ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Original Article

Efficacy and safety of house dust mite sublingual immunotherapy in children and adolescents with allergic rhinitis

Eficácia e segurança da imunoterapia sublingual para ácaros em crianças e adolescentes com rinite alérgica

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ABSTRACT

Objective: To describe the efficacy and safety of house dust mite sublingual immunotherapy (SLIT) in patients with allergic rhinitis (AR) over a 12-month period. **Methods:** This is a prospective, open-label study of children and adolescents aged 4 to 18 years with AR/asthma according to the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines, followed up at the outpatient clinics of the Hospital de Clínicas affiliated with the Federal University of Paraná, southern Brazil. All patients received SLIT drops (750 UBE/day) for *Dermatophagoides pteronyssinus* (DP) and *Blomia tropicalis* (BLO) at a concentration of 5000 UBE/mL for 12 months. Symptom and medication scores (RTSS) were assessed and skin prick tests for aeroallergens were performed from January 2022 to January 2023. **Results:** Twenty participants with an AR diagnosis for at least 4 years (range, 2-10) were included. The mean SLIT adherence rate was 89%. The mean DP wheal diameter reduced from 7.0 (SD 2.9) to 4.2 (SD 2.1) mm after 12 months (p=0.0002), while the median BLO wheal diameter reduced from 3.7 to 3.0 mm (p=0.0001). Patients showed a reduction in rescue medication use, symptom score, and combined symptom and medication scores (p<0.05). The mean visual analog scale score reduced from 9.3

RESUMO

Objetivo: Descrever a eficácia e segurança da imunoterapia com alérgenos sublingual (SLIT) com ácaros em pacientes com rinite alérgica durante um período de 12 meses. **Métodos:** Estudo experimental aberto, prospectivo que envolveu crianças e adolescentes de 4 a 18 anos com rinite alérgica/asma segundo as diretrizes *Allergic Rhinitis and its Impact on Asthma* (ARIA), acompanhados nos ambulatórios do Hospital de Clínicas da Universidade Federal do Paraná. Todos os pacientes receberam gotas (750 UBE/dia) de SLIT para *Dermatophagoides pteronyssinus* (DP) e *Blomia tropicalis* (BLO) na concentração de 5.000 UBE/mL durante 12 meses. Foram aplicados escores de medicação (RTSS), testes cutâneos para aeroalérgenos entre janeiro de 2022 e janeiro de 2023. **Resultados:** Vinte participantes com pelo menos 4 (variação de 2 a 10) anos de diagnóstico de RA. A adesão média à SLIT foi de 89%. Houve redução no diâmetro médio da pápula DP de 7 ± 2,9 mm para 4,2 ± 2,1 mm após 12 meses (p = 0,0002), bem como na mediana do diâmetro médio da pápula BLO de 3,7 mm a 3 mm (p = 0,0001). Os pacientes apresentaram redução no consumo de medicamentos de resgate, no escore de sintomas e no escore combinado de sintomas e medicamentos (p < 0,05). A

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(SD 0.7) to 5.2 (SD 1.4) (p<0.05). There was no difference in asthma control (p=0.16). The rate of mild adverse effects was low and did not differ throughout the study (p=0.62). There were no anaphylactic reactions. **Conclusion:** SLIT may provide short-term benefits to patients with AR, reducing the need for medication and improving nasal symptoms. SLIT was well tolerated and safe, with no serious adverse events.

Keywords: Allergen-specific immunotherapy, sublingual immunotherapy, allergic rhinitis.

pontuação da escala visual analógica reduziu de 9,3 ± 0,7 para 5,2 ± 1,4 ao final do estudo (p < 0,05). Não houve diferença no controle da asma (p = 0,16). A taxa de efeitos adversos leves foi baixa e não diferiu ao longo do estudo (p = 0,62), e não houve reações anafiláticas. **Conclusão:** A SLIT pode trazer benefícios em curto prazo em pacientes com RA, reduzindo a necessidade de medicação e melhorando os sintomas nasais. Foi bem tolerada e segura, sem eventos adversos graves.

Descritores: Imunoterapia alérgeno-específica, imunoterapia sublingual, rinite alérgica.

