Original Article

# Effects of Sublingual Immunotherapy (SLIT) in Allergic Rhinitis Our early experience

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**Abstract-** Allergic Rhinitis(AR) represents a global health concern and many of the patients are resistant to usual pharmacotherapy .This subgroup of patients may respond when treated with allergen specific immunotherapy. Our aim of this study was to study the effects of Sublingualimmunotherapy(SLIT) inrandomised cases where immunotherapy was indicated for the same following a positive skin prick test .The patients who attended ENT out patient departmentat Swagat Superspeciality hospital were included based on the symptoms and laboratory tests reports .We found more than 50% patients had significant improvement in clinical symptoms and reduction in severity of disease with immunotherapy ,which was considered as successful.

**Keywords-** Allergic Rhinitis, skin prick test, immunotherapy

**Introduction-**

Allergic Rhinitis(AR) represents a global health concernand it is estimated to affect approximately 400 million people worldwide.In western countriesAllergic Rhinitis and asthma have a considerableimpact on quality of life. It affects school performancein children and impairs sleep and work performance. Recent studies have shown increase in prevalence of 1.4-45% over the past decades and the leading causes thought to be are increased urbanisation and environmental pollutants [1,2]

Diagnosis of AR is made based on clinical symptoms such as sneezing, rhinorrhea, itchy nose,eyes and nasal congestion when there is no sign of lower respiratory tract infections or anatomic abnormalities of the nose3.Further diagnostic testing using skin-prick tests or allergen-specific IgE tests is usually required to confirm that underlying allergies cause the rhinitis.

The treatment of allergic rhinitis initially includes the avoidance of allergens especially indoor allergens such as house dust mites (HDM) in bed and house fungi which grow in damp places besides pets, indoor plants, grass, trees and grass pollen[3].Treatment modalities available are nasal saline irrigation, oral antihistamines(AH), intranasal corticosteroids,leukotriene receptor antagonists (LTRAs)/oral corticosteroid(OCS) alone or in combination.

Mild to moderate allergic rhinitis can be controlled with Antihistamine/intranasal corticosteroids,however severe cases may require OCS which also have serious long term side effects.

A small proportion of patients do not respond to pharmacotherapy and in these patients,allergen specific immunotherapy may be of importance.Though traditionally it has been administered bysubcutaneous route,there are reports of death and adverse reactions and sublingual approach ofimmunotherapy has emerged as a safer and better alternative route.[4]

Sublingual immunotherapy is a way of desensitizing patients and involves placing small amount of allergen extract under the tongue until it is dissolved. It is currently available for the treatment of grass and ragweed allergy, as well as house dust mite-induced allergic rhinitis (with or without conjunctivitis). This route offers multiple potential benefits over the subcutaneous route including the comfort of avoiding injections, the convenience of home administration, and a favourable safety profile.[5]

**Effects of allergen immunotherapy on early and late phase responses :**

Both the early and the late phase allergic responses are suppressed after Allergic immunotherapy (AIT), starting with the late phase response approximately2 weeks after the start of treatment. Suppression of the IgE-mediated early cutaneous response is less pronounced and occurs 8–12 weeks after the first dose. Reduction in nasal responsehave also been reported for grass pollen, and cat allergens

Various studies have shown that in immunotherapy B-cells show a shift from producing the allergenic IgE to the more 'protective' IgG4. Eventually there is a gradual decrease of serum IgE in serum over years of treatment .After discontinuation of treatment, IgG4 decreases again; however it still remains elevated compared with baseline levels[5]

**Materials and method:**

A total number of 90 cases of Allergic Rhinitis were selected for skin prick test who attended OPD in thedepartment of ENT, Swagat super speciality hospital for the period from May 2018 to May 2020(The number of cases were a bit reduced during COVID period) and the follow up period of those patients was for one year.

We selected these patients on the basis of high serum IgE, AECand deficient serum Vitamin D3 levels.

