



## EFFECTIVENESS OF SUBLINGUAL IMMUNOTHERAPY IN PATIENTS WITH ALLERGIC RHINITIS CAUSED BY COTTON DUST

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### Abstract

**Introduction:** SLIT has been considered to have more advantages than SCIT in treating allergic rhinitis. Allergic rhinitis caused by cotton dust were concerned in Viet Nam. The study aimed to evaluate the effectiveness of SLIT in patients with allergic rhinitis caused by cotton dust.

**Materials and methods:** We used standard cotton dust allergen to treat patients with allergic rhinitis caused by cotton dust in 3 years. The functional symptoms, physical symptoms and igE, igG4 concentration, prick test were compared before and after treatment, and adverse effects were recorded.

**Results:** Before treatment, all patients had symptoms with severe or moderate level. After treatment, 98.1% of patients no longer had nose itching; 100% of patients had mild or no sneezing; 100% of patients did not suffer from runny nose or had in mild degree; 100% of patients did not suffer from nasal congestion or had in mild degree. The condition of nasal mucosa and inferior turbinate were also significantly improved (73,1% and 78,85% turned normal, respectively). For subclinical symptoms, the positive skin prick test, the serum IgE concentration in the patients decreased statistically,  $p < 0.001$  and the serum IgG4 level increased statistically with  $p < 0.001$ .

**Conclusion:** SLIT showed good effectiveness with low adverse effects.

**Keywords:** SLIT, allergic rhinitis, cotton dust

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### Introduction

Recently, in countries around the world as well as in Vietnam, the incidence of allergic rhinitis has increased. According to a statistic in 10 European countries in 2004, the prevalence of allergic rhinitis was about 20% of the population [1]. For occupational allergic rhinitis, although the etiological factors of allergies are diverse, cotton dust allergy has been a common disease during the period of industrial development. Divya Aggarwal conducted a study to identify the common allergen causing allergic rhinitis and found 9% patients had positive skin prick test with cotton dust [2]. Among methods of treatment for allergic rhinitis, immunotherapy has been recognized as a method basing the pathogenetic mechanism, prevent the progress of the allergic disease, it has been effective and economical [3]. Immunotherapy in the treatment of allergic rhinitis includes subcutaneous immunotherapy - SCIT or SLIT - Sublingual Immunotherapy. Of which, SLIT is effective and it limits the side effects of SCIT. The method of treating allergic

rhinitis caused by cotton dust with SLIT may offer clinicians an additional viable treatment option. Stemming from the above problems, the research was deployed with the goal: *To evaluate changes in clinical symptoms and some immunological tests in patients with allergic rhinitis caused by cotton dust antigen treated by sublingual immunotherapy.*

### Materials and methods

A clinical trial study was conducted at the Department of Otorhinolaryngology of 103 Military Hospital-Vietnam Military Medical University from May 2016 to May 2019 and was approved by the ethics committee of Vietnam Military Medical University.

### Subjects

Patients with allergic rhinitis caused by cotton dust allergen received sublingual-specific immunotherapy in 3 years. Patients were pregnant or expected to have baby or patients with some diseases (cardiovascular, liver, kidney, chronic respiratory disease, mental illness,

autoimmune diseases) or patient refused to participate in the study were excluded from the study. In total, 52 patients were recruited. Functional and physical symptoms, skin prick test and some unexpected effects was recorded before treatment and after the treatment 3 years in order to evaluate the effectiveness of treatment.

**Clinical trial**

Using cotton dust allergen produced by the National Otorhinorhynology Hospital of Vietnam for sublingual-specific immunotherapy. The treatment consisted of initiation and maintenance stage.

**Table 1.** Treatment procedure for allergic rhinitis by sublingual immunotherapy

Initiation phase (24 days)			
Day 1 – 4 1 – 3 – 4 – 6 drop <b>1 IR/ml</b>	Day 5 – 8 1– 3 – 6 – 10 drop <b>10 IR/ml</b>	Day 9 – 16 1 – 2 – 4 – 6 – 8 – 12 – 16 – 20 drop <b>100 IR/ml</b>	Day 17 – 25 5 – 6 – 8 – 10 – 12 – 14 – 16 – 18 – 20 drop <b>300 IR/ml</b>
Maintenance phase (36 months): 20 drops /day (300 IR/ ml)			

**Evaluation of treatment effect**

**- Clinical examination**

Functional symptoms: sneezing, runny nose, stuffy nose, itchy nose.

Physical symptoms: the condition of the nasal mucosa, the condition of the inferior turbinate.

There were 4 level for each symptom: normal (no symptom); mild (symptoms clearly present but easily tolerated); moderate symptoms (bothersome but tolerable symptoms), and severe symptoms (symptoms hard to tolerate).

**- Skin prick test:** The method of conducting and evaluating the response was assessed according to Sullivan T. J. et al (1981) [4].