Introduction

Allergic rhinitis (AR), with or without associated conjunctivitis, is a common disease that affects between 10 and 40% of the population worldwide and has a significant impact on patients' quality of life. In some countries, more than 50% of adolescents have symptoms of AR.[1-3] In Brazil, it affects approximately 20% of the pediatric population.[4]

Although it is not a serious disease, AR has a significant socioeconomic impact. Direct costs include expenditures on medical care, tests, and medications, while indirect costs include reduced productivity and absenteeism at school and work. Among children, the disease also affects quality of life significantly, and can cause irritability and decreased cognitive performance.[1,5,6]. Long-term chronic nasal obstruction leads to changes in facial growth pattern, as well as functional complications and aesthetic issues.[7]

The main recommendations for patients with AR are avoidance of allergens, drug therapy for symptom management (mainly antihistamines and topical nasal corticosteroids), and, for patients with difficult-to-control disease, specific immunotherapy.[1,5,8] Subcutaneous injection of immunotherapeutics has been used for decades. The exact mechanism of action is not fully understood but includes changes in serum antibody levels and cellular immunity, including a shift from a Th2 to a Th1 response, among other regulatory mechanisms. The realization that the rich vascular bed located under the tongue could serve as a novel approach for allergen delivery led to the development of rapidly disintegrating tablets or aqueous extracts that could be efficiently absorbed by this route[9-11].

The immunomodulation resulting from this treatment has been shown to induce immune tolerance, with a significant reduction in symptoms and need for medication.[12]

The decision to start allergen-based immunotherapy should rely on clinical assessment and physical examination findings, with supplemental in vivo or in vitro testing as appropriate to identify sensitivity to specific relevant allergens, as well as a detailed discussion on treatment goals, risk versus benefit, and long-term commitment to a treatment plan. Because sublingual allergen immunotherapy (SLIT) involves long-term daily therapy, it requires patient or caregiver commitment to help maximize adherence.[12,13]

Control of AR symptoms remains satisfactory in the long term even after completion of immunotherapy, reducing or, in some cases, even altogether eliminating the need for medication. Therefore, this therapy can be considered potentially capable of inducing complete disease remission.[13]

The Allergic Rhinitis and its Impact on Asthma (ARIA), European Academy of Allergy, Asthma and Immunology (EAACI), Brazilian Association of Allergy and Immunology (ASBAI), and American Academy of Allergy, Asthma and Immunology (AAAAI) guidelines all recognize immunotherapy performed with allergen extracts as a valid form of treatment, as long as the extracts are of high quality (preferably standardized) and care is taken when selecting the antigen mix, since some allergens may contain proteolytic enzymes capable of inactivating other components of the mixture.[1,2,5,9]

The primary objective of this study is to ascertain whether SLIT constitutes an effective and safe therapy for pediatric patients with allergic rhinitis, with or

without conjunctivitis. Our secondary objectives were to assess the safety of SLIT and the degree of skin reaction before and after immunotherapy.

Methods

This open-label, prospective experimental study was conducted from January 2022 through December 2023. The study protocol was approved by the Research Ethics Committee of Universidade Federal do Paraná (opinion no. 74790323.6.0000.0096).

Data were obtained from the medical records of patients with persistent moderate/severe allergic rhinitis and/or rhinoconjunctivitis who underwent SLIT with *Dermatophagoides pteronyssinus* (DP) and *Blomia tropicalis* (BLO) extract for 12 months at the Outpatient Pediatric Allergy and Immunology Clinic, Hospital de Clínicas da UFPR (CHC-UFPR). The diagnosis of AR followed the ARIA guideline recommendations.

The sample comprised children and adolescents aged 4 to 18 years with moderate-severe allergic rhinitis/rhinoconjunctivitis, with or without comorbid asthma (mild or moderate, with FEV_1 >80% of baseline), exclusively sensitized to DP and BLO, and in whom pharmacotherapy plus specific environmental control measures had not been sufficient to control symptoms.

Patients with serious diseases of the immune system (such as autoimmune conditions), active infections (such as tuberculosis), heart disease, severe high blood pressure (even if controlled), severe kidney disease, severe atopic dermatitis, malignancies, or psychiatric diseases that would preclude full consent were excluded, as were those taking beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, or immunosuppressants.