**Inclusion criteria-** Patients were selected who had typical signs of Allergic Rhinitis(AR) and had above mentioned altered blood levels results and symptoms not adequately controlled by Anti histamines(AH) /corticosteroids nasal sprays and frequently requiring OCS(oral corticosteroids)

**Exclusion criteria-** Patients below 8 years and above 60 years of age were excluded.

Those with associated skin conditions like urticaria, dermatitis and pregnantpatientsor those on beta blockers, and patients with severe intractable asthma were also excluded.

**Procedure-** Antihistamines were stopped 5 to 7 days prior to the skin prick test in all selected patients under the study.

Both the anterior aspects of the forearms were cleaned and prilox cream (25mg lignocaine +25 mg prilocaine) was applied and kept for 30 minutes for the local anaesthesia effect.

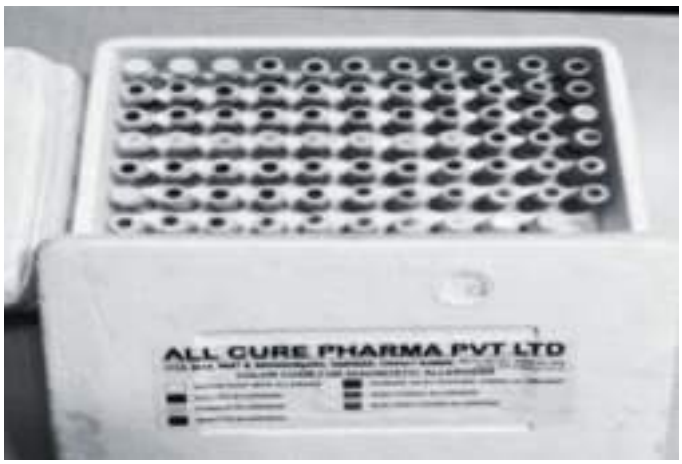


*Fig 1: Allergen kit*

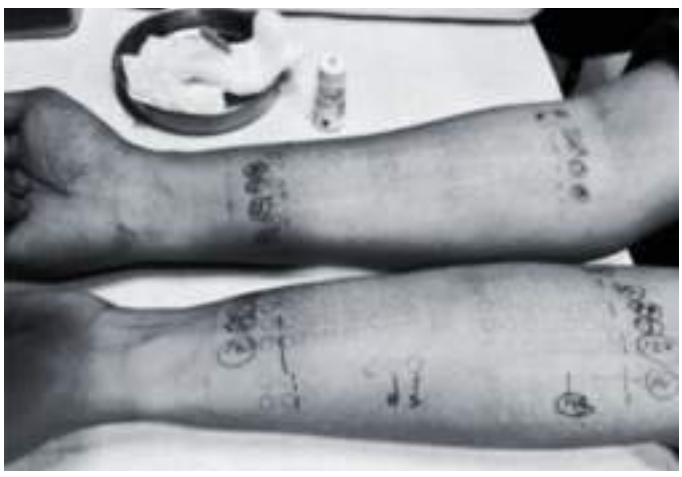

*Fig 2: Numbered marking for the skin prick test*

The allergen kit contains 142 allergens in the test kit ,ranging from house dust mites, pollens,different species of fungi,food,insects, animal, dander,dust,fabric allergens(provided by All Cure pharmaceuticals pvt. Limited).

We considered positive results for wheal reaction of 3mm diameter or of a size equal or larger than positive control in histamine after 15 minutes for minimum 2 allergens .

**Results-**

Out of 90 Patients selected for skin prick test, 58 were females and 37 were males.

The Male female ratio was 2:3 ,with female preponderance

The age group was maximum in the adolescent ages (8-20 yrs)-42

(20-45 yrs)- 28

( 45-60yrs)- 20

The most common symptoms were sneezing, itchy nose, watery eyes, and nasal discharge .

Out of 90 patients who underwent allergic skin prick 58 patients(64.4%) showed positive results and were advised to undergo immunotherapy and 11 patients(12.2%) had negative results.

