Efficacy Of Sublingual Immunotherapy For Cotton Dust Induced Allergic Rhinitis

Nam Thanh Quan[1*], Thuan Duc Nghiem[2], Thuc Minh Vu[1], Uyen Hanh Tran[3]

Abstract

Introduction: Sublingual immunotherapy (SLIT) has been considered to have more advantages than Subcutaneous immunotherapy (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: The study is a cross-sectional study to review 52 patients with cotton dust induced allergic rhinitis who were treated with standard cotton dust allergen in 3 years. The functional symptoms, physical symptoms, prick test were compared before and after treatment, and adverse effects were recorded.

Results: After 3 years of treatment with SLIT, all patients (100%) showed no or mild level of sneezing, runny nose, and nasal congestion. Most of thepatients (98.1%) did not have nose itching. Normal mucosa of nasal cavity and inferior turbinate by nasal endoscopewas 73.1% and 78.85% respectively. The concentration of serum IgE decrease significantly.The skin prick test was negative, accounted for 63.5%. There was no record of severe or life-threatening side effects.

Conclusion:SLIT is effective with low adverse effects.

Keywords:SLIT, allergic rhinitis, cotton dust
DOINumber: 10.48047/nq.2023.21.01.NQ20076 **NeuroQuantology2023;21(1):997-1001**

INTRODUCTION

Recently, in countries around the worldas well as in Vietnam, the incidence of allergicrhinitis has increased. According to a statistic in 10 Europeancountries in 2004, the prevalence ofallergic rhinitis was about 20% of thepopulation [1]. For occupational allergicrhinitis, although the etiologicalfactors of allergies are diverse, cottondust allergy has been a common diseaseduring the period of industrial development.Divya Aggarwalconducted a study to identify the common allergen causing allergic rhinitis and found 9% patientshad positive skin prick test with cotton dust[2]. Immunotherapy is a treatment for allergicrhinitis base onpathogenetic mechanism, prevent [illegible] prove to be effective and economical [3]. Of which,SLIT is more effective with fewer side effects than SCIT.The method of treating allergic rhinitiscaused by cotton dust with SLIT may offerclinicians an additional viable treatmentoption. Stemming from the above problems,the research was deployed with the goal:*To evaluate changes in clinical symptomsand some immunological tests in patientswith allergic rhinitis caused by cotton dustantigen treated by sublingual immunotherapy.*

MATERIALS AND METHODS

Research period

A clinical trial study was conducted at the Department of Otorhinolaryngology of 103

***Corresponding Author:** Nam Thanh Quan
Address:[1*]Otorhinolaryngology Department, Military Hospital 103, Vietnam Military Medical University
E-mail: quanthanhnamb6@vmmu.edu.vn
[2]Vietnam Military Medical University, Ha Noi, Viet Nam
[3] Otorhinolaryngology Department, Cho Ray Hospital, Ho Chi Minh City, Vietnam
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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

52 patients with allergic rhinitis caused by cotton dust allergen received sublingual-specific immunotherapy in 3 years.

Patients who were pregnant or expected to have baby or havingsevere diseases (cardiovascular, liver, kidney, chronic respiratory disease, mental illness, autoimmune diseases) or refused to participate in the study were excluded from the study.

Functional and physical symptoms, skin prick test, igE, igG4 concentrationand side effects wererecorded before treatment and after 3 years of treatment to evaluate the effectiveness of treatment.

Clinical trial :

a. Induce cotton dust allergen to patients

Using cotton dust allergen produced by the National Otorhinorarynology 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 ***1 IR/ml***	Day 5 – 8 1– 3 – 6 – 10 drop ***10 IR/ml***	Day 9 – 16 1 – 2 – 4 – 6 – 8 – 12 –16 – 20drop ***100 IR/ml***	Day 17 – 25 5 – 6 – 8 – 10 – 12 – 14 – 16 – 18 – 20 drop ***300 IR/ml***
Maintenance phase(36 months): 20 drops /day (300 IR/ ml)			

b. Follow up and assessment :

- 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.

According to TNSS (TotalNasal Symptom score), there were 4 levels 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 wasdeterminedby the kit with name Antibody Isotyping 7-Plex Human ProcartaPlex™ Panel based on sandwich principle.

c. Statistical Analysis

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:

All 52 patients with allergic rhinitis received SLIT for 3 years. The functional and physical symptoms, skin prick testand side effects were recorded before treatment and after 3 years of treatment. The results were following:

The average age of patients was 32.69 ± 6,09.

Of all participants, 57.4% of them fit into the 25- to 34-year-old age range. A total of 79.49 % of patients were female. 60% of patients have a history of allergies.

After the treatment of SLIT, all the patients reported feeling much better. All the functional symptoms such as sneezing, itching nose, runny nose, stuffy nose improve significantly($p< 0.001$), there is no record of severe or moderate level. Over 63% of all patients in the study were negative with prick test. None of the patients show hypertrophy or edema of mucosal membrane of nasal cavity and inferior turbinate by nasal endoscope. Of the side effects, limited caseswas reported, with the incidence of never have side effects was 86.54%. 5 patients (9.62%) with swelling of the floor of the mouth was closely follow up, and no intervention was needed. Another patient (1.92%) with severe urticaria was subsequently treated with anti-histamine. Concentration of serum IgE decreased significantly, from 1,227,756 UI/ml to 676,805 UI/ml.

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 comparision 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 desensitizationtreatment [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 resultsshowed that, after treatment, the majorityof patients with negative skin prick testaccounted for 63.5%. In the group withpositive prick test, the results all were 1(+) and 2 (+) level. It was better when compared to before treatment.

