Medical and Research Publications
International Open Access

Research Article **Journal of MAR Pulmonology (Volume 5 Issue 6)**

Clinical Effectiveness of Subcutaneous Immunotherapy in Allergy.

Binu Krishnan [1]*, Sruthy S S [2], Rajalekshmi Krishnamoorthy [3], Ancy Robin [4]

1. Senior consultant pulmonologist, Department of Pulmonary and Sleep medicine, PRS Hospital, India.
2. Clinical pharmacist, Department of Pulmonary and Sleep medicine, PRS Hospital, India.
3. Clinical pharmacist, Department of Pulmonary and Sleep medicine, PRS Hospital, India.
4. Junior medical officer, Department of Pulmonary and Sleep medicine, PRS Hospital, India.

Corresponding Author: Binu Krishnan, MD, FCCP, FAPSR. Senior consultant Pulmonologist, PRS Hospital, Kerala, India.

Received Date: February 12, 2023

Published Date: March 01, 2023

Abstract

Background and objective: *In India, very few studies are available regarding the effect of immunotherapy in allergic rhinitis and asthma. The objective was to evaluate the effectiveness of subcutaneous immunotherapy in various allergies.*

Methodology: *All adult patients who underwent subcutaneous immunotherapy at a tertiary care centre in India were retrospectively analyzed for a period of 60 months. Subcutaneous immunotherapy is indicated for the treatment of allergic conditions affecting the nose and eyes (allergic rhino conjunctivitis), ears (allergic otitis media), lungs (bronchial asthma) as well as for severe insect sting allergy.*

Results: *213 patients were included in the study. Females constituted the majority with 60.09% (N=128) than males 39.9 % (N= 85). The mean age of patients was 37.07 +/- 40.30. The majority of patients included in the study was age below 40 that is, 63.37% (n=135). The mean IGE level was 320.61 +/- 125.479 IU/ml. The success rate of immunotherapy was 64.31% (n= 137) and failure rate was 35.68% (n= 76). The highest successful outcome was for a combination of allergic rhinitis and atopic dermatitis (35.68%) followed by allergic rhinitis, atopic dermatitis and asthma which was present in 29 patients (13.61%).*

Conclusions: *SCIT is an effective treatment option for management of allergies especially in allergic rhinitis and atopic dermatitis.*

Key-words*: allergy, atopic hypersensitivity, asthma, immunotherapy allergic rhinitis.*

Abbreviations

SCIT: Subcutaneous Immunotherapy

BHR: bronchial Hyper Responsiveness

IgE: Immunoglobulin

SD: Standard Deviation.

HDM: House Dust Mite

Introduction

Subcutaneous immunotherapy (SCIT) is a unique type of therapy for allergic diseases because it provides symptomatic relief while modifying the allergic disease by targeting the underlying immunological mechanism. Its efficacy and safety have been established in the treatment of asthma, allergic rhinitis and stinging insect hypersensitivity. Allergy skin tests are used to find out which substances cause a person to have an allergic reaction. Immunotherapy for allergic disease involves the administration of allergens to which the patient is sensitive, for the purpose of modulating the immune response to that allergen and alleviating allergic symptoms. Immunotherapy is the only treatment that alters the abnormal immune response underlying allergic disease.

SCIT with allergens, such as venoms or food allergens is reviewed distinctly. SCIT may be administered via a conventional, cluster, or rush schedule. In conventional SCIT, the allergen is administered via once-weekly injections at increasing concentrations until a maintenance dose is obtained, followed by injections typically at 4-week intervals. In a cluster schedule, multiple injections, usually 2–3, are administered on nonconsecutive days, while in a rush protocol, multiple injections are administered on consecutive days, allowing the patient to reach maintenance typically in 1–3 days. A typical course of immunotherapy is 3–5 years in duration, as studies with SCIT have demonstrated prolonged remission after 3–4 years of treatment. Three years of SCIT may be sufficient in asthmatic patients **[**1**]**. The decision to stop or continue immunotherapy is based on the severity of the disease, benefits sustained from treatment, and convenience of treatment.