21 patients (23%)had sensitivity to food allergens and insect ,animal dander for which avoidance was advised and these patients were advised to continueantihistamine and intranasal corticosteroidtherapy as immunotherapy is not available for these specific types of allergens and is not effective.

8 patients(8.8%) opted out of immunotherapy option advised.

Thereforeout of total 90 patients who underwent skin prick test, 50 patients (55.5%) received the sublingual immunotherapy.

Table 1: List of the major sensitive allergens for patients who were given immunotherapy

| Name of the allergens | number of patients showing positive SPT/Percentage | |
|---|---|---|
| **HDM(house dust mites)** | | |
| D. Ferehae | 58 | 64.55% |
| D. Pteronyssinus | 53 | 53.8% |
| **Pollens** | | |
| A. arabica | 34 | 37.7% |
| A.vasica | 28 | 31.1% |
| A. conyzoides | 39 | 43.3% |
| A.Excelsa | 21 | 23.3% |
| AmaranthusSpinosus | 28 | 31.1% |
| C. fistula | 32 | 35.5% |
| C. Siamea | 37 | 41.1% |
| C. ciliaris | 28 | 31.1% |
| P. hysterophorus | 31 | 34.4% |

Sublingual Immunotherapy(SLIT) was given to these patients based on their sensitivity particularly seen most commonly to house dust mites like D.Ferehae and D.pteronyssinus (64.5 % and 53.8% ) followed by pollen varieties mostly sensitive like A.arabica (37.7%),A.conyzoides (43.3%),c.siamea(41.1%),C.fistula 35%.

All the patients under the studyreceivedimmunotherapy for a duration of 1year(All Cure pharmaceuticals).


*Fig 3: Immunotherapy kit*

The immunotherapy kit comes with three coloured vials(Green,blue and red). Each vial contains 5.5ml of allergen extract.

The initial dosage from the green vial is one drop on 1st day ,then gradually increasing till 5 drops on 5th day, in empty stomach before breakfast and then switching to twice daily dosage weekly for the 2nd vial .

The maintenance dose provided with the 3rd(red vial) is administered once a week .

We followed up these patients for 1 year post receiving the SLIT for one year. At the end of 2 years ,we reviewed with the aim for assessing the efficacy of the therapy.

Out of 50 patients,5 patients reverted to use of oral corticosteroids in between for symptom control and were considered as failed candidates.

14 patients required occasional steroid nasal spray for control of symptoms,though no oral corticosteroids was used and they had a good response with immunotherapy and was considered as successful.

9 patients required nasal spray and short term Antihistamines(AH) in between ,and also didn't have to be switched over to oral Corticosteroids and had good symptom control in due course of studywith immunotherapy

Hence we found that more than 50% patients had significant improvement in clinical symptoms and reduction in severity of disease on SLIT,which was considered as successful.

Moreover 18-25 % of patients had satisfactory improvement in their allergic symptoms and that were adequately controlled by Sublingual immunotherapy (SLIT),though they occasionally had to use intra nasal steroid spray and Antihistamines but their frequency of use gradually reduced.

The remaining 10 % cases who had to use oral corticosteroids during the courseof SLIT were considered as failed candidates which was a criteria for deciding the efficacy of SLIT .

No complications were reported in the study period.

Hence we found SLIT as a good therapeutic option for moderate to severe allergic rhinitis as itis very safe and effective though we need study with a large volume of patients for further validation .

**Discussion-**

Allergen immunotherapy modifies the allergic disease ,mitigates the development of asthma and new allergen sensitivity and also seen to improve the disease by inducing clinical improvement that persists for years after discontinuation of a successful course of treatment.[6]

Pharmacotherapy which includes topical nasal sprays and Oral AnithistaminesLeukotrine modifiers (monteleukast, zafirleukast) are used regularly to control symptoms or an as need basis.Studies over the years have suggested none of these medicines have disease modifying effect and generally provide only symptomatic relief.[6]

Since Immunotherapy has disease modifying properties we can hope that those patients who have improvement in symptoms during the 1 year studyperiod may have further reduction in symptoms if we continue further follow up of these patients.