Patients (or their guardians) kept a daily record of symptoms and medication use during the follow-up period. Mean scores were calculated for the assessment instruments administered during monthly study visits. Records of patients meeting the aforementioned criteria were retrieved from a database and analyzed according to the following variables: sex (male or female), age (in years), underlying disease that led to SLIT, presence of concomitant asthma, total IgE measurement, visual analogue scale (VAS) score (assessed at all visits), results of skin prick testing (SPT) with DP and BLO extracts (carried out at the start of treatment and after 12 months of treatment), adherence (assessed according to the clinician's judgment), medications required to control symptoms, symptom score, treatment-emergent adverse events, and clinical progress (after 12 months of treatment). The safety of SLIT in participants and their severity of skin reaction to house dust mites DP and BLO were recorded by comparing the mean wheal diameter on SPT before and after 12 months of SLIT. The frequency of adverse effects related to SLIT was ascertained with a questionnaire administered during study visits. Treatment adherence was assessed subjectively by the treating physician.

Clinical findings, symptom progression, adverse effects, concomitant medication, SPT results, and treatment adherence were reported descriptively and subsequently analyzed.

A simple ARIA-standard VAS was used to score the severity of rhinitis symptoms such as nasal congestion, itching, sneezing, and discharge, as well as conjunctival symptoms. In addition to the general perception of such symptoms' effect on quality of life, they are jointly measured on a ruler-type scale marked with figures and patients are asked to point out which point along this ruler best matches their current status, ranging from zero (completely asymptomatic) to 10 (awful, completely uncontrolled symptoms).

Symptom scores and medication scores were assigned according to symptom severity and the need for medication use respectively, as recorded in diaries kept by the patient or their guardians; these diaries were reviewed at regular intervals by the investigators. Visits were scheduled every three months starting from the SLIT induction phase. SPTs for DP and BLO were performed using standardized allergen extracts, positive control, and negative control. One drop of each allergen was applied to the volar surface of the forearm and the skin was pricked with a lancet. After 15 minutes, the reaction was read; a wheal diameter greater than or equal to 3 mm was considered positive. SPTs were used to monitor SLIT efficacy at the start of treatment and at 12-month follow-up. Reduction in wheal size was used as a secondary parameter to assess treatment efficacy. Allergen extracts were provided by FDA Allergenic Pharmaceuticals, Rio de Janeiro, Brazil.

The liquid extract administered in this study consisted of a standardized mixture of equal proportions of DP and BLO extracts at a concentration of 5,000 biological allergy units (BAU)/mL.

The study medication was titrated incrementally every day for 5 days (induction phase) up to a

maximum maintenance dose of 750 BAU/day for 12 months. Again, the extract was provided by FDA Allergenic Pharmaceuticals, Rio de Janeiro, Brazil (Table 1).

After enrollment, participants received vials of the SLIT extract, which were administered at home by the patient or guardian. Every 21 days, the parents or guardians of the participants collected the new vials in person at the study center.

The induction dose was 1 sublingual drop of the standardized DP/BLO extract for 5 days, followed by 3 sublingual drops daily for 12 months. The first dose was administered by a physician at the study center, and patients were kept for 1 hour under observation.

At a series of follow-up visits and at the end of treatment (or at the end-of-study visit), the following data were recorded: changes in SLIT treatment (dose modification, early discontinuation, etc.); changes in medications taken for symptom control; symptom progression; and any adverse events. Patient adherence and satisfaction, as perceived by the treating physician, were also recorded at each follow-up visit. Events such as failure to attend prearranged follow-up appointments and delay in collecting SLIT refills were deemed indicative of treatment non-adherence.

Primary outcome

The primary parameter for evaluating efficacy was a combination of the symptom score (SS) and use of rescue medication score (MS), the so-called Combined Symptom and Medication Score (CSMS), as proposed in the 2014 European Academy of Allergy and Clinical Immunology (EAACI) Position Paper on standardization of clinical outcomes used in allergen immunotherapy trials.[14] The CSMS was calculated with the following formula:

$$\textbf{CSMS} = SS/6\ (0\text{-}3) + MS\ (0\text{-}3) = 0\text{-}6$$

where: SS was the sum score from 0 to 3 (absent, mild, moderate, or severe) of four nasal symptoms (itchy nose, runny nose, blocked nose, and sneezing) and two conjunctival symptoms (itchy eyes and watery eyes). The maximum possible SS is 18; and MS was the sum score based on daily rescue medication use: topical nasal corticosteroid (1 or 2 sprays – 1 or 2 points, respectively) and loratadine (3 points), as shown in Table 2.

