

Clinical Efficacy of Sublingual Immunotherapy in Respiratory Allergy Patients; A preliminary study

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Abstract

A total of 30 patients with respiratory allergies were studied for sublingual immunotherapy (SLIT) with incremental doses. All these patients were positive by skin prick test for house dust, dust mites, tree pollen, grass pollen and weed pollen either singly or in combination. The effect of SLIT was assessed by symptom diary and treatment diary maintained by the patients for one year. There was relief of symptoms in 80% of these patients. There were no adverse systemic reactions and only one patient had local event in the form of taste disturbance which subsided on its own. It is concluded that SLIT is efficacious and safe in patients with allergic asthma and rhinitis or both.

Key words: Allergens, Skin tests, Sublingual immunotherapy

INTRODUCTION

Allergic disorders are common with a estimated prevalence of 15%¹ and increasing over the last few decades in industrialized nations². Respiratory allergy is one of the most common of allergic disorders. In the treatment of allergy, there are three approaches. The first method is avoidance of exposure to the allergen, which is not always possible³. The second method is pharmacotherapy in which the patient will be symptom free as long as he is on medication and the drugs used may have their own side effects. The third method is immunotherapy (IT) which gives long lasting symptom free interval. Among the methods of immunotherapy

the subcutaneous injection (IT) is conventional and standard method³. However, this needs a doctor or a paramedical staff to give injection and is associated with pain and sometimes with severe systemic reaction. The other methods - Oral, local bronchial and nasal have limited clinical efficacy and practically not in use. The sublingual immunotherapy is a novel method, patient friendly, easy to administer with least adverse reactions and efficacious. The present study was undertaken to assess the benefit of SLIT in patients of respiratory allergy.

MATERIAL AND METHODS

The patients were recruited at outpatient department of allergy center, Kempegowda Institute of Medical Sciences Hospital and Research Centre, Bangalore. The inclusion criteria were patients aged 5-55 years, suffering with asthma, rhinitis and or both. Patient with severe asthma, high blood pressure, ischemic

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heart disease, pregnancy, immune disorders, history of anaphylaxis to immunotherapy and patients who were receiving immunosuppressive medications were excluded. The protocol was approved by institutional ethics committee.

A total of 30 patients, 15 males and 15 females were recruited for the study after confirming the diagnosis and informed consent. Skin prick tests with allergen extracts were performed and those positive were selected for sublingual immunotherapy. All these patients were given symptom diary and treatment diary and were instructed to enter the nature and frequency of symptoms and treatment taken and these were reviewed during monthly follow-up. They were followed up for one year to assess the safety, clinical efficacy and compliance of sublingual immunotherapy.

PREPARATION OF ALLERGEN EXTRACT FOR SUBLINGUAL IMMUNOTHERAPY

The vials containing allergens in concentrated form (1:99) were obtained from Creative Drug Industries Navi Mumbai. Patients who were allergic to 4 allergens, 10ml of 1:99 dilution were prescribed (maximum 4 allergens can be mixed), from this, maintenance vial (1:99) was prepared by taking 1.5ml from each allergen extract and making it 6ml. If the patient was allergic to 3/2/1 allergens, then the 3rd strength was prepared by taking 2ml/3ml/6ml, respectively from each extract and making it 6ml. This 6ml of 1:99 dilutions was the 3rd strength (vial3), which is the maintenance dose. From the 3rd strength, 2nd strength was prepared by adding 0.5ml from the 3rd strength to 4.5ml of dilution fluid (glycerin) (vial2) (1:999). The 1st strength was prepared by adding 0.5ml from the 2nd strength to 4.5ml of dilution fluid (vial 1). This forms the initial strength (1:9999) of sublingual immunotherapy.

ADMINISTRATION OF SLIT

After a thorough physical examination, appropriate allergen extract was administered. Two drops of vial 1 was diluted in 10ml of distilled water and then it was administered sublingually, patient was advised to keep it for one minute below the tongue and then swallow. The patient was given sublingual immunotherapy on empty stomach preferably in the morning. The dose

was increased by 2 drops, once in every 3 days. The patient was asked to maintain a symptom diary and treatment diary. If the patient was able to tolerate the increasing dosage, then asked to report once in 4 weeks.

Similarly vial 2 and vial 3 was continued with 2 drops initially and increased by 2 drops once in every 3 days. However, if the patient was not able to tolerate a particular dose (due to adverse effects), then instructed to take the previous tolerable dose and continue that dose as maintenance dose.

