

Usefulness of specific immunotherapy in patients with severe perennial allergic rhinitis induced by house dust mite: a double-blind, randomized, placebo-controlled trial

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Summary

Objectives To evaluate the effectiveness of specific immunotherapy (SIT) in patients with severe house dust mite (HDM)-induced perennial allergic rhinitis using diary cards and objective endpoints.

Patients and Methods Thirty-six adult patients were selected with moderate to severe allergic rhinitis due to HDM allergy uncontrolled by regular anti-allergic drugs. Twenty-eight patients completed the study, 22 of these patients also had mild asthma. Subjects were stratified for HDM sensitivity on the basis of their 4-week diary card score and the size of their immediate and late-phase skin reaction to HDM. The groups were well matched for all relevant parameters. Patients were randomized to receive active preparation (Alutard®-SQ, ALK, *Dermatophagoides pteronyssinus* extract) or an identical placebo preparation. Increasing doses were administered until the maintenance dose was reached. This dose was then given once a month for 12 months.

Results Clinical efficacy was evaluated by symptom medication diary cards recorded for 4 weeks after 12 months of continuous treatment and compared with pre-treatment scores. Skin test reactivity was re-measured after 12 months of treatment to HDM, cat dander and codeine phosphate. After 1 year of treatment, the actively treated group showed a 58% reduction in diary card symptom scores ($P < 0.002$) and a 20% reduction in the use of rescue medication. The placebo group had a 32% reduction in symptom scores ($P = \text{NS}$), but no reduction in rescue medication requirements. The active group showed 36% reduction in skin prick test sensitivity to *D. pteronyssinus* ($P = 0.006$), while the placebo group values were unchanged. Skin reactivity to codeine was unchanged in both groups. No significant adverse reactions to SIT were encountered.

Conclusions One year of SIT for *D. pteronyssinus* in patients with poorly controlled rhinitis ($\pm$ mild asthma) produced clinically useful improvement as shown by symptom–medication diary cards and reductions in immediate skin reactions compared with placebo treatment.

Keywords house dust mite (HDM), late-phase reactions (LPR), specific immunotherapy (SIT), rhinitis

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Introduction

Over the past five decades, there has been a substantial increase in the prevalence of IgE-mediated allergic conditions, including perennial allergic rhinitis induced by house dust mite (HDM) [1].

Allergy to HDM is one of the most common causes of allergic disease worldwide with over 50% of asthmatic children in the UK sensitized [2]. Mite allergy frequently starts with symptoms of rhinitis, but over the longer term many patients may develop symptoms of bronchial asthma.

The management of HDM-induced allergic conditions includes avoidance measures and pharmacological treatment. Many sufferers are aware of their sensitivity yet find avoidance difficult or ineffective. Over the past 15 years, there have been improvements in treatments, including selective H_1 non-sedating antihistamines and topical nasal corticosteroids. These are usually effective for those with mild to moderate allergy if used regularly. A minority of people with HDM-induced allergic rhinitis respond poorly to treatment. In this subgroup of patients, specific immunotherapy (SIT) would be the treatment of choice in many countries throughout the world, including the United States, Scandinavia and continental Europe [3, 4]. In the UK, SIT for HDM allergy is rarely offered since the Committee on Safety of Medicines report in 1986. This questioned the efficacy and

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safety of SIT after a number of deaths from severe bronchospasm and anaphylaxis [5], many of these involved the use of HDM extracts. The benefits of SIT for hymenoptera venom [6] and grass pollen allergy [7] are now well established, and we have recently reported the benefits of SIT in cat-induced allergic rhinoconjunctivitis and asthma [8]. In the present study, the effects of HDM SIT were examined in a double-blind, randomized, placebo-controlled study, using the Alutard[®]-SQ vaccine (ALK, Hørsholm, Denmark), which is a highly purified and biologically standardized depot preparation of HDM with a low reported incidence of systemic reactions and high efficacy.

Materials and methods

Patients

Thirty-six adults (16 M, 20 F) were selected from the allergy clinics at Southampton General Hospital or the Royal Bournemouth Hospital.