Loratadine (10 mg) was only indicated when nasal corticosteroids alone were not sufficient to control symptoms. Information on medications was recorded daily in a journal of rescue medication use.

Table 1
SLIT treatment regimen with *Dermatophagoides pteronyssinus* (DP) and *Blomia tropicalis* (BLO) extracts

Concentration	Phase	Dose	Frequency	Der p 1, M phase	Blo t 5, M phase	Dose (BAU), M phase
5,000 BAU/mL	I	1 drop	QD for 5 days	0.6 µg/day	22.5 ng/day	750 BAU/day
	M	3 drops	QD for 12 months			
5,000 BAU/mL	I	1 drop	QD for 5 days	0.6 µg/day	22.5 ng/day	750 BAU/day
	M	3 drops	QD for 12 months			

BAU = biological allergy unit, I = induction, M = maintenance.

Table 2
European Academy of Allergy and Clinical Immunology (EAACI) Task Force Recommendation for standardization of clinical outcomes used in efficacy trials of with allergen immunotherapy

A)	Symptom score		
	Nasal symptoms	(Score 0-3)	0 = no symptoms 1 = mild symptoms [a] 2 = moderate symptoms [b] 3 = severe symptoms [c]
		Itchy nose	0-3a
		Sneezing	0-3
		Runny nose	0-3
		Blocked nose	0-3
	Conjunctival symptoms	Itchy eyes	0-3
		Watery eyes	0-3
	Total daily symptom score (dSS)		0-3 (max score is 18÷6=3)
B)	Medication score		
		Intranasal corticosteroids QD	1 point
		Intranasal corticosteroids BID	2 points
		Oral antihistamine QD	3 points
	Total daily medication score (dMS)		0-3 (max score is 3)
C)	Combined symptom and medication score		
	CSMS	dSS (0-3) + dMS (0-3)	0-6

[a] Sign/symptom clearly present, but minimal awareness; easily tolerated.
[b] Definite awareness of sign/symptom that is bothersome but tolerable.
[c] sign/symptom that is hard to tolerate; causes interference with activities of daily living and/or sleeping.
Adapted from EAACI Position Paper, Pfaar, et al.[19].

To assess safety, participants or their guardians recorded a daily journal of any emergent local and systemic adverse effects.

Safety outcomes were assessed by the number of patients who experienced any treatment-related adverse events (TRAEs) leading to treatment discontinuation.

Adverse events (AE) were evaluated and categorized according to the World Allergy Organization (WAO) definition[15] as follows:

Local AEs: oral itching, swelling of the lips or tongue, and nausea/abdominal pain/diarrhea.

Systemic AEs: urticaria, exacerbation of rhinitis and/or asthma, angioedema, and hypotension.

Eight follow-up visits were prearranged at the start of treatment. Patients who were overdue more than 15 days for a study visit or SLIT refill were excluded from the study, as this was deemed indicative of treatment nonadherence by the participant as perceived by the treating physician.

For statistical analysis, categorical variables were presented as frequency distributions and proportions. The chi-square test was used to compare proportions. Continuous variables were expressed as means and standard deviations or medians and ranges as appropriate.

Student's *t* test was used to compare means, and the Wilcoxon test to compare medians. Statistical analyses were carried out in Stat Plus version 5.9.5.0 software (Analyst Soft Inc., USA). A p-value < 0.05 was considered to rule out the null hypothesis.

Results

Data from 20 patients aged 4 to 18 years diagnosed with persistent moderate-severe AR induced by house dust mites, with symptoms ranging from 2 to 10 years in duration, were analyzed.

Baseline demographic data and clinical characteristics of the population of children and adolescents on SLIT are presented in Table 3.

All patients who had comorbid asthma were sensitized to DP and BLO, and all had normal lung function.

At 1-year follow-up, IgE and eosinophil levels did not show significant changes during SLIT (p = 0.6).

The mean diameter of the DP wheal did show a reduction after 12 months. The median diameter of the BLO wheal showed the same behavior.

SPT with the allergen extract itself was also associated with a lessened reaction at the end of treatment (Table 3).