The study results also showed a decrease in serum IgGE concentrationafter 3 years of treatment. Some domesticauthors also showed similar results.According to aresearch of R Djurup and et al., thespecific IgE levels decreased, and reducedsignificantly in clinical symptoms and skinprick test results[15]. The authors Ohashi Y,Nakai Y and colleagues also noted similarresults when treating patients with allergicrhinitis by SLIT and concluded that thechanges of IgE confirm the immunemodulation of the body [16]. Thus, thethedecrease of serum IgE level after trialdemonstrated an altered immune response,as indicated by prick tests, which significantlyreduces the positive level. All these changeswere in line with the improvement ofclinical 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.

Acknowledgement

Thank to staffs in Otorhinolaryngology Department, Military Hospital 103, Vietnam Military Medical University.

Thank to staffs in Immunology Labo, Department of Immunology, Vietnam Military Medical University.

All of them partly helped me in performed the skin prick test and determined the concentration of igE, igG4 as well as recording the data.

Interest conflicts

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

References

Desiderio Passali, Cemal Cingi, Paola Staffa, et al. (2018). The International Study of the Allergic Rhinitis Survey: outcomes from 4 geographical regions. *Asia Pacific Allergy*. 8(1).

D Aggarwal, S Abhilash, S Kapur, et al. (2019). Study of causal aeroallergens in allergic rhinitis. *Otorhinolaryngol Head Neck Surg*. 5: 916-21.

Eli O Meltzer và Don A Bukstein (2011). The economic impact of allergic rhinitis and current guidelines for treatment. *Annals of Allergy, Asthma*. 106(2): S12-S16.

Sullivan T. J, Wedner H. J, Shatz GS, et al. (1981). Skin testing to detect penicillin allergy. *J Allergy Clin Immunol*. 68:171-80.

Stephen R Durham và Martin Penagos (2016). Sublingual or subcutaneous immunotherapy for allergic rhinitis? *Journal of Allergy Clinical Immunology*. 137(2): 339-349. e10.

Vu Van San (2002). Clinical features of patients with occupational allergic rhinitis caused by cotton dust-woollen in textile company Hai Phong. *Medical PhD*. Viet nam Military Medical University, Ha Noi.

Guy W Scadding, Moises A Calderon, Mohamed H Shamji,

et al. (2017). Effect of 2 years of treatment with sublingual grass pollen immunotherapy on nasal response to allergen challenge at 3 years among patients with moderate to severe seasonal allergic rhinitis: the GRASS randomized clinical trial. *Jama*. 317(6): 615-625.

Flavia CL Hoyte và Harold S Nelson (2018). Recent advances in allergic rhinitis. *FResearch*. 7.

Rauf Tahamiler, Gkioukxel Saritzali, và Salih Canakcioglu (2007). Long-term efficacy of sublingual immunotherapy in patients with perennial rhinitis. *The Laryngoscope*. 117(6): 965-969.

Helen Smith, Peter White, Ilkka Annila, et al. (2004). Randomized controlled trial of high-dose sublingual immunotherapy to treat seasonal allergic rhinitis. *Journal of allergy clinical immunology*. 114(4): 831-837.

Desiderio Passali, Luisa Maria Bellussi, Dario Gregori, et al. (2012). Nasal obstruction as a key symptom in allergic rhinitis: efficacy and safety of a medical device in children. *Otolaryngologia Polska*. 66(4): 249-253.

Els Mehuys, Philippe Gevaert, Guy Brusselle, et al. (2014). Self-medication in persistent rhinitis: overuse of decongestants in half of the patients. *The Journal of Allergy Clinical Immunology: In Practice*. 2(3): 313-319.

Khaltaev N. Bousquet J., Cruz A. A., et al. (2008). Allergic rhinitis and its impact on asthma (ARIA) 2008 Update (in collaboration with the World Health Organization, GA2LEN*and AllerGen**). *Allergy*: 63:8-160.

Gianna Moscato, Olivier Vandenplas, Roy Gerth Van Wijk, et al. (2009). EAACI position paper on occupational rhinitis. *Respiratory research*. 10(1): 1-20.

R Djurup (1985). The subclass nature and clinical significance of the IgG antibody response in patients undergoing allergen-specific immunotherapy. *Allergy*. 40(7): 469-486.

Yoshihiro Ohashi, Ayaki Tanaka, Yasushi Kakinoki, et al. (1997). Effect of Immunotherapy on Seasonal Changes in Serum-Specific IgE and IgG4 in Patients With Pollen Allergic Rhinitis. *The Laryngoscope*. 107(9): 1270-1275.

Jennifer Maloney, David I Bernstein, Harold Nelson, et al. (2014). Efficacy and safety of grass sublingual immunotherapy tablet, MK-7243: a large randomized controlled trial. *Annals of Allergy, Asthma Immunology*. 112(2): 146-153. e2.

J Maloney, S Durham, D Skoner, et al. (2015). Safety of sublingual immunotherapy Timothy grass tablet in subjects with allergic rhinitis with or without conjunctivitis and history of asthma. *Allergy*. 70(3): 302-309.

Hendrik Nolte, David I Bernstein, Harold S Nelson, et al. (2016). Efficacy of house dust mite sublingual immunotherapy tablet in North American adolescents and adults in a randomized, placebo-controlled trial. *Journal of Allergy Clinical Immunology*. 138(6): 1631-1638.

Giovanni Passalacqua, Anna Nowak-Węgrzyn, và Giorgio Walter Canonica (2017). Local side effects of sublingual and oral immunotherapy. *The Journal of Allergy Clinical Immunology: In Practice*. 5(1): 13-21.

Pascal Demoly, Jonathan Corren, Peter Creticos, et al. (2021). A 300 IR sublingual tablet is an effective, safe treatment for house dust mite–induced allergic rhinitis: An international, double-blind, placebo-controlled, randomized phase III clinical trial. 147(3): 1020-1030. e10.