Inclusion criteria:

- Troublesome clinical symptoms of moderate to severe HDM-induced perennial allergic rhinitis despite standard therapy and avoidance measures (standard therapy included anti-histamines, intranasal corticosteroids, $\pm$ sodium cromoglycate). Mild asthma was present in 28 of 36 subjects and did not exclude the subject, provided their chest symptoms were well controlled on treatment with a normal FEV₁ and less than 10% variation in PEFR monitoring on their regular asthma medication.
- Diary card assessments of symptoms and medication use over 1 month were completed prior to entry to the study and randomization. This was to confirm severity and to observe compliance with regular medication.
- A positive skin prick test (weal diameter of 5 mm or more) to *Dermatophagoides pteronyssinus* Soluprick[®], 10 Heps ALK was essential, as this corresponded exactly with the desensitizing vaccine used throughout the study.
- A late-phase reaction of 10 mm or more to 45 biological units of intradermal *D. pteronyssinus* was required for entry to the study.

Exclusion criteria:

- A significant clinical history of other allergies.
- An SPT greater than 3 mm to *D. farinae* (Soluprick, ALK Laboratories, Denmark)
- A history of SIT in the previous 5 years.
- A history of cardiovascular or other medical or immunological diseases contraindicated for SIT.

All patients had a baseline full medical examination with basic pulmonary function tests (PEFR, FVC, FEV₁) and routine blood tests. Of the 36 patients who were selected, eight subjects (four active, four placebo) dropped out early from the study due to difficulties in attending for the injections with work commitments. There were insufficient data on the subjects for an intention-to-treat analysis. Dust

samples from each patient's mattress and living room carpet were assessed once during the study. This was deliberately scheduled just prior to the 12-month reassessment, so that comparison of mite levels between the groups could be available at the time of their final symptom-medication diary card. All the subjects were instructed not to undertake additional anti-mite measures during the course of the study. ALK Laboratories, measured the allergen content of dust samples.

Study design and ethics

The trial was performed as a double-blind, randomized, placebo-controlled study, and was approved by the Southampton University Hospital joint ethics committee and Royal Bournemouth Hospital ethics committee, UK. All patients gave written informed consent. Each patient's GP was informed of the participation of their patient in the study and all gave written permission.

Stratification and randomization

In order to achieve an even randomization of patients in the active and placebo groups, the patients were carefully stratified on the basis of diary card symptom scores, immediate and 24 h late cutaneous reactions to HDM before randomization (Table 1).

After stratification, three groups (A, B and C) were randomized separately to active or placebo by the use of computer-generated random numbers. Group A was judged to be mild. Group B had moderate sensitivity and Group C had severe sensitivity. Four dropouts occurred from Groups A and B shortly after enrolment, later decoding showed these subjects to be four active and four placebo subjects.

Table 1. Stratification criteria for randomization γ from skin prick test reaction, late cutaneous reaction (LPR) and diary cards

Stratification criteria for randomization			Total possible score
Diary card			
Symptoms only (weekly average)	< 100 scored = 0 > 100 scored = 1		1
SPT (mm)			
Soluprick HDM	5 mm = scored 1		
At 15 min	6–9 mm = scored 2 10–15 mm = scored 3		3
24 h LPR			
To HDM (45 BU)	10–15 mm = scored 1 16–30 mm = scored 2 31–45 mm = scored 3 45–60 mm = scored 4		4
Total possible score			8
Group	No. of subjects	Total score	Grade
A	10	4	Mild sensitivity
B	16	5–6	Moderate sensitivity
C	10	7–8	Severe sensitivity

HDM, house dust mite.

Diary cards

Diary cards were commenced in early April following the reduction in the prevalence of winter viruses and prior to the grass pollen season, since 14 patients were grass pollen reactive. Four patients in the study showed a tree pollen reaction mean of 3 mm that was considered unlikely to interfere with diary card recording.

Patients kept a diary card for daily assessment of their rhinitis and chest symptoms, and recorded both PEFR measurements and medication use and any viral illness. Diary cards were completed for a minimum of 4–6 weeks before randomization, and again after 1 year of treatment. During this period, the subjects were seen twice a week to ensure compliance. The presence of a viral illness resulted in an extension of the diary card recording, so the illness period could be deleted from the analysis. Participants used their anti-allergic drugs (inhaled asthma therapy or intranasal steroids) regularly to control symptoms as they had done prior to enrolment for the study, but were asked to record this and the use of all rescue medication on their diary cards. Rescue medication included antihistamines, inhaled B_2 agonist and increased use of steroids (oral, intranasal and inhaled). The severity of individual symptoms for nose (sneezing, running, itching and blocking), and chest (cough, wheeze, tightness and breathlessness) were scored on a scale from 0 to 3 with 0 = no symptoms, 1 = mild, 2 = moderate and 3 = severe. A total 4-week score for each symptom was calculated. The maximum possible score per week was 21 for each symptom. 'Illness periods' were excluded from the diary card analysis. The total weekly symptom scores were added together to derive a total 'symptom score' for the 4-week observation period. The final symptom score was the total score of 4 weeks.