RESULTS

A total of 30 patients with respiratory allergy were treated by SLIT. They were equal in number i.e. Males and females (15 each). The age of the patients ranged from 5 years to 55 years (Table 1)

Table 1. The patients of respiratory allergy (age group and sex recruited for sub lingual immunotherapy)

Age (years)	Sub-Lingual Immunotherapy		Total
	Male	Female	
5-14	2(13.3)	1(6.6)	3(10.0)
15-24	2(13.3)	2(13.3)	4(13.0)
25-34	6(40.0)	5(33.3)	11(37.0)
35-44	5(33.4)	4(26.6)	9(30.0)
45-55	-	3(20)	3(10.0)
Total	15(100.0)	15(100)	30(100.0)

Majority of the patients (37%) belonged to the age group of 25-34 years. Among the patients studied, 43% had allergic rhinitis, 7% patients had allergic asthma and 50% were having asthma with rhinitis. There was family history of allergy in 56.6% of patients. All the 30 patients had positive skin prick test and majority, 21 (70%) were allergic to house dust and dust mites (*Dermatophagoides pteronyssinus* and *D. farinae*). Remaining 9 (30%) patients were allergic to tree, grass and weed-pollens.

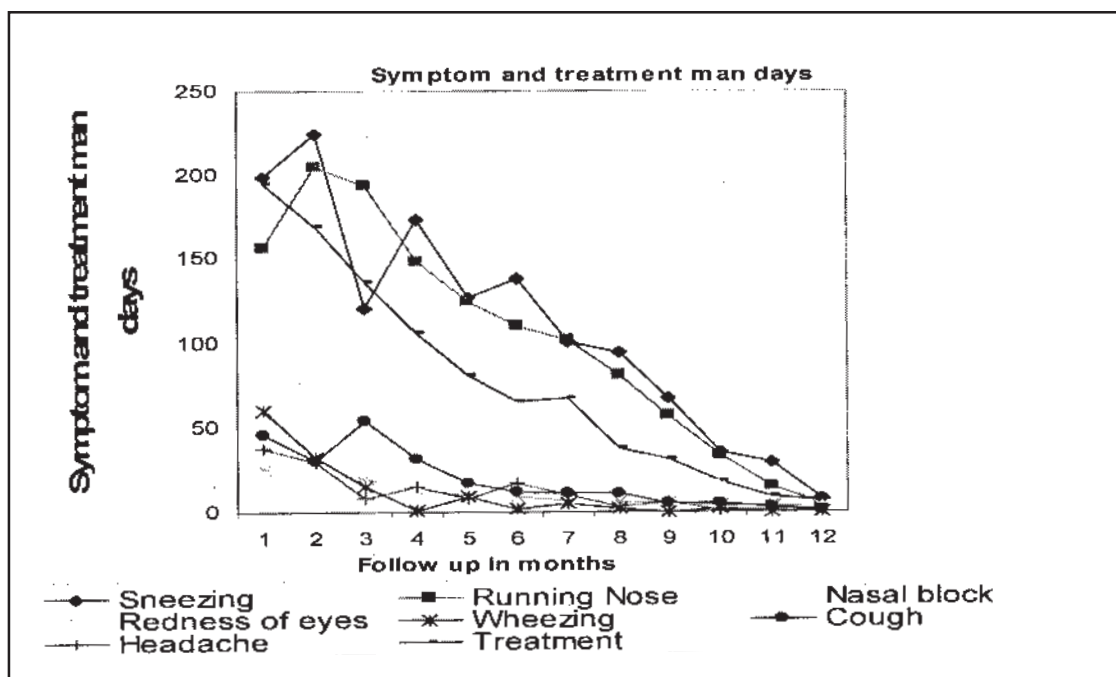


Fig 1. Symptoms and treatment (pharmacotherapy) analysis at '0' and after 1 year of sub lingual immunotherapy

CLINICAL EFFICACY OF SLIT

Analysis of improvement of symptoms was done by studying the symptom diary and treatment diary and also by interrogation during follow up visits. Use of concomitant medications was also assessed. (Fig. 1)

It was observed that 24(80%) patients showed relief of allergic symptoms by SLIT. The symptoms of sneezing, running nose, nasal block, redness of eyes, cough, wheeze and headache were all decreased at the end of one year as shown in the above graph.