Materials and Methods

This was a retrospective analysis of all out- patients who underwent subcutaneous immunotherapy in the Pulmonology department of PRS hospital, Trivandrum, India over a period of 5 years from January 2012 to December 2016.The department had a dedicated allergy wing where both intradermal drugs as well as antigen allergies were tested. Subcutaneous immunotherapy was given for patients who were considered suitable for the treatment. The medical records of all consecutive patients who had undergone immunotherapy in PRS Hospital were analyzed for the study. This study was performed in accordance with the Declaration of Helsinki.

Patients with diagnosis of allergic rhinitis, asthma, and /or atopic dermatitis were considered for treatment with immunotherapy. Patients below the age of eighteen years and pregnant females and were excluded from the procedure.

The standard panels of allergens were considered for all intradermal allergy tests done in our centre. The allergens were widely classified as pollens, fungus, dust, food and others. The same panel was used in all patients. Allergens were used in the concentration of 1:500. Intradermal allergy was conducted as per the standard international practice. Buffered saline (1: 500) was used as the control for the entire test. Prior to the procedure, informed consent was obtained from all patients. Vital signs including pulse rate and oxygen saturation were monitored throughout the procedure using pulse oximeter. The entire procedure was done in the allergy clinic by pulmonologist. To address any potential medical emergency, all resuscitatory measures including crash-cart were available in the allergy clinic.

Allergens for treatment were prepared according to the allergy profile of each patient. The allergens were administered at increasing concentrations as once weekly injections subcutaneously until a maintenance dose was obtained. Thereafter, the dosing intervals were adjusted until a four- weekly interval was reached. Injections were started in 1/5000 concentrations which was gradually increased to 1/500 and then to 1/50 concentration. Those patients who took treatment for less than 18 months were considered as defaulters. The success of immunotherapy was defined as amelioration of symptoms of the primary disease at the completion of treatment. Those patients who had persisting symptoms at the end of treatment or defaulted treatment were considered as failures.

Statistical analysis

Categorical and quantitative variables were expressed as frequency (percentage) and mean ± SD respectively. The data were entered into Microsoft Excel 2013 and subsequently analyzed.

Results

The medical records of patients who underwent antigen allergy test in the Pulmonology department in PRS Hospital, Trivandrum, Kerala from 2012 to 2016 (60 months) were studied. Two hundred and thirteen patients were included in the study. Females constituted the majority with 60.09% (N=128) than males 39.9 % (N= 85). The mean age of patients was 37.07 +/- 40.30. The majority of patients included in the

study were below the age of forty (63.37%, n=135**[**Table 1**]**. Mean absolute eosinophil count was 479.92 +/- 2.86 cells/ micro liter. The mean IGE level was 320.61 +/- 125.479 IU/ml.

Most common allergen was house dust mite, which was present in 201 patients (94.36%), followed by house dust present in 200 patients (93.89%), grocery dust present in 181 patients (84.97%), hevea present in 169 patients (79.34%)**[**Table 2**]**. The mean number of allergen per patient was 9.16 +/- 1.97.

Most of the patients included in the study had a diagnosis of both allergic rhinitis and atopic dermatitis was 60.09% (n= 128). Other diagnosis included a combination of allergic rhinitis, atopic dermatitis and asthma was 16.43% (n= 35). Atopic dermatitis alone was 14.55% (n= 31) **[**Table 3**]**. Most of them (51.6%) had treatment with subcutaneous immunotherapy alone. The mean treatment duration of patients constituted of 26.12 +/- 12.02 **[**Table 4**]**.

The success rate of immunotherapy was 64.31% (n= 137) and failure rate was 35.68% (n= 76). The defaulted constituted of 10.79% (n= 23). The highest successful outcome of each diagnosis included a combination of allergic rhinitis, atopic dermatitis was present in 76 patients (35.68%) followed by allergic rhinitis, atopic dermatitis and asthma present in 29 patients (13.61%)**[**Table 5**]**. The mean number of vials per patients was 7.11 +/- 2.08.