**Table 2.** Prick test reaction degrees

Degree	Expression
(-)	Like negative
(+)	Diameter of papules from 3 - 5mm, itch, erythematous
(++)	Diameter of papules from 6 - 8mm, itch, erythematous
(+++)	Diameter of papules from 9 -12mm, having prosthetic legs
(++++)	Diameter of papules > 12mm, having many prosthetic legs

**- Immunoassays:** The concentration of globulins were determined by the kit with name Antibody Isotyping 7-Plex Human ProcartaPlex™ Panel based on sandwich principle.

**Statistics**

The data was analyzed by SPSS 22.0. Qualitative variables were described through numbers and percentages. For Quantitative variables with non-normal distribution: described through median values, min - max, compare medians of 2 paired groups by Wilcoxon test. Compare 2 or more percentages using chi-squared test (test X2). P-values ≤0.05 were considered significant.

**Results**

**Table 3.** Changes in the level of functional symptoms (n = 52)

Levels of functional symptoms	Before treatment		After 3 years of treatment		p
	Frequency	Percentage (%)	Frequency	Percentage (%)	
<b>Itchy nose</b>					
Severe	13	25	0	0	< 0.001
Moderate	16	30.8	0	0	
Mild	23	44.2	1	1.9	
Normal	0	0	51	98.1	
<b>Sneezing</b>					
Severe	42	80.8	0	0	< 0.001
Moderate	4	7.7	0	0	
Mild	6	11.5	27	51.9	
Normal	0	0	25	48.1	

<b>Runny nose</b>					
Severe	20	38.4	0	0	< 0.001
Moderate	30	57.7	0	0	
Mild	2	3.9	9	17.31	
Normal	0	0,0	43	82.69	
<b>Stuffy nose</b>					
Severe	28	53.9	0	0	< 0.001
Moderate	23	44.2	0	0	
Mild	1	1.9	23	44.2	
Normal	0	0	29	55.8	

Before treatment, all patients had 4 nasal functional symptoms, major part was severe and moderate level. After treatment, no patient was at severe and moderate level in each functional symptom. The difference was significant,  $p < 0.001$ .

**Table 4.** Changes in the level of physical symptoms (n = 52)

Levels of functional symptoms	Before treatment		After 3 years of treatment		2, p
	Frequency	Percentage (%)	Frequency	Percentage (%)	
<b>Nasal mucosa</b>					
Severe	26	50.0	0	0	< 0.001
Moderate	15	28.8	0	0	
Mild	11	21.2	14	26.9	
Normal	0	0	38	73.1	
<b>Inferior turbinate</b>					
Severe	0	0.00	0	0.00	< 0.001
Moderate	35	67.31	0	0.00	
Mild	16	30.77	11	21.15	
Normal	1	1.92	41	78.85	

The proportion of patients with severe and moderate nose mucous membrane damage after treatment was lower when compared to before treatment (0% and 78,8%, respectively). The difference was statistically significant ( $p < 0.001$ ).

Initially, inferior turbinate lesions were mainly moderate and mild. After 3 years of treatment, the majority of patients no longer had inferior turbinate lesions (78.85%).

**Table 5.** Changes in skin prick test

Prick test result	Before treatment (n=52)		After 3 years (n=52)		p	
	n	(%)	n	(%)		
Negative	0	0	33	63.5	< 0,001	
Positive	1 (+)	0	12	23.1		
	2 (+)	26	50.0	7		13.4
	3 (+)	21	40.4	0		0.0
	4 (+)	5	9.6	0		0.0
Total	52	100	52	100		

Before treatment, the majority of patients had positive skin prick test resulting 2 (+), 3 (+) with the rate of 90.4%, no patients had negative result. After treatment, the percentage of patients with prick test (-) was 63.5%, positive 1 (+) was 23.1%, 2 (+) was 13.5%, no patient positive 3 (+), 4 (+). The difference was statistically significant with  $p < 0.001$ .

**Table 6.** Changes in serum IgE, IgG4 concentration (n = 52).

Index	Min	Max	Median	p*	
Serum IgE concentration	Before treatment	575,424	38,008,333	1,227,756	< 0.001
	After treatment	177,855	24,762,500	676,805	
Serum IgG4 concentration	Before treatment	4,823	362,322	45,937	< 0.001
	After treatment	28,472	604,536	94,792	

(\*: Wilcoxon test)

After treatment, serum IgE concentration decreased statistically with  $p < 0.001$  in comparison to baseline. Serum Ig G4 concentration increased statistically with  $p < 0.001$ .

**Table 7.** Some adverse effects during treatment (n=52)

Type of adverse effect	n	(%)
Oedema under the tongue	5	9.62
Digestive disorders	1	1.92
Papules, urticaria	1	1.92
Total	7	13.46

The rate of patients had side effects was 13.46%, of which, the percentage of patients had oedema under the tongue is biggest (9.62%).