Asthma control was evaluated at two time points during this first year of treatment using the ACT (Asthma Control Test) as an assessment tool. The first assessment took place at induction (ACT 20.5 ± 2.1) and the second after at least 6 months of SLIT (ACT 21.1 ± 2). There was no significant difference between these two time points (p = 0.16).

No deaths, cases of anaphylactic shock, or other life-threatening events were reported during the study.

Table 4 shows a summary of treatment safety. No serious TRAE was reported in this study.

Ten TRAEs occurred in the study group over the 12-month follow-up: five cases of oral symptoms or pruritus at the application site, two of lip angioedema, and three of worsening allergic symptoms/asthma exacerbation. The total TRAE rate was 15% at induction, 15% in the first month of SLIT, 5% in the third month, 10% in the sixth month, and 5% at the last (12-month) assessment, respectively.

Table 3
Demographic distribution of study patients undergoing sublingual immunotherapy (SLIT)

Characteristics	Pre	Post	p
Male sex	10 (50%)		
BMI	19.3 ± 1.5		
Age at initiation of SLIT, mean ± SD in years	10.3 ± 2.8		
Moderate/severe rhinitis	20 (100%)		
Duration of symptoms in years, median (range)	4 (2-10)		
Asthma	20 (100%)		
FEV_1, % of predicted	109.1 ± 13.5		
Total IgE, geometric mean in KU/L	493.9	438.8	0.6
Eosinophils/mm^3, median (range)	385 (130-1,110)	350 (108-720)	0.6
Wheal diameter with *Dermatophagoides pteronyssinus* extract, mean ± SD in mm	7 ± 2.9	4.2 ± 2.1	0.0002
Wheal diameter with *Blomia tropicalis* extract, median (range) in mm	3.7 (3-15)	3 (0-7)	0.0001
Wheal diameter with SLIT extract, mean ± SD in mm	3.8 ± 1.6	2.7 ± 1.8	0.02
Wheal diameter with histamine 10 mg/mL, mean ± SD in mm	5.7 ± 1.7	5.1 ± 2.1	0.03

BMI = body mass index, FEV_1 = forced expiratory volume in the first second, IgE = immunoglobulin E.

Table 4
Assessment of adverse events

Variable	Induction	1 month	3 months	6 months	12 months	p
Local TRAE	3 (15%)	1 (5%)	1 (5%)	1 (5%)	1 (5%)	0.62
Systemic TRAE	0	2 (10%)	0	1 (5%)	0	0.7

TRAE = treatment-related adverse events.

There was no significant difference in TRAE between the time points of assessment ($p > 0.05$).

Primary outcome analysis after one year of SLIT showed that patients had significant improvements in MS, SS, and CSMS (Figures 1, 2, and 3).

The average treatment adherence in the 12-month follow-up period was higher than 89%, which is expected for SLIT. The maximum tolerated delay in attending scheduled interview visits or collecting medication refills was 15 days (Figure 4).

The VAS score decreased from baseline to the end of the follow-up period ($p < 0.05$) (Figure 5).

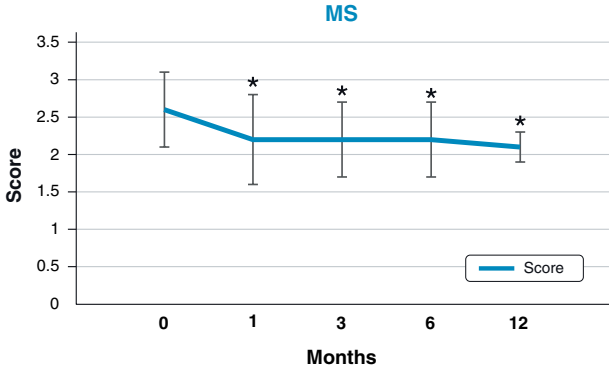

Figure 1
Comparison of rescue medication scores between baseline and months 1, 3, 6, and 12

* $p < 0.05$. Data expressed as means and standard deviations.

Discussion

Allergen immunotherapy (AIT) is an immune-based, disease-modifying treatment option for IgE-mediated allergies such as allergic rhinoconjunctivitis and allergic asthma. However, studies on the long-term efficacy of SLIT for AR, especially in pediatric patients, are still scarce.

