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# ORIGINAL ARTICLE

# DOES IMMUNOTHERAPY IN ALLERGIC RHINITIS WITH INCREASED IGE LEVELS OFFER CONSISTENT RELIEF FROM NASAL SYMPTOMS, AN INSTITUTIONAL STUDY?

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**ABSTRACT: OBJECTIVES:** 1. To evaluate the efficacy of Immunotherapy in improvement of nasal symptoms in patients with Allergic Rhinitis. 2. To evaluate the adverse reactions of Immunotherapy in patients suffering with allergic rhinitis. **MATERIALS AND METHODS:** Study group included 138 patients with Allergic rhinitis, who presented in Department of ENT, during July 2011 to March 2014. Patients with clinical history of allergic rhinitis were screened with total serum IgE. Patients with elevated total serum IgE were investigated with skin prick test. Patients with positive skin reactions were treated with sub cutaneous immunotherapy. Development of adverse reactions during administration of immunotherapy was assessed. A follow up period of 18 months was considered for the study. A relief in clinical symptoms of allergic rhinitis at the end of 18 months was considered. **CONCLUSION:** Immunotherapy offers significant improvement in relief of clinical symptoms of allergic rhinitis with minimal adverse reactions over a long time. Total serum IgE forms an affective screening tool in diagnosis of allergic rhinitis. Immunotherapy appears as a safe alternative treatment for the management of allergic rhinitis.

**KEYWORDS:** Allergic Rhinitis, Immunotherapy, Allergen sensitivity, Total serum IgE, Skin prick test, adverse reactions.

**INTRODUCTION:** Allergic rhinitis is the most common allergic disease affecting the human population. Apart from causing nasal congestion, difficulty in breathing, sneezes, Allergic rhinitis also presents with fatigue, difficulty in concentrating, poor school and work performance. Most common investigations preferred in diagnosing allergic rhinitis are elevated total serum IgE and skin prick test. (1)

Patients of allergic rhinitis with a positive clinical history on exposure to the allergen often show specific IgE antibodies against the offending allergens.(2) RAST or ELISA are preferred to be more precise investigations in diagnosis but purified proteins and antibodies are not available for characterization based on major allergen content in India.(3)

The main stay of management of allergic rhinitis is focused on suppression of inflammatory reactions by medications like antihistamines, nasal steroids, and leukotriene receptor antagonists.

Apart from these since long time Immunotherapy is recognized as an alternative therapeutic option to alter the natural history of allergic rhinitis. It alters the biochemical nature of the disease by a shift of TH2 response towards TH1 and down regulates IL-4. This will lead to a decrease in release of inflammatory mediators, specific IgE levels, allergen specific airway hyper-responsiveness producing clinical improvement of symptoms.(4)

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**OBJECTIVES:**

1. To evaluate the efficacy of Immunotherapy in improvement of nasal symptoms in patients with Allergic Rhinitis.
2. To evaluate the adverse reactions of Immunotherapy in patients suffering with allergic rhinitis.

**METHODOLOGY:**

**Study Population:** Study group included 138 patients of Allergic Rhinitis with symptoms persisting for more than 3 months, who presented in Department of Otolaryngology, Narayana Medical College and Hospital, Chinthareddypalem, Nellore during July 2011 to March 2014.

**Inclusion Criteria:** Patients with a clinical history of allergic rhinitis with elevated total Serum IgE were included in the study in addition to symptoms of nasal itching, sneezing and rhinorrhea for more than 3 months with itching disturbing sleep in night, sneezing attacks of 5 or more per episode with minimum 5 episodes per day and rhinorrhea if patient has to use hand kerchief to wipe off mucous secretions at least once during a day were included.

**Exclusion Criteria:** Patients of Allergic rhinitis less than 3 months with normal values of total serum IgE, Patients of Bronchial asthma, Atopic dermatitis, patients with local nasal diseases like deviated nasal septum, Turbinate Hypertrophy, Rhino sinusitis, Nasal polyposis were strictly excluded from the study.