Allergen immunotherapy (AIT), first reported by Leonard Noon in the early 20th century, is a highly effective treatment in individuals with immunoglobulin (Ig)E-mediated diseases.[5]

It is an effective treatment for allergic rhinitis, particularly for patients with intermittent (seasonal) allergic rhinitis caused by pollens, including tree, grass and ragweed pollens. It has also been shown to be effective for the treatment of allergic rhinitis caused by house dust mites, Alternaria, cockroach, and cat and dog dander .

AIT can be administered either by a subcutaneous (SCIT) or sublingual (SLIT) route.

The subcutaneous route has been for decades the traditional route of administration, but in recent years the sublingual route emerged as an actual treatment option .The main reason to introduce sublingual immunotherapy (SLIT) was the safety problems with subcutaneous immunotherapy (SCIT), which may include systemic reactions, sometimes severe and, though very rarely, even fatal .[6]

The advantages in regard the compliance, is higher with SLIT as it does not need to be administered in a medical setting, the cost-effectiveness because there is noadditional cost of injections[7]

The most common side effects of sublingual immunotherapy are local reactions such as oral pruritus, throat irritation, which resolve after the 1st week of therapy or rarely generalised reactions like urticaria .[7]

Immunotherapy is contraindicated in patients with severe, unstable or uncontrolled asthma ,pregnancy and lactation period and also ideally be avoided in patients on beta-blocker therapy as well as in those with active oral inflammation or sores .[8]

Rondon et al inferred in their trials that allergy immunotherapy provided for the common house dust mites like D.*Pteronyssinus* is safe and clinically effective treatment for Allergic rhinitis.[9]

In a study done by Wang W,Yin J et al, where duration of SLIT was 3 years they suggested that treatment to be reassessed if there is no sign of success after 1- 2 years. Hence if therapeutic efficacy can be predicted before 1 year ,the patients who are predicted to benefit from AIT could be motivated to continue so and the patient who do not respond can choose over other modality of therapy as early as possible.[10]

In another study done by Tahamiler R, Saritzali G et al, to study the long term efficacy of SIT where they did the study for 2 years ,the sneezing ,total symptoms and prick test scores was reduced at the end of 1st year and secretion score significantly reduced at the end of 2nd year.[11]

Hence most of the studies includes immunotherapy for 2-3 years ,but in our study we wanted to see if it provided symptom free period at the conclusion of an year,as it might be inconvenient to continue for 2-3 years.

In a study done by Matricardi M, Kuna P et al where four RCT was done to study comparison between SIT and pharmacotherapy ,they stated immunotherapy has not only a disease-modifyingaction and creates a reduction in drug consumption, but also has a rather powerful antisymptomatic effect starting as early as the first season after treatment onset[12].

In a study done by Aasbjerg J, they found individuals treated with SCIT had the largest decrease in steroid injections when receiving 1 year of treatment; the decrease diminished with increasing length of treatment from 1 to 5 years. [8]

Therefore our study too we have found that even after completion of 1year of immunotherapy the requirement of intra nasal corticosteroids and antihistamines have gradually reduced in comparison to therequirementat the beginning of the therapy. But if we continue further follow up we may find there is better control of allergic symptoms without use of pharmacotherapy.

**Conclusion** : In our study a significantdecrease was observed in theclinicalsymptoms of allergic rhinitis patients after immunotherapy.When allergen avoidance and pharmacotherapy are not sufficientfor disease control, AIT is advised underavailableguidelines.Hence we conclude that although ours is a small volume study ,sublingual immunotherapy is indeed future of the treatment of allergic rhinitis. And it is the best modality of treatment so far for moderate to severe cases not responding to the first line pharmacotherapy and also if we consider the long term side effects of oral corticosteroids. Though some patients may respond differently based upon the severity of the allergies.

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