Previous studies have demonstrated the effectiveness of SLIT in relieving AR symptoms and reducing medication use.[16] Total symptom score, total medication score, and VAS have been recommended as possible outcomes for assessing efficacy in SLIT studies. Most meta-analyses on SLIT in children have proven its efficacy in reducing symptom scores and medication use compared to placebo groups in allergic respiratory diseases.[17] In the present study, we found significant decreases in MS, SS, and CSMS compared to baseline, proving the effectiveness of SLIT in our

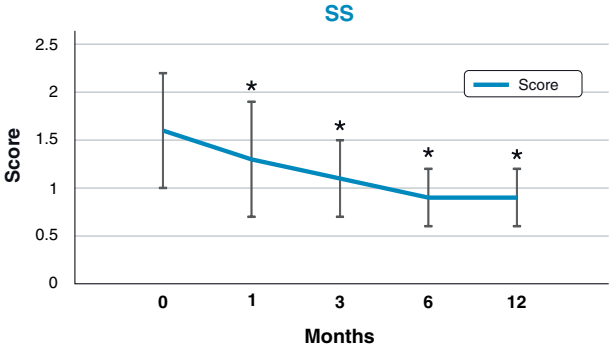

Figure 2
Comparison of symptom scores between baseline and months 1, 3, 6, and 12

* $p < 0.05$. Data expressed as means and standard deviations.

cohort, which is in agreement with other studies,[17] and further supporting the short-term clinical benefits of SLIT for patients with house dust mite-induced AR.

Although it has not been used in practice as a good biomarker of response, the mean wheal diameter on DP and BLO skin prick testing reduced significantly after treatment, showing a rapid reduction in allergic sensitization by SLIT.

AIT has among its mechanisms of action very early desensitization effects, modulation of T- and B-cell responses and related antibody isotypes, as well as inhibition of eosinophil, basophil, and mast cell migration into tissues and release of their respective mediators.[25] In the present study, the 12-month period of observation was too short to observe such reductions; further investigation is required to corroborate and supplement our findings.

Allergen-specific IgE shows an early rise and relatively late decline. These events occur in parallel with increases in IgG4, which rises continuously as treatment continues. After several months, the allergen-specific IgE/IgG4 ratio decreases. After a few months, reductions are seen in tissue mast cell and eosinophil populations, in release of their mediators, and in the late-phase response of the skin.[25]

SLIT may be associated with milder AEs (mainly pruritus or oropharyngeal edema), while serious side effects are rare. However, reports of AEs after immunotherapy are very heterogeneous in the literature.

The World Allergy Organization (WAO) standardized grading system for local reactions after SLIT, or mild symptoms of systemic reactions, should be used in future immunotherapy trial protocols.[18] In the present study, there were few local AEs and only three reports of systemic AEs, management of which did not require medication.

SLIT is self-administered and, therefore, many adverse effects likely go unreported.[19] In the present study, symptom assessments for pediatric patients were conducted by their parents or guardians to ensure unified assessment.

The VAS method has been widely used to assess the overall severity of AR and is recommended as a secondary outcome in SLIT trials. Del Cuvillo et al. proposed a classification method to assess the severity of AR based on VAS scores, which are also mentioned in the Chinese guideline for the diagnosis and treatment of AR.[20,21] In a retrospective study, patients who completed 3 and 4 years of SLIT showed

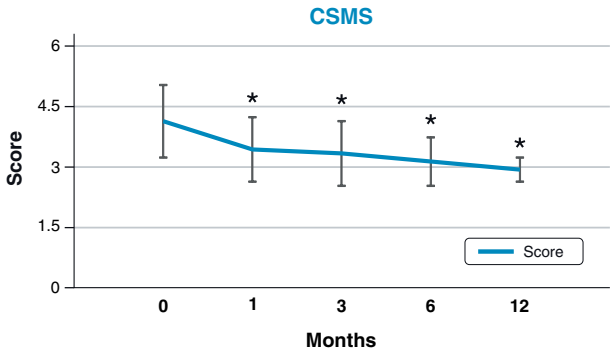

Figure 3
Comparison of combined symptom and medication scores between baseline and months 1, 3, 6, and 12
* $p < 0.05$. Data expressed as means and standard deviations.

