Mean Sleep	2.24	+ 1.82	1.18	+ 1.38	<0.0001
Mean Non Nose/Eye	2.67	+ 1.66	1.35	+ 1.20	<0.0001
Mean Practical	2.49	+ 1.68	1.16	+ 1.06	<0.0001
Mean Nasal Symptoms	2.71	+ 1.57	1.44	+ 1.17	<0.0001
Mean Eye Symptoms	2.21	+ 1.72	1.13	+ 1.26	<0.0001
Mean Emotional	2.43	+ 1.66	1.03	+ 1.23	<0.0001

**ADHERENCE**

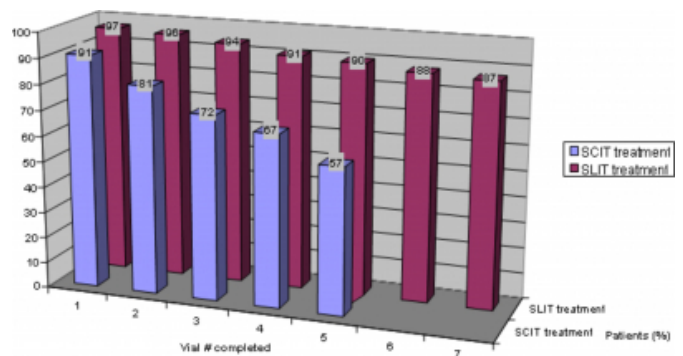
A series of 200 multi sensitive patients affected with Perennial Allergic Rhinitis that entered desensitization protocols. We did observe adherence to treatment protocol from beginning to maintenance levels of immunotherapy treatment.

Two treatment groups consisting of 100 patients each received either SLIT or SCIT treatments. The latter treatment was administered in a manner consistent with that described by Nelson(4) The average age was 34.8 years, 68

female, 32 males for the SLIT group. The average age was 42.1 years, 73 females, and 27 males in the SCIT group. We did observed a gradual decline in the adherence to both treatment modalities as the protocols progressed. The decline was steeper in the SCIT group and at maintenance levels of treatment, and adherence in SLIT group was 87% compared with 57% in the SCIT treatment group (Figure 1). 2 adverse events occurred in the SLIT group and included sublingual irritation and swelling (only in one) that were managed by reducing the dosage and complying with more thorough avoidance measures after which the dosage was increased again with no further problems.

**Figure 3**

Figure 1: Adherence to Treatment of SLIT vs. SCIT Protocols



**DISCUSSION**

We found SLIT to be a useful and promising therapeutic intervention in the management of patients affected with allergies. The clinical response is documented by highly significant differences in quality of life at post treatment compared with baseline. The substantial difference as documented in adherence to both kinds of treatment is justified by the safety that has been documented in SLIT and enables treatment to be administered at home, whereas the SCIT protocols are highly regulated and must be administered in a clinical setting. This paradigm may no longer fit current social trends, lifestyles, and dynamics of the American family.

The protocols of SCIT, though uncommon, are affected by other factors including: schedules, reactions, slow improvement, and economic issues. It is with interest that we witnessed the trends of this population once they were switched to SLIT. SLIT protocols are shorter in time and the patients do experience a clinical benefit that is evident sooner than with SCIT and this may also play a role in increased adherence.

The dosage we found possible according to the strength of the stock solutions available to allergists in the United States, range from ten to fifteen times the achieved dosage with standard injectable immunotherapy. In general, these dosages are lower than those thought to be necessary in the past for SLIT to be effective. We did mix individual allergens to construct individual treatment sets following Nelson's guidelines for such mixes and dosages<sup>(3)</sup>.

The European academy of Allergy and Immunology has a position paper advising against the use of mixed allergens and non standardized allergens extracts for SLIT<sup>(1)</sup>. The standard American allergen immunotherapy preparation of individual allergens extracts are mixed according to the individual skin test results<sup>(2)</sup>. Only Ragweed, D. Pteronyssinus, D. Farinea, Cat, Rye, Timothy, and Bahia grasses are standardized allergens available to American allergists for use at this time. Given the complexity of the American allergen landscape, the use of standardized allergens only would be limiting in the treatment of the vast majority of patients in the USA.

One case of anaphylaxis with SLIT was associated with a mix of allergens that did not follow Nelson's guidelines, did not have a build up phase, and exposed the patient to an extremely high dosage from the onset of therapy (2,000 BAUs of cat and 500 BAUs of grass mix.)<sup>(5)</sup>. In addition, no clinical supervision of this treatment took place. We have

mixed individual allergens in a fashion that adheres to Nelson's guidelines and have used a build up phase that mirrors concentration and schedule of SCIT in our practice. The daily home self administration of each dosage has enabled us to move through each vial faster, (1 week each) and thus achieve maintenance levels sooner, enhancing adherence. We did monitor the patients after vial 1 and then after each set of 2 vials, a total of 4 visits during build up phase.

As this was an observational non-randomized retrospective study, we recognize that selection bias could have affected the results. Never-the-less, it is hoped that these findings illustrate the feasibility of using SLIT in the United States.

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