**INTERVENTIONS:**

Initial selection of patients for the study was based on a clinical evaluation by a panel of three Doctors experienced in management of Allergic rhinitis. After obtaining a written informed consent from the patients for the treatment and follow up they were evaluated with a clinical questionnaire for nasal itching, sneezes and rhinorrhea. These patients with positive clinical history of allergic rhinitis were investigated with total serum IgE. Total serum IgE exceeding 500 IU/ml was considered elevated in the study group. [5]

Skin prick test was performed in patients having elevated total serum IgE. A total number of eleven allergens which included Pollen, dusts, Mite and fungi were selected for the study. Patients with positive skin reactions were given sub cutaneous immunotherapy. We selected a total of 11 allergens Dusts - common House dust, wood and spider web dust, mite- Dermatophagoides, Fungus - Aspergillus and Pollen from Xanthium, Parthenium, Argemone and Brassica considering the local climatic conditions.[6] Other specific allergens which include epithelia, insects and food allergens were excluded.

Skin prick test is performed on the fore arm with positive and negative controls. Histamine diphosphate is used as positive control to compare the cutaneous response to injected allergen extracts. Diluent normal saline buffer is used as negative control to rule out the possibility of getting false positive skin response due to trauma or sensitization induced by skin test device.[7]

Drugs which alter the response of the test like Antihistamines are discontinued for 3 weeks prior to skin test. The allergen drops were deposited in longitudinal rows, 3 to 3.5 cm apart. In the prick technique, a drop of an allergen is applied on the skin. The skin is then pricked using a sterile blood lancet.

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Each blood lancet is used only once so as to avoid contamination. Grading of skin reaction is done after 20 minutes in comparison with negative control normal saline and positive control Histamine diphosphate. Skin prick test reactions with more than 3mm wheal were considered as positive.

| Skin prick test wheal | Result | Grading |
|---|---|---|
| 0mm | Negative | |
| Up to3mm | Positive | 1+ |
| 3-5mm | Positive | 2+ |
| 5-7mm | Positive | 3+ |
| 7mm and above | Positive | 4+ |

Table 1: Grading of skin prick test response[8]

Results of skin prick test were observed based on the response obtained in the form of wheal to each allergen. Depending on the response to allergen the results were graded and a mixture of solution was prepared in optimal concentration to each allergen after considering the cross reactions. Immunotherapy is administered subcutaneously in all the patients.

Immunotherapy was started with 1:5000 w/v diluted antigen and the injections are given two times a week starting from 0.05 ml and increased in every injection by 0.05 ml, increased to 0.1ml. In the patients who were not able to tolerate an incremental dosage of 0.1ml per injection dosage is titrated and continued at 0.05ml per injection.

The injections are given subcutaneously with insulin syringe with increased concentrations as per the schedule. The further schedule is as follows:1:5000 – once in three days, from 0.05 ml to 0.9 ml with an increase in dose by 0.1ml per each injection, 1:500 – once in three days, from 0.1 ml to 0.9 ml in increments of 0.1ml, 1:50 – one time a week, from 0.05 ml to 0.5 ml, 1:50 – one time in 2 weeks at a dose of 0.6 ml, 1:50 – one time in 3 weeks at a dose of 0.7 ml, 1:50 – one time a month at a dose of 0.8 ml, 1:50 – one time a month at 0.9 ml, 1:50 – one time a month at 1.0 ml which we considered Highest maintenance dose.(8) After each injection patients were observed for acute hypersensitivity reactions.

**Main Outcomes Measures:** Patients were instructed to note the number of episodes of nasal itching, sneezes and rhinorrhea during immunotherapy and follow up. We preferred a Clinical improvement of symptoms of allergic rhinitis if there was a decrease in appearance of symptom severity. A decrease in number of episodes of nasal itching to less than 2 in a month, sneezes to less than 3 episodes per month with not more than 2 sneezes per episode and an improvement of rhinorrhea if the use of hand kerchief to wipe off nasal secretions limited to not more than 2 episodesin a month, in a patient as positive responders to immunotherapy. In all these patients total serum IgE was repeated at the end of follow up of 18 months.