## Discussion

### Functional symptoms

Allergic rhinitis has four basic symptoms: sneezing, runny and stuffy nose, and nose itching. These symptoms go along with each other and brings a lot of complaints to patients and can affect quality of life. Our research results have shown that after treatment, all functional symptoms reduced in comparison with those before treatment. The difference was statistically significant with  $p < 0.001$ . In which, in symptoms of nose itching and runny nose, the rate of patients improved symptoms were biggest. After 3 years of treatment, 98.1% and 82.7% of patients no longer had symptom of nose itching and runny nose, respectively.

Runny nose, along with sneezing, was two symptoms that occur in the early phase of an allergic reaction, because mast cells, when stimulated, secrete histamine, prostaglandins, and leukotrienes. (In addition, nasal discharge also had the involvement of a neural mechanism). Research results have shown similar treatment effects for both these symptoms. After 3 years of treatment, no patient had severe and moderate sneezing, and 48.1% of patients no longer sneeze. Our results are consistent with most of the previous studies. Authors Durham S. R. et al (2016) have provided positive results showing the effectiveness of specific sublingual and parenteral desensitization treatment [5].

The percentage of patients improved these symptoms in our study results were higher than those of Vu Van San who evaluated symptoms after 9 months of specific desensitization of allergic rhinitis caused by cotton dust allergens by subcutaneous injection [6]. The difference in our study results compared to other authors may stem from the fact that patients in our study were treated specifically and evaluated after 3 years, so the effect may be higher. This was also the conclusion of some studies when comparing the

treatment effectiveness of two groups of allergic rhinitis patients with specific desensitization of the sublingual route for two years and three years. The authors found that the treatment effect of the 3-year group was better [7], [8], [9], [10].

The degree of stuffy nose had a statistically significant change with  $p < 0.001$  between the time before and after 3 years of treatment. Stuffy nose was a manifestation of the slow phase of an allergic reaction, usually manifests about 6 hours after allergen exposure, and decreased slowly. This was also one of the main symptoms in allergic rhinitis and was also very difficult to treat, according to Passali D. et al (2012) [11].

### Physical symptoms

Our studies have shown that the treatment had a positive effect on the condition of the nasal mucosa. The patients had better status of nasal mucosa were corresponded with better functional status. Perhaps differences in allergen administration, duration, and adherence to treatment regimens contributed to these differences.

The inferior turbinate changed less after specific desensitization treatment than the change in nose mucous membrane after treatment. For patients with a severe condition, it is necessary to apply an orthopedic measure to ensure ventilation through the nose, thereby reducing the risk of other ENT diseases and lower respiratory tract infections. However, we found that when using specific desensitization treatment with a period of 3 years, there was a significant change. This statement is also consistent with other authors Mehuys E. et al [12].

The hypertrophy and degeneration of the nose mucous membrane can be considered as a common consequence of a prolonged pathological process here, these manifestations were not in the context of an allergic reaction in the nose. Perhaps the disease period was relatively long, some

patients have been ill for decades, plus the lack of knowledge about vasoconstrictor drugs, patients often self-administer vasoconstrictor nasal drops for a long time, has caused damage to the nose mucous membrane that was difficult to recover. These lesions have also been referred to as drug-induced rhinitis.

### **Subclinical symptoms**

It can be said that skin prick test is an important test for planning the diagnosis and treatment [13], [14]. The improvement in the positive degree of the prick test in the patient indicated that the treatment was effective. Our results showed that, after treatment, the majority of patients with negative skin prick test accounted for 63.5%. In the group with positive prick test, the results all were 1 (+) and 2 (+) level. It was better when compared to before treatment.

The study results also showed an increase in serum IgE concentration and a decrease in serum IgG4 concentration after 3 years of treatment. Some domestic authors also showed similar results. According to a research of R Djurup and et al., the specific IgE levels decreased, the IgG1 and the IgG4 increased, and reduced significantly in clinical symptoms and skin prick test results [15]. The authors Ohashi Y, Nakai Y and colleagues also noted similar results when treating patients with allergic rhinitis by SLIT and concluded that the changes of IgE, IgG4 confirm the immune modulation of the body [16]. Thus, the increase in serum IgG4 content and the decrease of serum IgE level after trial demonstrated an altered immune response, as indicated by prick tests, which significantly reduces the positive level. All these changes were in line with the improvement of clinical symptoms after treatment.

### **Side effects**

During desensitization treatment, the percentage of patients with side effects was quite low (13.46%). These side effects were all mild, mostly self-resolving and did not require any cure. There was 1 case of urticaria that was treated with an antihistamine. This result was consistent with the previous studies about the safety of the sublingual desensitization method in the treatment of allergic rhinitis [17], [18], [19], [20], [21].

### **Conclusion**

The study showed the effectiveness of SLIT in treating allergic rhinitis caused by cotton dust with low rate of adverse effects.

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### **Interest conflicts**

There is no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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