AGE	18-20	14	6.57
	21-30	57	26.76
	31-40	64	30.04
	41-50	46	21.59
	51-60	22	10.32
	61-70	9	4.22
	>70	1	0.46

Table 1. Age distribution among 213 patients.

MAJOR ANTIGENS	NUMBER	PERCENTAGE
ALBIZIA	68	31.92
HEVEA	169	79.34
ORIDOXA	91	42.72
ASPERGILLUS FLAVUS	4	1.87
ASPERGILLUS NIGER	33	15.49
ASPERGILLUS FUMIGATUS	133	62.44
CANDIDA ALBICANS	47	22.06
GROCERY DUST	181	84.97
HOUSE DUST	200	93.89
OLD PAPER DUST	121	56.80
WHEAT GRAIN DUST	141	66.19
HDM	201	94.36
PRAWN	64	30.04

Table 2. Sensitivity profile of various allergens.

DIAGNOSIS	NUMBER	PERCENTAGE
Allergic Rhinitis	9	4.22
Allergic Rhinitis and Atopy	128	60.09
Atopy Alone	31	14.55
Allergic Rhinitis, Asthma	7	3.28
Allergic Rhinitis, Atopy, Asthma	35	16.43
Atopy, Asthma	3	1.40

Table 3. Diagnostic Profile.

TREATMENT	NUMBER	PERCENTAGE
SCIT	110	51.6
SCIT, NASAL SPRAY	55	25.8
SCIT, NASAL SPRAY, METERED DOSE INHLER	38	17.8
SCIT, METERED DOSE INHALER	10	4.7

Table 4 . Various treatment modalities used

OUTCOME IN EACH DIAGNOSIS	NUMBER	PERCENTAGE
ALLERGIC RHINITIS	4	1.87
ALLERGIC RHINITIS AND ATOPY	76	35.68
ATOPY ALONE	26	12.20
ALLERGIC RHINITIS, ASTHMA	5	2.34
ALLERGIC RHINITIS, ATOPY AND ASTHMA	29	13.61
ATOPY, ASTHMA	1	0.46

Table 5. Treatment outcome in each diagnosis

Discussion

In the study on allergen skin-test reactivity in a community-based sample, Maureen Sabit et al found that the sensitivity and specificity of the skin tests were more in the 35 to 40 age group for most of the allergens and decreased thereafter with advancing age **[**2**]**. The study also showed a sensitization profile of 54% to a specific allergen tested in the respective study. Increased frequency of positive skin test was demonstrated in males (p =0.003). But females demonstrated more asymptomatic sensitization (p= 0.04). In the present study, mean age of patients was 37.07+/-40.30. Majority of patients included in the study was age below 40. Females encompassed the majority with 60.09% (N= 128) compared to males 39.9% (N =85). It was analysed that the risk of allergy was greater for boys during childhood compared to females. Females show a marked shift in this trend starting from adolescent age group onwards. This was even more manifested in the case of atopic disorders like asthma, food allergies and anaphylaxis.

According to Humbles et al the contribution of eosinophils, cells associated with asthma and allergy remains to be established. Their study suggest that eosinophils contribute substantially to airway remodelling but are not obligatory for allergen – induced lung dysfunction and support an important role for eosinophil – targeted therapies in chronic asthma. Eosinophilia could be characterized as mild (450–1500 eosinophils per micro liter), moderate (1500–5000 eosinophils per micro liter) and severe (greater than 5000 eosinophils per micro liter) **[**3**]**. In a study on IgE and asthma, Kumar R et al found that that

serum IgE value increased with the increase severity of airway obstruction. In the present study, mean eosinophil count was 479.92 +/-2.86 cells/ micro liter. The IgE level was also significantly elevated with a mean of 320.61 +/- 125.48. The raised IgE levels might be a marker of phenotype of patients who benefit from anti-IgE therapies like Omalizumab **[**4**]**.