We observed and enquired the patients for the development of adverse reactions to Immunotherapy like tightness of chest, difficulty in breathing, abdominal pain, development of intense skin itching, swelling of lips or tongue immediately after the injection and lassitude, headache, papular rash over the malar bones, gastro intestinal disturbances, photo dermatitis over the exposed areas and a change of voice when the patient came for the next injection for late phase

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allergic reactions during the course of immunotherapy.[9] Also we enquired the patient for the development of similar adverse reactions during the follow up period after immunotherapy.

**RESULTS:** A total No. of 138 patients with Allergic Rhinitis formed the study population. Of them 109 (78.99%) patients showed elevated levels of total Serum IgE. These 109 patients with elevated total serum IgE were investigated with skin prick test. Prior to Immunotherapy Skin prick test revealed allergen sensitization in 92(84.40%) for pollen, 97(88.99%) for dusts and 87 (79.81%) for mite and fungi. Most of the patients had a mixed response to allergens in skin prick test. These results were documented in table 2.

Prior to Immunotherapy it was observed that in allergen sensitive patients to pollen nasal itching was seen in 89 (81.65%), to dusts in 92 (84.40%) and to mite and fungi in 79 (72.48%). Allergen sensitivity to Sneezes revealed that 84 (77.06%) patients sensitive to pollen, 89 (81.65%) to dusts and 82 (75.23%) to mite and fungi. Episodes of Rhinorrhea were observed in 87(79.81%) patients on exposure to Pollen, 91 (83.49%) to dusts and 83(76.14%) to mite and fungi. These results were documented in tables 3, 4, 5.

A decrease in number of episodes of clinical symptoms of allergic rhinitis was observed for nasal itching, sneezes and rhinorrhea during follow up. Episodes of nasal itching were reduced by 86.78%, Sneezes were reduced by 89.53%andepisodes of rhinorrhea were reduced to 87.63%at the end of 18 months. These results were evident in the form of a graph and represented in figure 1.

Post immunotherapy allergen sensitivity was reduced for Nasal itching in 72(80.90%) patients for pollen, 71 (77.17%) to dusts and 61 (77.21%) to mite and fungi. Sneezes reduced in 65(77.38%) patients to pollen, 66 (74.15%) to dusts and 58 (70.73%) to mite and fungi.

Similarly episodes of rhinorrhea were reduced in 66 (75.86%) patients to pollen, 69 (75.82%) to dusts and 64 (77.10%) to mite and fungi. These results were documented in tables 3, 4, 5. Post Immunotherapy total serum IgE estimation repeated at the end of follow up. Elevated total serum IgE was seen in 23 (21.10%) of patients.

During Immunotherapy we observed itching and redness in13 (11.92%) patients at the site of injection which subsided without any medication. 7 (6.42%) patients expressed lassitude during the course of Immunotherapy. 2 (1.83%) patients developed abdominal pain. One patient developed intense itching all over the body during immunotherapy.

In our study we observed that there was no change in blood pressure, difficulty in breathing or chest tightness and none of our patients developed lip or tongue swelling or other severe systemic anaphylactic reactions in early or late phases of Immunotherapy. Also no adverse reactions were noted during follow up.

| Skin prick test | positive | Negative | Total |
|---|---|---|---|
| Pollen | 92 | 17 | 109 |
| Dusts | 97 | 12 | 109 |
| Mite and Fungi | 87 | 22 | 109 |

Table 2: Allergen sensitivity of Skin prick test

DOI: 10.14260/jemds/2014/3264



| Nasal Itching | Pre treatment | Post treatment | Relief |
|---|---|---|---|
| Pollen | 89 | 17 | 72(80.90%) |
| Dusts | 92 | 21 | 71(77.17%) |
| Mite and Fungi | 79 | 18 | 61(77.21%) |

Table 3: Specific allergen response to Nasal Itching in Immunotherapy

| Sneezes | Pre treatment | Post treatment | Relief (%) |
|---|---|---|---|
| Pollen | 84 | 19 | 65(77.38%) |
| Dusts | 89 | 23 | 66(74.15%) |
| Mite and Fungi | 82 | 24 | 58(70.73%) |