Drugs were scored as follows:

- (a) Each nasal spray or inhalation = 1.
- (b) Each antihistamine tablet or prednisolone tablet (5 mg) = '2' (paracetamol or similar tablets were not counted).

Peak expiratory flow was measured twice daily with a Mini-Wright[®] peak flow meter in the asthmatic subjects and recorded on the diary card. To ensure consistency, each patient was supplied with their own peak flow meter.

Immunotherapy protocol

The depot preparation of Alutard[®]-SQ extract for *D. pteronyssinus* was used. The maintenance dose of 1.0 mL (100 000 SQ-U/mL) contained 7 µg/mL of Der p1 absorbed onto aluminium hydroxide for slow release. Its biological activity was equivalent to 10 000 biological units/mL. A single batch of Alutard[®]-SQ was used throughout the study. Identical placebo packs contained diluent and had progressive concentrations of histamine (ALK). The doctors carrying out the SIT had no knowledge of, nor access to the randomization code, which was kept locked and sealed by a doctor not involved with the study. The code was only opened after all the data had been collected and were ready for statistical analysis. Before each injection, the patient's general condition and reaction to the last injections were assessed and PEFR was measured with a Mini-Wright[®] peak

Table 2. HDM immunotherapy schedule for the induction course

Injection number	Vial allergen concentration (SQ-U/mL)	Dose (SQ-U)	Dose volume (mL)
1	100	10	0.1
2	100	50	0.5
3	1000	100	0.1
4	1000	500	0.5
5	10 000	1000	0.1
6	10 000	5000	0.5
7	100 000	10 000	0.1
8	100 000	20 000	0.2
9	100 000	40 000	0.4
10	100 000	60 000	0.6
11	100 000	80 000	0.8
12	100 000	100 000	1.0
Maintenance	100 000	100 000	1.0

HDM, house dust mite.

flow meter. All SIT injections were given by doctors who were experienced in this form of treatment. The SIT schedule is shown in Table 2. Patients received an up dosing injection twice weekly and reached a maintenance dose of 100 000 SQ-U within 8–10 weeks. An observation period of 1 h postinjection was followed in line with the August 1994 CSM recommendations. Maintenance injections were administered monthly for 1 year. Adjustments in the schedule were made on an individual basis according to standard guidelines for SIT [4]. Injections were postponed if the subject was at all unwell. Patients were carefully observed for 1 h after each injection, during which PEFR was recorded at 30-min intervals. Any observed changes would be judged to be manifestations of SIT-induced reactions. Appropriate drugs and resuscitation equipment for the treatment of anaphylaxis were available, but never required.

Asthmatic subjects (Table 3)

Twenty-two subjects had mild asthma, all took B_2 agonists either regularly or as required. Only two subjects used long-acting B_2 agonists. Seventeen subjects were taking long-term (5 years +) regular inhaled steroids. Thirteen subjects were taking beclomethasone (200–800 µg daily), two budesonide 400 µg daily and two fluticasone (250 µg daily).

Skin tests

- (a) At screening, skin prick tests were performed with appropriate controls on the flexor aspect of the forearm using common airborne allergens, including HDM.
- (b) Skin tests to *D. pteronyssinus* (Soluprick[®]-SQ, ALK) plus *D. farinae* (Solupricks SQ) were performed. These extracts correspond with desensitizing vaccines, but only those patients with dominant *D. pteronyssinus* reactions were selected for the study. The weal diameter at 15 min of 5 mm(+) was required for entry to the study.
- (c) Duplicate titration skin prick tests were carried out on entry into the study (before randomization), and after 1 year of treatment. These titration tests were performed on