In a study on different risk factor patterns for adult asthma, rhinitis and eczema Erik P Ronmark et al found that there are different risk factor patterns for asthma, rhinitis and eczema in adults but some risk factors are overlapping between some of the conditions Their study also recorded that at least 2.3 % had all three conditions while 13.9 % had at least two conditions. The prevalence of current asthma was 11.8 %, current rhinitis 42.8 %, current eczema 13.5 in their study **[**5**]**. These values were different in the present study. Most of the patients included in the study had a diagnosis of both allergic rhinitis and atopic dermatitis was 60.09% (n= 128). Other diagnosis included a combination of allergic rhinitis, atopic dermatitis and asthma was 16.43% (n= 35). Atopic dermatitis alone was 14.55% (n= 31). It was also noted that there were contrasting differences in the prevalence of atopic dermatitis in open population and general practice setting when self-reported and physician diagnosed.

According to the opinion by Chang Keun Kim et al, SCIT was associated with greater improvements in lung function and bronchial hyper responsiveness and reductions in nasal and sputum eosinophilia and allergen reactivity. Changes in symptom scores were also much greater in patients receiving SCIT when compared to those who did not receive it **[**6**]**.

In the present study, the highest successful outcome of each diagnosis included allergic rhinitis, atopic dermatitis was present in 76 patients (35.68%) followed by allergic rhinitis, atopic dermatitis and asthma present in 29 patients (13.61%). Wanting Zhu et al suggested that their meta-analysis justifies that SCIT has a significant effect on improving symptoms and reducing medicine consumption for local allergic rhinitis patients **[**7**]**.

Nkiruka Erekosima et al suggested that SCIT reduces asthma symptoms, asthma medication usage, rhinitis/rhino conjunctivitis symptoms, conjunctivitis symptoms, and rhinitis/rhino conjunctivitis disease-specific quality of life in comparison to placebo or usual care. Respiratory reactions were the most common systemic reactions. Generally moderate to strong evidence supports the effectiveness of SCIT for treatment of allergic rhinitis and asthma, particularly with single-allergen immunotherapy regimens **[**8**]**.

In the present study, the highest successful outcome of each diagnosis included allergic rhinitis, atopic dermatitis was present in 76 patients (35.68%) followed by allergic rhinitis, atopic dermatitis and asthma present in 29 patients (13.61%).

Myung Hyun Sohn et al suggested that SCIT is an effective and well-tolerated treatment option in the management of AR which has been practiced for almost a century and the only treatment that can affect the natural course of disease **[**9**]**.

Lee et al reported a valuable study on the efficacy and safety of SCIT in routine clinical practice in Korean adults with allergic rhinitis sensitized to house dust mites (HDM). This large retrospective cohort study reviewed 304 patients with allergic rhinitis treated using SCIT targeting HDM alone or with pollens for at least 1 year, and showed that SCIT facilitated remission in 76.6% of patients with allergic rhinitis within 4.9 years on average. They also demonstrated that severe allergic rhinitis, specific IgE levels to HDM ≥17.5 k U/L, and duration of immunotherapy ≥3 years were identified as significant predictors of clinical remission during SCIT for patients with AR sensitized to HDM **[**10**]**.

In the present study, most common allergen was house dust mite, which was present in 201 patients (94.36%), followed by house dust present in 200 patients (93.89%). Mean absolute eosinophil count was 479.92 +/- 2.86 cells/ micro liter. The mean IGE level was 320.61 +/- 125.479 IU/ml. Larger and multicenter clinical trials are needed to clarify the safety and long-term efficacy. The limitation was that the present study was a retrospective analysis of the effect of immunotherapy. Also, long term outcome of subcutaneous immunotherapy in allergy could not be assessed from the present study.

Conclusion

Subcutaneous immunotherapy is an effective treatment option for management of allergies especially in allergic rhinitis and atopic dermatitis. Larger clinical trials are required to determine the long-term outcome of immunotherapy in various allergies.

References

1. Heather Ellen Hoch MD, Stanley James Szefler MD, in Kendig's Disorders of the Respiratory Tract (Ninth Edition), 2019. Pages 747-755.e3.