Table 4: Specific allergen response to Sneezes in Immunotherapy

| Rhinorrhea | Pre treatment | Post treatment | Relief (%) |
|---|---|---|---|
| Pollen | 87 | 21 | 66(75.86%) |
| Dust | 91 | 22 | 69(75.82%) |
| Mite and Fungi | 83 | 19 | 64(77.10%) |

Table 5: Specific allergen response to Rhinorrhea in Immunotherapy

**Figure 1:** Chart showing assessment of clinical Symptoms of nasal itching, sneezes, rhinorrhea during follow up of Immunotherapy.

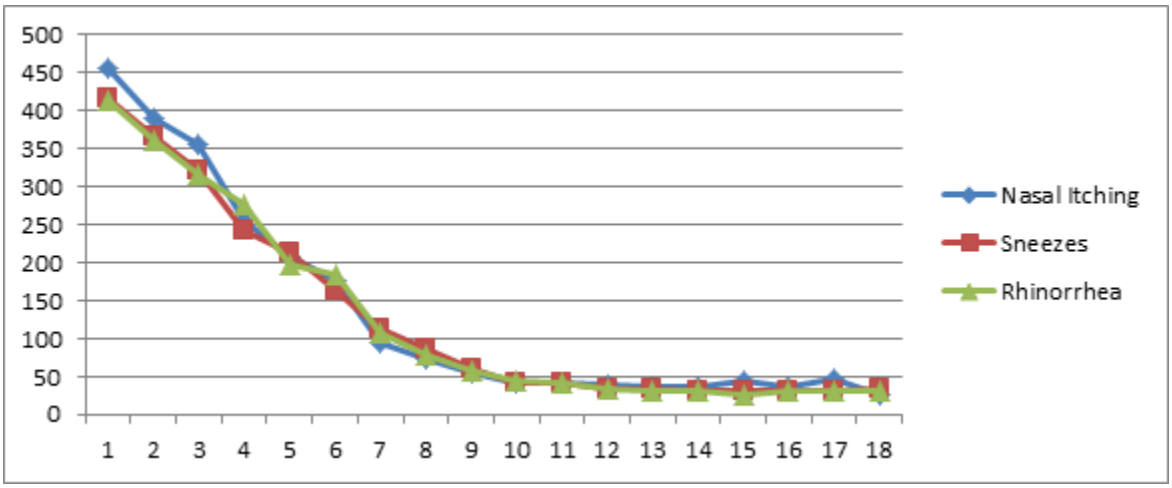


**Fig. 1**

**DISCUSSION:** An assessment of the response of immunotherapy in allergic rhinitis is done by assessing an improvement of clinical symptoms, serological investigations like total serum IgE, skin tests, and estimation of specific immunological parameters. [10]

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After completion of immunotherapy, we observed relief in clinical symptoms of Allergic rhinitis which were maintained during the follow up.

In our study post immunotherapy at the end of 18 months of follow up we observed an individual relief in symptoms of allergic rhinitis in patients desensitized for pollen where 80.90%relief was observed for nasal itching, 77.38%patients were relieved from sneezes and episodes of rhinorrhea reduced in75.86%

Following immunotherapy to dusts it was observed that the episodes of Clinical symptoms of allergic rhinitis were reduced in77.17% patients for nasal itching, sneezes in74.15% and episodes of rhinorrhea in75.82% in patients at the end of 18 months. Similarly in patients desensitized to mite and fungi a decrease in episodes of nasal itching was seen in 77.21% of patients, sneezes were reduced in 70.73% of patients and episodes of rhinorrhea in77.10% of patients.

In our study a relief of symptoms of nasal itching for all the allergens post immunotherapy was observed in 78.42% of patients. Similarly in a study by Yuri Zeldin et al [11] it was observed that a decrease in episodes of nasal itching was seen in 62% of patients. In another study by Rao Sukhesh [12] there was a relief in nasal itching in 65.3% of patients.

