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*Original Article*

# Efficacy of dust mite specific immunotherapy for allergic rhinitis in dust mite-sensitive subjects

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**Abstract:** Objective: To evaluate the therapeutic effect of specific immunotherapy (SIT) with a standardized dust mite vaccine in 35 dust mite-sensitive subjects with allergic rhinitis (AR). Methods: AR symptoms and signs and AR-related distress were scored before SIT treatment and after 1 year and 2 years of SIT treatment. Total scores before and after treatment were compared to determine treatment efficacy. Results: After treatment for 1 year, all symptoms, signs and distress scores were significantly reduced compared to before treatment ($P<0.05$). After 2 years of SIT treatment, all scores were significantly reduced compared to 1 year of treatment. Efficacy rates were compared between children and adults at 1 and 2 years of treatment; no significant differences were found. No serious adverse reactions were experienced during treatment. Conclusion: Standardized dust mite allergen vaccine is a safe, effective treatment for AR in dust mite-sensitive patients, and should be considered as a routine treatment. Two years of treatment is more effective than one year treatment.

**Keywords:** Allergic rhinitis, specific immunotherapy, allergen vaccines, therapeutic efficacy

## Introduction

Allergic rhinitis (AR) is an allergic inflammation of the nasal airways, which is induced by interactions between environmental and genetic factors [1]. AR is characterized by release of inflammatory mediators induced by IgE and by involvement of active immune cells, specifically those involved in the Th2 immune response, when atopic individuals come in contact with allergens [2, 3]. The global incidence of AR, like other allergic diseases, exhibits a gradually increasing trend, which is especially obvious in developed countries. This indicates that AR is not only a public health problem, but also a problem related to social economy [4]. In 2010 the World Health Organization (WHO) published *Allergic Rhinitis and Its Impact on Asthma* (ARIA), which lists AR treatment options as avoiding contact with allergens, medication, specific immunotherapy (SIT), education and surgery [5]. Many patients are sensitive to multiple antigens, both indoor and outdoor, making clinical improvement through antigen avoidance alone difficult or impossible. Nasal corticosteroids and antihistamines can alleviate symptoms for most patients [6], but since these drugs do not regulate immune status they fail to provide long-term maintenance after drug withdrawal. As a biological response regulator, immunotherapy is the only way to prevent the immune responses that lead to AR and thereby alter the natural course of the disease. The effect of immunotherapy on AR has been fully affirmed and recommended by the WHO, and the standardized allergen vaccine was recommended for use in SIT [7].

In the present work, we studied the efficacy and safety of dust mite allergen vaccine treatment in dust mite-sensitive patients with AR in Shanghai, China. Subjects were followed for two years. Our results show that this treatment is indeed effective and safe.

## Materials and methods

### *Study subjects*

This study was carried out from November, 2012 to November, 2014, at the No. Eight

**Table 1.** AR symptom scoring

| Score | Sneezing* | Rhinorrhea# | Nasal Obstruction | Rhinocnesmus |
|---|---|---|---|---|
| 1 point | 3-5 | ≤4 | Felt on inspiration | Intermittent |
| 2 points | 6-10 | 5-9 | Intermittent | Formication, tolerable |
| 3 points | ≥11 | ≥10 | All day | Formication, intolerable |

*Number of continuous sneezes; #Number of times nose was blown per day.

**Table 2.** SIT efficacy after 1 and 2 years of treatment

| Period | Highly effective (%, n) | Effective (%, n) | Ineffective (%, n) | Total effective rate (%, n) |
|---|---|---|---|---|
| 1 year | 11.43 (4) | 65.71 (23) | 22.86 (8) | 77.14 (27) |
| 2 years | 45.71 (16) | 51.43 (18) | 2.86 (1) | 97.14 (34) |

People's Hospital of Shanghai Department of Otorhinolaryngology. Inclusion criteria included AR diagnosis according to Guidelines for Diagnosis and Treatment of Allergic Rhinitis [8], lack of symptom control by antihistamines or moderate or higher doses of inhaled corticosteroid hormone, skin prick test (SPT) result of at least ++ for dust mite allergen, and willingness to accept long-term immunotherapy. Exclusion criteria included presence of severe immune system disease, moderate or severe asthma (forced expiratory volume (FEV) <70% of predicted), cardiovascular disease, cancer, chronic infectious disease, mental disease or pregnancy, as well as evidence of poor treatment adherence.

40 patients were enrolled in the study, but 5 left the study before completion. Of the 35 subjects who completed the study, 19 were male and 16 were female. Their ages ranged from 6 to 50 years, with a mean age of 21.7±10.4 years. Disease duration ranged from 2 to 25 years.

This study was approved by the No. Eight People's Hospital ethics committee, and informed consent was obtained from all subjects or from their parents or guardians.