2. Maureen Sabit, Cecil Wong, Agnes Andaya4 and John Donnie Ramos. Allergy Asthma Clinical Immunology (2020) PMC 7477877DOI: 10.1186/s13223-020-00471-9.

3. Humbles, A. A., Lloyd, C. M., McMillan, S. J., Friend, D. S., Xanthou, G., Erin. E. McKenna, Ghiran, S., Gerard, N. P., Yu, C., Orkin, S. H., & Gerard, C. (2004). A Critical Role for Eosinophils in Allergic Airways Remodeling. Science, 305(5691), 1776–1779. http://www.jstor.org/stable/3837771

4. Kumar R, Singh BP, Srivastava P, Sridhara S, Arora N, Gaur SN. Relevance of serum IgE estimation in allergic bronchial asthma with special reference to food allergy. Asian Pac J Allergy Immunol. 2006 Dec;24(4):191-9. PMID: 17348241.

5. Erik P. Ronmark, Linda Ekerljung, Roxana Mincheva, Sigrid Sjölander,Stig Hagstad, Göran Wennergren,Eva Rönmark,Jan Lötvall,Bo Lundbäck Different risk factor patterns for adult asthma, rhinitis and eczema: results from West Sweden Asthma Study (doi: 10.1186/s13601-016-0112-0)

6. Kim CK, Callaway Z, Park JS, Kwon E. Efficacy of subcutaneous immunotherapy for patients with asthma and allergic rhinitis in Korea: effect on eosinophilic inflammation. Asia Pac Allergy. 2021 Oct 25;11(4):e43. doi: 10.5415/apallergy.2021.11.e43. PMID: 34786373; PMCID: PMC8563102.

7. Zhu W, Gao P, Zhang Q, Chen J. Efficacy and Safety of Subcutaneous Immunotherapy for Local Allergic Rhinitis: A Meta-Analysis of Randomized Controlled Trials. Am J Rhinol Allergy. 2022 Mar;36(2):245-252. doi: 10.1177/19458924211050547. Epub 2021 Oct 19. PMID: 34664513.

8. Erekosima N, Suarez-Cuervo C, Ramanathan M, Kim JM, Chelladurai Y, Segal JB, Lin SY. Effectiveness of subcutaneous immunotherapy for allergic rhinoconjunctivitis and asthma: a systematic review. Laryngoscope. 2014 Mar;124(3):616-27. doi: 10.1002/lary.24295. Epub 2013 Aug 5. PMID: 23832632.

9. Sohn MH. Efficacy and Safety of Subcutaneous Allergen Immunotherapy for Allergic Rhinitis. Allergy Asthma Immunol Res. 2018 Jan;10(1):1-3. doi: 10.4168/aair.2018.10.1.1. PMID: 29178670; PMCID: PMC5705477.

10. Lee JH, Kim SC, Choi H, Jung CG, Ban GY, Shin YS, Nahm DH, Park HS, Ye YM. A Retrospective Study of Clinical Response Predictors in Subcutaneous Allergen Immunotherapy With House Dust Mites for Allergic Rhinitis. Allergy Asthma Immunol Res. 2018 Jan;10(1):18-24. doi: 10.4168/aair.2018.10.1.18. PMID: 29178674; PMCID: PMC5705479.

11. Agache, Ioana; Laculiceanu, Alexandru; Cojanu, Catalina; Spanu, Daniela; Rogozea, Liliana Advances in allergen immunotherapy for asthma 2004Sep17;305(5691):1776-9.doi: 10.1126/science.110028.

12. Jensen-Jarolim E, Untersmayr E. Gender-medicine aspects in allergology. Allergy. 2008 May; 63(5):610-5. Doi: 10.1111/j.1398-9995.2008.01645.x. PMID: 18394135; PMCID: PMC2999751.

13. Fulkerson PC, Rothenberg ME. Targeting eosinophils in allergy, inflammation and beyond. Nat Rev Drug Discov. 2013 Feb; 12(2):117-29. Doi: 10.1038/nrd3838. Epub 2013 Jan 21. PMID: 23334207; PMCID: PMC3822762.