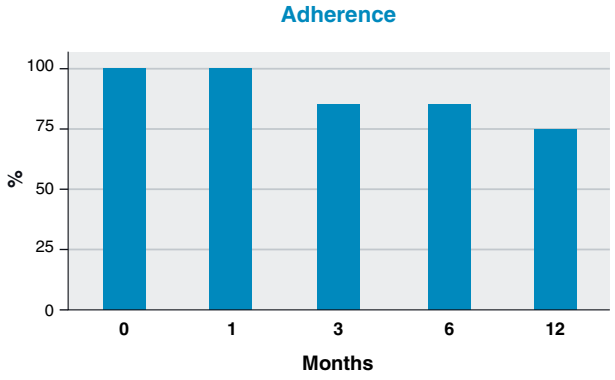

Figure 4
Comparison of percent adherence over 12 months of sublingual allergen immunotherapy (SLIT)

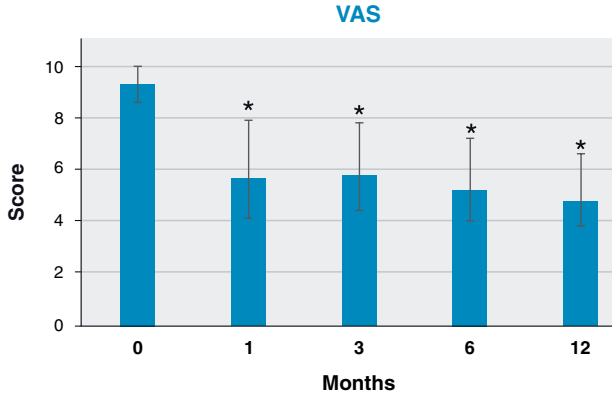

Figure 5
VAS scores of nasal and conjunctival symptoms at 12 months
VAS = visual analogue scale.
*Compared with baseline score, $p < 0.05$.
Data expressed as means and standard deviations.

a significant decrease in VAS scores compared with those who completed a 2-year course of SLIT.[21] Our study was not placebo-controlled, but our results are consistent with the literature regarding improvement of nasal and conjunctival symptom scores.

A real-life retrospective study by Bahceciler et al. of 90 children undergoing SLIT suggested it results in short- and long-term avoidance of inhaled corticosteroid (ICS) use in patients with allergic asthma.[22] Although several studies have evaluated the effectiveness of SLIT in preventing ICS use in patients with asthma, there is a dearth of studies on the efficacy of SLIT in patients with allergic asthma. In our study, we did not observe a significant symptom reduction in asthmatics over the two semesters analyzed, although their AR was moderate to severe, lung function was normal, and the ACT did not differ significantly across time points ($p = 0.16$).

We followed patients on SLIT for 12 months, but their treatment course did not end there; all are on a 3-4-year plan, which highlights the importance of long-term SLIT to maintain lasting effects. Lin et al. enrolled 500 participants to receive 1-3 years of SLIT and found that, in patients with AR, a 3-year course of SLIT was more effective than 1 year or 2 years.[23] Hamada et al. documented a significant decrease in nasal discharge, sneezing, nasal obstruction symptoms, and CSMS in patients receiving 4-5 years of SLIT compared with those receiving 1 year of SLIT,[10] thus showing that clinical outcomes tend to be even more satisfactory with more prolonged courses of SLIT.

Because SLIT requires daily administration of the allergen for at least 3 years to achieve clinical efficacy, adherence is a major issue from the perspective of patients, providers, and payers. However, adherence to SLIT is characterized by widely variable discontinuation rates. Based on controlled and observational studies that provided information on adherence over different treatment times, overall discontinuation rates have been approximated for the first to third years of treatment for SCIT (subcutaneous immunotherapy) (22%, 34%, and 26% respectively) and SLIT (42%, 29%, and 27% respectively).[17] In our study, no patient discontinued SLIT; however, there were cases of nonadherence.

In conclusion, the results obtained in this study suggest that SLIT should be administered for longer periods to allow assessment of broader outcomes. However, we also observed that SLIT is able to consistently provide short-term benefit in patients with moderate-severe AR, improving nasal symptoms, reducing the need for medication, and improving quality of life—a disease-modifying effect. SLIT was well tolerated by all patients and there were no treatment-related anaphylaxis events.

Acknowledgments

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