*SIT treatment*

Subjects received standardized dust mite allergen immunotherapy with Mites Allergens ALK(503) D.p (ALK-Abello, Denmark), known commercially as Alutard SQ. The agent was injected slowly subcutaneously in the lateral upper arm, under aseptic conditions. SIT included two stages: the treatment stage in which subjects received an initial dose of 20SQ-U (SQ-U is the standard unit dose) followed by increasing doses (40, 80, 200, 400, 800, 2000, 4000, 8000, 10000, 20000, 40000, 60000, 80000 and 100000 SQ-U) every week for 15 weeks, and the maintenance stage in which 100000 SQ-U was injected every 4-8 weeks for approximately 2 years. Subjects who experienced symptoms of allergic rhinitis during SIT were treated with antihistamines or intranasal corticosteroids in the acute stage, and these drugs were stopped during the remission stage and 2 weeks before evaluation.

*Data collection*

Before beginning SIT treatment, each subject's pretreatment, or baseline, condition was evaluated and scored by a physician. The following AR symptoms were scored on a 3 point scale: sneezing, rhinorrhea (nasal discharge), nasal obstruction and rhinocnesmus. The symptom scoring system is shown in **Table 1**. AR signs were also scored on a 3 point scale as follows: 1 point for turbinate swelling with visible nasal septum and middle turbinate; 2 points for small gap between inferior turbinate and nasal base; 3 points for inability to visualize middle turbinate.AR-induced distress was reported by subjects using a visual analogue scale (VAS) [9]. VAS scores were recorded subjectively, with scores of 1-3 defined as mild distress, 4-7 as moderate distress and 8-10 as severe distress. Subjects' condition, as well as efficacy and safety of the treatment, was evaluated and scored again after one and two years of SIT via outpatient follow-up and telephone follow-up.

*Therapeutic effect of SIT*

SIT efficacy was evaluated according to the criterion established in Chongqin 2010 [10], with curative effect calculated as (pretreatment score-post-treatment score)/(pretreatment score) ×100%, with the score being the sum of the individual symptom and signs scores. Curative effect was calculated after one year of treatment and after two years of treatment.

Efficacy results were categorized into three levels based on the curative effect score: highly

**Table 3.** Effect of SIT on AR symptoms and signs

| Item | Pre-SIT | 1 yr after SIT | 2 yr after SIT | $t_1$ | $t_2$ | P |
|---|---|---|---|---|---|---|
| Sneezing | 2.31±0.57 | 1.23±0.60 | 0.87±0.38 | 7.72 | 2.29 | 0.013 |
| Rhinorrhea | 2.25±0.60 | 1.34±0.64 | 0.81±0.52 | 6.14 | 3.8 | 0.026 |
| Nasal obstruction | 1.81±0.58 | 1.11±0.57 | 0.73±0.52 | 5.09 | 2.91 | 0.017 |
| Rhinocnesmus | 1.93±0.61 | 0.97±0.65 | 0.45±0.40 | 4.86 | 4.03 | 0.032 |
| Signs score | 1.60±0.35 | 1.15±0.45 | 0.76±0.40 | 4.67 | 3.83 | 0.028 |
| Total score | 9.90±1.67 | 5.80±2.25 | 3.42±1.54 | 9.17 | 5.49 | 0.009 |

$t_1$ is the comparison between pretreatment and 1 year of SIT, using the paired Student's t test; $t_2$ is the comparison between 1 year and 2 years of SIT.

**Table 4.** Effect of SIT on VAS

| Treatment period | VAS value | t | P |
|---|---|---|---|
| Pretreatment | 7.34±1.58 | - | - |
| 1 year | 3.35±1.79 | $t_1$=9.89 | 0.027 |
| 2 years | 0.71±1.07 | $t_2$=7.49 | 0.032 |

$t_1$ is the comparison between pretreatment and 1 year of SIT, using the paired Student's t test; $t_2$ is the comparison between 1 year and 2 years of SIT.

effective (≥66%), effective (26-65%), and ineffective (≤25%). Meanwhile, according to VAS standard, definite clinical significance was defined as the improvement of overall subjective symptoms >25% [9].

*Adverse reaction*

Reactions to SIT were recorded by the subject after each injection. Reactions were rated level 1, 2, 3 or 4 based on the following criteria: 1) local allergic reaction (swelling, redness and itching) after injection; 2) eye redness and swelling within 24 hours of injection; 3) urticarial or asthma within 24 hours of injection; 4) allergic shock after injection.

*Statistical analysis*

Software SPSS16.0 was used to analyze the data. Symptoms score, signs score and VAS score before SIT treatment and after SIT treatment for 1 or 2 years was compared using the paired Student's t test. The data were expressed as mean ± standard deviation. Statistical significance is defined as $P<0.05$.