Table 3. Baseline data for the two groups

Parameter	Active	Placebo	P-value
Number of patients	15	13	
Sex (male/female)	6/9	7/6	
Age			
Mean	33	37	
(range)	(19–48)	(23–55)	
Asthmatic	14	8	NS
Eczema	9	3	NS
Intranasal steroids	15	13	
Oral antihistamines	15	13	
B ₂ Agonists–prn	12	2	
Regular	2	6	
Inhaled steroids	11	6	
Theophyllines	2	0	
HDM SPT (mm)	6.30 ± 0.61	5.38 ± 0.4	NS
HDM RAST (IU/mL) (mean)	2.77 ± 0.85	3.66 ± 0.84	NS
HDM SPT AUC	33.11 ± 2.80	34.72 ± 3.43	NS
HDM LPR (mm) 24 h	30.18 ± 3.29	36.79 ± 4.78	NS
Cat SPT (mm)	4.69 ± 0.74	4.00 ± 0.89	NS
Cat SPT AUC	25.41 ± 4.62	27.86 ± 5.39	NS

HDM, house dust mite.

both *D. pteronyssinus* and cat dander. This was to assess whether a separate allergen (cat) also showed skin sensitivity changes during HDM SIT. The volar aspect of both forearms was used with a parallel line bioassay design [9]. Aqueous extracts of *D. pteronyssinus* and cat dander (Aquagen[®]-SQ, ALK) were used at log+1/2 log concentrations as follows – 100, 300, 1000, 3000, 10 000, 30 000 and 100 000 SQ-U/mL. The same batch of allergen was used throughout the whole study. Titration tests with codeine phosphate were also performed on both occasions to assess non-specific mast cell releasability. Codeine phosphate was used at 10, 30 and 60 mg/mL.

Area under the curve estimations

All titration weals were outlined in ink at 15 min with a permanent record taken by applying transparent adhesive tape, which was then transferred to the case record card. The mean diameters were calculated for each allergen concentration (HDM, cat and codeine phosphate). A graph of mean skin test diameter (mm) vs. log concentration in SQ-units was plotted for each patient. This allowed assessment of sensitivity changes after 1 year of immunotherapy for each extract and the area under the curve (AUC) was calculated for comparisons in each individual (pre–post treatment) and between active and placebo groups.

- (d) Late-phase reactions to HDM (45 biological units) were assessed in duplicate at enrolment to the study using diluted aqueous extracts (Aquagen SQ). A volume of 0.03 mL was injected intradermally giving a dose of 45 BU of *D. pteronyssinus*.

This dose had been shown to produce an adequate LPR without inducing systemic reactions. The immediate weal diameters were measured at 15 min and the LPR diameter

was measured at 24 h. Aquagen SQ is a freeze-dried extract for reconstitution with aqueous Aquagen[®] diluent. Measurements of these reactions were repeated at 12 months. The single diluted batch for the repeat late reactions was discarded accidentally by an assistant before all subjects were injected. The post-treatment LPRs have therefore been omitted due to this protocol violation.

HDM measurements in bed and living room carpet

This was measured once just prior to the 12-month reassessment. An HDM Hoover sampler with filters was used. A 2-min Hoover of the mattress was performed and a separate one square metre of living room carpet was sampled for 2 min. The samples were measured by ALK.

Quantification and statistics

All data were collected double-blind with respect to the clinical protocol, entered onto a PC and analysed with the aid of the Statistical Package for Social Sciences (SPSS-PC) [10]. Group comparisons were made by parametric tests where appropriate and intragroup paired data were compared by paired Student's *t*-tests. Values of *P* < 0.05 were regarded as statistically significant.

Results

Baseline group comparisons (pre-treatment) (Table 3)

The active and placebo groups were well matched for age and gender. The active group contained more patients with eczema (nine vs. three) but this was not a randomization criterion. Specific IgE levels to HDM pre-treatment were also matched in each group (*P* = 0.489).

Baseline skin test comparisons (pre-treatment) (Table 3)

The two groups had similar sensitivity to HDM as assessed by skin tests (mean SPT 6.30 mm active vs. 5.38 mm placebo). The AUC for HDM titration SPT showed no significant difference. The late-phase reaction to HDM was also similar (30.18 mm active vs. 36.79 mm; placebo). All subjects showed similar cat dander sensitivity (Table 3).

Assessment of local and systemic reactions

A mean of 16 injections was required to reach the maintenance dose for both the groups. Large local reactions at the injection sites were not troublesome and no treatment was given. Seven mild systemic reactions occurred during the induction phase. All were associated with active treatment. Five of these occurred in the same subject requiring dose reductions and more injections (21 injections) to reach the maintenance dose. All seven reactions produced cough and rhinorrhoea. These reactions occurred within 30 min of allergen injection and responded promptly to inhaled salbutamol and/or sublingual adrenaline from a Medihaler-Epi[®] Spray. No severe systemic reactions were encountered in any patient.