Out of 13 patients with allergic rhinitis, 10 (76%) patients had relief of symptoms with SLIT. Of the remaining 17 patients having allergic rhinitis with asthma, 14(82%) showed relief of symptoms by SLIT. Overall out of 30 patients studied, 24 (80%) patients had relief of symptoms and the remaining 6 patients did not respond.

SAFETY

Analysis of local and systemic side effects of SLIT revealed, that there were no systemic reactions. Only

one patient had mild local reaction in the form of taste disturbance which subsided on its own without any intervention and the patient continued SLIT. This shows that SLIT is safe without any significant side effects. However, 5 patients (16%) had mild aggravation of the existing symptoms for the third strength (3rd vial). They responded well after reducing the dosage and SLIT was completed as per the protocol.

COMPLIANCE

Compliance was assessed during the review of symptom diary and treatment diary and their visits during follow up. It was observed that all patients were taking SLIT as per the protocol.

DISCUSSION

Allergic rhinitis and allergic bronchial asthma are quite common, particularly in urban areas may be due to higher atmospheric pollution. The standard modalities of treatment consist of avoidance of exposure to allergen that is not always practical, pharmacotherapy gives relief as long as the patient is

on medication and immunotherapy gives long lasting relief of symptoms and can change the course of disease.

Subcutaneous immunotherapy (SCIT) is the standard method for desensitizing patients with respiratory allergy. Although this method has proven efficacy and good safety record³, it has disadvantages since it requires injection particularly problematic in children and the need for a doctor or a paramedical staff for giving injection and at times associated with side effects.

Sublingual immunotherapy (SLIT) has been studied fairly extensively and found to be effective, has least side effects and does not require injection and hence is becoming popular. The present study was undertaken to study the safety and clinical efficacy of SLIT among patients suffering with respiratory allergy.

Among the 30 patients who received SLIT, 13 had allergic rhinitis, 2 had allergic bronchial asthma and 15 had both allergic rhinitis and bronchial asthma. In the present study, age range of patients recruited was 5 to 55 years, which differ from the study conducted by Di Rienzo et al⁴ and Pajno et al⁵ where SLIT was carried out in children with asthma. Bosquet et al⁶ studied SLIT in asthma in an age group of 7 to 42 years.

In the present study, 21 (70%) patients were allergic to house dust and dust mites and the remaining 9 (30%) patients were allergic to grass, tree and weed pollens whereas in other studies it was observed that the patients were allergic to *Parietaria judaica*⁷ mite⁸, house dust mite⁶ and grass pollen^{9,10}.

Among the 13 patients of allergic rhinitis, (with running nose, sneezing and nasal blocks) 10 showed relief of symptoms with SLIT. In remaining 17 patients who had bronchial asthma (2 patients) and allergic rhinitis with asthma (15 patients), relief of symptom was seen in 14 (82%) patients (i.e. the number of episodes of wheezing and sneezing were decreased). The number of rescue medication taken by them was also decreased over a period of one year. This is in accordance with other studies¹⁰ where high dose of SLIT has beneficial effect on nasal symptoms in patients with seasonal allergic rhinitis, and in patients with seasonal asthma⁹. Pajno et al⁵ observed clinical

efficacy and safety of SLIT in children with mild to moderate asthma and La Rosa et al⁷ observed clinical benefit in children allergic to *Parietaria*. In the present study, it was observed that there was relief of symptoms in 80% of patients, La Rosa et al⁷ have reported 88% of their patients with rhinoconjunctivitis got relief in symptoms with SLIT. Durham et al.¹¹ in their study of sublingual immunotherapy (sublingual tablets) in seasonal allergic rhinoconjunctivitis reported significant reduction of symptoms and improvement in quality of life.

In the present study, it has been demonstrated that SLIT is safe. There was only one patient who had local reaction which subsided on its own. There was no systemic reaction in any of the patients in the present study. Mild aggravation of existing symptoms was observed in 5 (16%) patients for the third strength (3rd vial) who responded well for reduced dosage and SLIT was continued and completed as per protocol. Other studies¹¹⁻¹⁴ also found no significant adverse effect of SLIT.

It is concluded from this study that SLIT is clinically effective, safe with least side effects and easy to administer in allergic rhinitis, allergic asthma and allergic rhinitis with asthma.

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