## Results

*Therapeutic effect of SIT*

40 subjects were enrolled, but only 35 completed the 2 year SIT treatment. Statistical analysis was based on the complete data from these 35 subjects. Therapeutic effect of SIT was calculated as described in Materials and Methods after one year of SIT and after two years of SIT. As shown in **Table 2**, the total effective rate was 77.14% (27/35) after one year of SIT, including 11.43% (4/35) highly effective, 65.71% effective (23/35), 22.86% ineffective (8/35). After two years' SIT, the total effective rate had increased to 97.14% (34/35), including 45.71% (16/35) highly effective, 51.43% (18/35) effective, and only 2.86% ineffective (1/35). Total effective rate after two years of SIT was significantly higher than the rate after one year of SIT.

*Effect of SIT on symptoms and signs scores*

The effectiveness of SIT was evaluated based on the scores of symptoms and signs. The symptoms and signs scores (SSS) were accessed before treatments after subjects were treated with SIT for 1 year or 2 years. The results showed that individual and total SSS decreased with period of treatment increased. SSS after 1 year of SIT treatment was significantly lower than pretreatment SSS, and SSS after 2 years' SIT was significantly lower than after 1 year's SIT (**Table 3**).

*Effect of SIT on AR-related distress*

Subjects rated their AR-related distress before treatment and after one year and two years of SIT using a VAS, as described in Materials and Methods. Distress ratings were significantly lower after one year of SIT compared to pretreatment levels, andsignificantly lower with two years of SIT compared to one year of SIT (**Table 4**).

*Comparison of SIT efficacy in children and adults*

In this study, 18 subjects were children (<18 years) and 17 were adults (≥18 years). After one year of SIT, the total effective rate was 83.33% (15/18) for children and 70.59% for adults, with no statistical significance between two groups. After two years of SIT, the total

**Table 5.** Comparison of SIT efficacy in children and adults

| | Total (n=35) | Children (n=18) | Adults (n=17) | *P* |
|---|---|---|---|---|
| 1 year SIT | | | | |
| Highly effective | 4 | 3 | 1 | |
| Effective | 23 | 12 | 11 | |
| Ineffective | 8 | 3 | 5 | |
| Total effective rate (%) | 77.14 | 83.33 | 70.59 | 0.23 |
| 2 years SIT | | | | |
| Highly effective | 16 | 9 | 7 | |
| Effective | 18 | 10 | 8 | |
| Ineffective | 1 | 0 | 1 | |
| Total effective rate (%) | 97.14 | 100 | 93.75 | 0.16 |

effective rate was 100% (16/16) for children and 93.75% for adults, with no statistical significance between two groups (**Table 5**).

*Safety evaluation*

During the 2 years of SIT treatment, a total of 1015 injections were given to the 35 study subjects. The incidence of adverse reactions was 1.78%, with three subjects exhibiting systemic reactions, for a total of 18 times. Of the 18 adverse reactions, 17 were level one, 1 was level two, and none were level 3-4. Symptoms of the adverse effects were relieved completely after administration of symptomatic treatment.

## Discussion

The results of this study show that AR symptoms improved after SIT with standard allergen vaccine Alutard SQ in subjects known to be sensitive to dust mites after both one and two years of treatment. AR symptoms and signs scores and VAS scores were significantly lower after one year of treatment compared to pretreatment, and were significantly lower after two years of treatment compared to one year. The total effective rate of SIT was 77.14% (1 year) and 97.14% (2 years). Thus, dust mite specific immune therapy was effective for dust mite-sensitive patients with AR, and two years of treatment is more effective than one year.

Several studies of SIT effectiveness have used a longer time frame. A study by Aasbjerg et al [11] showed that SIT treatment for approximately 3 years is necessary to achieve a decrease in serum specific IgE to normal levels, but that longer treatment duration was necessary to significantly improve clinical symptoms. Milani et al [12] reported that sublingual SIT was able to significantly reduce the nasal symptoms of AR after three years of immunotherapy. In the present study, we confirmed that two years of SIT achieved better results than one year. Additional studies will be necessary to determine whether longer times of treatment with dust mite specific immunotherapy can achieve even better results.

According to Aasbjerg et al [11], specific immunotherapy is more effective in patients who are sensitive to a single definite allergen. Most of the subjects in the present study responded positively to other allergens in addition to house dust mite and dust mite, but overall symptoms and signs of AR improved after mite specific immunotherapy. Therefore, Alutard SQ is effective for AR patients who are sensitive to other antigens in addition to dust mites. It is unclear how specific immunotherapy can result in nonspecific desensitization. Further studies are needed to reveal the underlying mechanism.

Reports on the SIT efficacy in children compared to adults have shown various results. Takeuchi et al [13] reported no significant difference between children and adults, but Heinrich, Lee JE et al [14, 15] reported that the younger the age, the better the efficacy. In the present study the total effective rate after SIT treatment for one year or for two years was not significantly different between children and adults. Since the sample size was small in this study, this comparison should be repeated with a larger study population.

## Conclusions

Specific immunotherapy with standardized dust mite allergen vaccine is a safe, effective method to achieve relief of AR in dust mite sensitive patients, and therefore could be used as a routine treatment. Two years of SIT achieved better results than one year.

## Disclosure of conflict of interest

None.

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