HDM levels in beds and carpets

HDM allergen levels ng/g dust showed no statistical difference between the groups ($P = 0.379$) (Table 4). *D. pteronyssinus* was shown to be the highest compared with *D. farinae* and *D. microceras* and appropriate to the immunotherapy vaccine used. This sampling was completed at the time of final assessment, so that significant differences in mite level in beds and carpets could be assessed along with symptom medication diary card responses at 12 months. Visiting 28 homes was a large undertaking and quite informative. Ten subjects had HDM-proof covers on their mattresses, duvets or pillows. Most had excessive soft furnishing, dusty rooms with many rugs and longhaired carpets in the living room and bedroom. Most 'mite measures' when questioned again in the home at the time of sampling had consisted of:

1. Mattress hoovering 1 × week when sheets changed (26 subjects).
2. Washing bed linen very hot to kill mites (20 subjects).
3. Regular hoovering (28 subjects).
4. Efforts to avoid high humidity levels in the house (16 subjects).
5. Declutter of bedroom (22 subjects).
6. Carpet removal (eight subjects).

Table 4. Domestic house dust mite (HDM) allergen level in bed and carpets for the active and placebo groups

HDM levels Ng/g dust	Active group	Placebo group	<i>P</i> -value
	Mean	Mean	
Mattress			
<i>D. pteronyssinus</i>	6349.53	9230.58	0.571
<i>D. farinae</i>	1031.93	25.16	0.364
<i>D. microceras</i>	7.266	14.41	0.560
Living-room carpet			
<i>D. pteronyssinus</i>	1916.20	4802.03	0.176
<i>D. farinae</i>	18.70	25.33	0.730
<i>D. microceras</i>	0	0	0
Bedroom+living-room	9176.93	14098.00	0.379

The overall impression was that many of these patients had suffered HDM symptoms due, in part, to high mite levels in the house.

Symptom-medication diary card assessments after 12 months of treatment (Table 5)

After treatment, the active group showed a significant reduction in symptom scores by 58%, a 30% reduction was seen in the placebo group, but this was not statistically significant. The active group also showed a non-significant reduction in drug use by 20% (Table 5) supporting the recorded reduction in symptom scores. No similar reductions in drug use occurred in the placebo group (pre 65, post 66 $P = 0.0968$). Table 5 shows individual scores for chest and nasal symptoms and chest and nasal drug use.

Titration skin prick tests after 1 year SIT (Table 6)

In the active group, cutaneous sensitivity to HDM calculated by AUC showed a reduction after SIT by 36%. The placebo group showed no significant change at 1-year titration SPT to an unrelated allergen 'cat dander' and showed no significant change after 12 months of SIT for HDM. (Table 6).

Table 6. Skin tests: changes after 1 year of HDM SIT

Skin test	Active				<i>P</i> -value
	Pre-treatment		Post-treatment		
	Mean	SEM	Mean	SEM	
HDM SPT AUC	33.11	2.80	21.14	2.66	0.006
Cat SPT AUC	25.41	4.62	23.59	4.69	NS
Codeine 60 mg/mL SPT	7.00	0.58	7.36	0.34	NS
Placebo					
HDM SPT AUC	34.72	3.43	33.39	3.22	NS
Cat SPT AUC	27.86	5.39	27.58	5.25	NS
Codeine 60 mg/mL SPT	7.15	0.87	7.83	0.46	NS

HDM, house dust mite; AUC, area under curve.

Table 5. Diary card scores for active and placebo groups

Score	Active group		<i>P</i> -value Pre vs. Post	Placebo group		<i>P</i> -value Pre vs Post	Post-treatment active vs placebo <i>P</i> value
	Pre	Post		Pre	Post		
Total symptom score	171 ± 23	72 ± 26	0.002*	195 ± 42	132 ± 48	NS	NS
Total drug score	74 ± 31	59 ± 15	NS	65 ± 26	66 ± 35	NS	NS
Total chest score	35 ± 9	31 ± 6	NS	41 ± 9	20 ± 11	NS	NS
Total chest drugs	39 ± 9	40 ± 14	NS	29 ± 17	33 ± 11	NS	NS
Total nasal score	135 ± 18	40 ± 12	0.013*	153 ± 27	111 ± 18	NS	0.04
Total nasal drugs	45 ± 10	18 ± 36	0.04*	35 ± 9	32 ± 14	NS	NS
PEFR % predicted	96 ± 4%	98 ± 3%	NS	108 ± 10	113 ± 02	NS	NS

*Significant difference demonstrated.