In our study relief from sneezes to all allergens was seen in 74.08% of patients post immunotherapy. Yuri Zeldin et al [11] observed a reduction in sneezes in 72.5% of population. Rao Sukhesh [12] observed a reduction in sneezes in61.5% of patients. Episodes of rhinorrhea decreased collectively to all allergens in 76.26% of patients in our study.

Yuri Zeldin et al [11] observed a decrease in episodes of rhinorrhea in 84.5% of patients. Rao Sukhesh [12] observed a decrease in symptoms of rhinorrhea in 80.77% of patients. Yuri Zeldin et al[11] considered improvement in quality of life with visual analogue scale in their study which can be a factor for the percentage variation. Similarly In the study by Rao Sukhesh [12] we observed symptoms were graded as mild, moderate and severe. This can lead to a variation in response of symptom relief from our study.

In the present day scenario immunotherapy is indicated as a supplement to allergen avoidance and to pharmacotherapy.[13] In a study conducted by Shyam et al[14] in patients of Allergic rhinitis, it was observed that post immunotherapy and follow up there was a reduction in symptoms of allergic rhinitis of sneezes, Rhinorrhea, nasal block, redness of eyes, and headache in76% of patients. In this study symptom relief was studied at the end of 18 months.

In the study by Yuri Zeldin et al[11] it was observed that 73% of patients had a relief of overall symptoms of allergic rhinitis collectively where the symptom relief was analyzed at the end of 18 months. In the study by Rao Sukhesh[12] 69.21% of patients had relief in overall symptoms collectively.

In our study a collective decrease in symptoms of allergic rhinitis was seen to all the allergens was seen in 76.25% of patients at the end of 18 months. We infer that following immunotherapy a relief in symptoms of allergic rhinitis ranging from 69% to 76% can be obtained with a symptom free life over a long period.

Initially we investigated all the patients with clinical symptoms of allergic rhinitis patients with total serum IgE. Total serum IgE is believed to be elevated in cases of allergic rhinitis. In a study by V.S Chowdary et al [15] they opined that estimation of levels of total serum IgE in patients of allergic rhinitis helps in proper planning of treatment of the disease. Total serum IgE was repeated at the end of 18 months in our study.

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We observed that the levels of total serum IgE returned to normal in 86 (78.89%) of patients. According to Durham et al [16] who opined that after the successful completion of immunotherapy and at follow up post Immunotherapy there will be a reduction in release of inflammatory mediators and specific IgE levels. In a study by S. Manohar et al[17] it was reported that the levels of total serum IgE returned to normal in 90.2% of patients of allergic rhinitis and asthma.

We observed adverse reactions in the form of itching and redness in 11.92%, lassitude in 6.42% and 1.83% of patients developed abdominal pain and 0.91% of patients developed intense itching all over the body during immunotherapy.

In a study by J. Siedenberg et al[18] adverse reactions in the form of pruritus were seen in 79(40.93%), gastro intestinal disorders were seen in 4(2.07%), tiredness or lassitude seen in 1(0.51%), erythema in 9(4.66%). These findings suggest that Immunotherapy can be an effective alternative management with minimal adverse reactions apart from the other modalities of treatment available.

In our study we observed that estimation of total serum IgE forms an effective screening measure in diagnosis of Allergic rhinitis along with clinical history. Further investigation of these patients with skin prick test confirms the nature of the disease.

When these patients were given immunotherapy an improvement in clinical symptoms of allergic rhinitis was observed. Successful administration of immunotherapy depends on the proper patient selection, maintenance of quality of allergens, adequate titration of the doses of allergens, proper monitoring the timing and dosage of the allergens and follow up. Proper care has to be taken in the treatment with a careful observation to the development of adverse reactions which were to be monitored.

**CONCLUSIONS:** Immunotherapy offers significant improvement in relief of clinical symptoms of allergic rhinitis with minimal adverse reactions over a long time. Total serum IgE forms an affective screening tool in diagnosis of allergic rhinitis. Immunotherapy appears as a safe alternative treatment for the management of allergic rhinitis.

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