Discussion

This double-blind, randomized, placebo-controlled study indicates that 12 months of SIT for HDM allergy was useful and improved symptom scores by 58%. As a result, medication use was reduced by 20%. The treatment was well tolerated despite 22 of the 28 subjects having a diagnosis of mild asthma, normally a contradiction to SIT in the UK. HDM measurements in carpets and mattresses were made just prior to the 12-month reassessment, so differences in exposure levels were checked in case of possible bias. Fortunately, these results confirmed *D. pteronyssinus* to be the predominant allergen in carpets and mattresses of these patients and corresponded with the patient selection on the basis of their original skin tests. The difference in symptom medication diary cards at 12 months confirmed that differences in allergen exposure between the groups did not account for the improvement. Titration skin prick testing to *D. pteronyssinus* was reduced by 36% in the active group, confirming a reduction in objective sensitivity in line with the clinical improvement. Immediate SPTs were reduced by SIT, but this reduction may not last and does not correlate as well with clinical efficacy as a reduction in the late-phase reaction [11]. The groups were well matched at baseline for LPR diameter. After 12 months of SIT, the single batch of freshly diluted Aquagen for all repeat cutaneous LPR testing was discarded by an assistant. This occurred when only 50% of patients had been injected. As a result of this protocol violation, the late reactions at 12 months have been removed from the analysis. This would have been the most reliable of objective sensitivity changes. However, the authors were left only with titration SPT values. Although *D. pteronyssinus* sensitivity and cat sensitivity commonly coexist clinically, there is no serological evidence of cross-reactivity between the antigens of cat dander and *D. pteronyssinus* [12]. It was therefore not surprising that SPT to cat dander did not change at 12 months. The Alutard SQ extract maintenance dose of 100 000 Sq-U/mL for *D. pteronyssinus* is of lower biological unit potency (10 000 BU/mL) than Alutard SQ cat dander (100 000 BU/mL) or even grass pollen (30 000 B/mL). This could explain the low incidence of side effects from use of the *D. pteronyssinus* extract, but could equally limit its maximum clinical benefit. SIT is probably 'a high-dose tolerance' phenomena with higher systemic side-effects associated with the greater potency of the extracts, as shown in other studies of SIT with HDM [13–16]. In our study, all subjects reached the maintenance dose of 100 000 SQ-units, which represents 7 µg Der p1. Above this dose, the asthmatic subjects may have been problematic. The authors felt that many subjects could have tolerated a higher maintenance dose and reaped further clinical benefit. The clinical efficacy of SIT for HDM appears slow in onset with benefit continuing slowly with continued immunotherapy. Serious systemic reactions during SIT may occur especially in patients with asthma compared to rhinitic patients without asthma. This study showed no apparent difficulty in these patients with chronic, but mild, stable asthma having immunotherapy for HDM with this extract. In a retrospective study of fatalities associated with immunotherapy, acute asthma was listed as the most common cause of death [17]. A recent study has reported that both large local and mild systemic reactions

were much more common in patients with asthma (0.39% for each side-effect) compared to patients with perennial rhinitis, but no asthma [18]. No late systemic reactions were encountered in the present study; this is in accordance with other studies using a similar dosage schedule [19, 20]. Successful SIT may cause allergen-reactive T cells to be down-regulated or tolerized by modulation of a Th2-type lymphocytes response [21]. Unfortunately, our data on the LPR and the biopsies taken from the LPR sites were not analysable due to the error in post-treatment, late-phase induction and the difficulty in attempting to interpret the results. In conclusion, HDM-SIT appears to offer additional benefits (in terms of symptom control) over and above standard drug therapy and allergen avoidance, in patients with persistent symptoms despite optimal medical management. SIT with a depot HDM extract (Alutard®-SQ) significantly reduced symptoms and skin sensitivity with an acceptable minimal level of side-effects. The results of this study verify that SIT is useful, safe and can reduce symptoms in mite-sensitive adult patients with allergic rhinitis even when complicated by mild allergic asthma.

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