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IMMUNOTHERAPY VERSUS PHARMACOTHERAPY AMONG PATIENTS WITH ALLERGIC RHINITIS BASED ON TOTAL SYMPTOM SCORE AND MEDICATION SCORE.

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ABSTRACT **Objective:** To compare efficacy of immunotherapy and pharmacotherapy in patients with allergic rhinitis using total symptom score and rescue medication score. **Design:** Prospective analysis of outcomes of different treatment modalities in allergic rhinitis patients in a tertiary care centre. **Subjects:** Hundred and ten patients, diagnosed to have allergic rhinitis were included in this study, they were divided into 2 groups based on treatment modality i:e, pharmacotherapy (Group A) and immunotherapy group (Group B). Former contained 76 patients and latter 34 patients **Results:** The pretreatment mean total symptom score (TSS) in pharmacotherapy group was 7.76±3.8 and in immunotherapy group 10.88±2.45. Post treatment mean total symptom score was 7.31±3.68 and 6.29±3.01 respectively. Mean rescue medication score (RMS) in pharmacotherapy group was 0.40±0.22 and immunotherapy was 0.28±0.18. **Conclusion:** Both pharmacotherapy and immunotherapy was efficacious and safe in treating patients with AR , but the magnitude of reduction was more in immunotherapy group. Regardless of the sensitisation status of the patients (even if the patient is polysensitised) they responded well with single allergen immunotherapy. Reduction in rescue medication score was statistically significant in those receiving immunotherapy giving a stable control. Immunotherapy can also be used as anti symptomatic treatment and has the capacity to modify the course of illness

KEYWORDS :

INTRODUCTION

Allergic rhinitis(AR) is a global health problem which causes morbidity and disability worldwide. In India, AR is considered a minor disease[1] despite the fact that symptoms of AR are present in 75% children and 80% asthmatic adults. AR reduces the quality of life, impairs the quality of sleep and also affects the cognition and causes exhaustion and irritability. AR also affects the work and school performance. Preventable expenditure per patient who are inadequately treated for AR is significant due to absenteeism (absence from work) and also presenteeism (reduced productivity at work), that is, €2405 per untreated patient per year [2].

The great majority of patients (60–80 %) of AR consulting doctors are polysensitised[3]. As the age increases the polysensitisation becomes more prevalent[4]. Polysensitised patient have a risk of developing subsequent allergic diseases such as allergic asthma. Patient who are polysensitized may not be polyallergic, whereas a polyallergic patient is invariably polysensitised. Polyallergy is defined if patient has sensitisation to multiple allergen in skin prick test and has causative association with sensitising allergen exposure [5].

Allergin immunotherapy(AIT) is an immuno-modulatory method for the treatment of immunoglobulin E (IgE) mediated allergic diseases. AIT is given sequentially in increasing dose of antigen(s) which induces a shift from TH2 based immunological response to TH1. Recent data suggest that the activity of IL-10-secreting TR1-like cells and CD25+, CD4+, T regulatory(TReg) cells decreases in patients with AR but are increased in patient who are on SIT. Increase in the level of IL-10 and TReg cells decreases the allergic response[6]. With an aim to find a better alternative for the patients of allergic rhinitis , this study was carried out comparing the patient parameters in pharmacotherapy and immunotherapy cohorts.

Materials and Methods

The study was conducted in the Department of Otolaryngology Head and Neck surgery, Pgimer, Chandigarh, India from June 2017 to feb 2020. Instituitional ethics clearance was obtained prior to study. This was a prospective study with 110 Patients (with in age group of 12 to 60 years) , diagnosed to have AR and having a positive skin prick test to one or more allergens. They were divided into 2 groups based on treatment modality i:e, pharmacotherapy (Group A)and immunotherapy group (Group B). Former contained 76 patients and latter 34 patients. Detailed history, clinical examination and systemic examination was done. Pre treatment assessment total symptom score was done and all patients were subjected to skin prick test. Out of all those patients who had positive Skin prick test (SPT), 34 patients were selected for immunotherapy after meticulously correlating between patients clinical history and their SPT results. Inclusion to immunotherapy group also depended on patient's willingness to start immunotherapy, because of high cost and lack of easy availability of immunotherapy in our country. Rest of the patients i:e, 76 patients were included in pharmacotherapy group.

Group A – Patients in this group were given antihistamines and topical steroids ie, levocetrezine 5mg and montelukast 10mg tablets which was given once daily to the patients along with fluticasone nasal spray which was administered 2puffs per nostril twice daily for 2weeks followed by one puff twice a day for 2months.

Group B – Patients were given subcutaneous immunotherapy after meticulously correlating their clinical history and SPT results. Specific subcutaneous immunotherapy (SCIT) was administered after confirming allergens by skin prick test. SCIT preparation ALLERGOVIT® were given in those patients who have allergy to pollen and SCIT preparation ACAROID® was given in those patients who were allergic to HDM (house dust mite) . Subcutanous immunotherapy consist of initial treatment phase during which allergen dose is increased, and a maintenance phase where a constant allergen dose is administered at longer intervals (3years). The injection was given subcutaneously with insulin syringe. Dose was started with 0.1ml and increased weekly till 0.6-0.8ml depending upon the AIT.

Both these 2 group of patients were followed up after 2 months for assessment, total symptom score and rescue medication score.

Skin Prick Test (SPT)

We used standardised allergen extracts of a variety of allergens including mites, pollen, moulds, animal epithelia, and food. A positive control (1.7mg/ml histamine dihydrochloride) and a negative control (physiological saline) was included. Separate lancets were used for each allergen, testing and reading done after 15 minutes. Reactions >3 mm in a subject was regarded as positive. Use of concomitant medication had to be discontinued for specific time.

Total symptom scores(TSS)

Here we used 6 symptoms of AR ie, sneezing , running nose , nasal blockade itching and redness of eyes , itching of nose , watering of eyes. Each symptom was assigned a score ranging from 0 to 3 depending on their severity ie,

'0' means no symptoms
'1' : symptoms present; easily tolerable and lesser awareness
'2': moderate symptoms (awareness of symptoms present: bothersome but tolerable) and
'3': severe symptoms (difficult to tolerate; hampers day to day activities and sleep).

So total score ranged from 0 to 18.

Average rescue medication score

Instructions were given to the patients to follow a stepwise regimen, stepped up if symptoms were not reduced with previous regimen;

Step 1 OAH (oral antihistaminics)
Step 2 INCS (intranasal corticosteroids)
Step 3 Oral corticosteroids

RMS of present day is the highest score recorded the same day. Average RMS (ARMS) average of daily RMS in the given period . ARMS ranged from 0 to 3.

Scores were assigned as follows
0 = no medication
1 = patient took OAH;
2 = patient took INCS and
3 = patient had to take oral corticosteroids to alleviate the symptoms.

RESULTS

Study population included 110 patients with mean age of 32.61±11.58. Out of 76 patients in pharmacotherapy group 40 were males and 36 were females . Out of 34 immunotherapy patients 20 females and 14 were males. Most common presenting symptom in the present study was sneezing accounting for 97%. seventy nine had persistent symptoms and patients had intermediate symptoms. Out of 110 patients, 79 had perennial symptoms, 19 patients had seasonal symptoms,12 patients had perennial with seasonal exacerbations. Sixty seven patients had indoor symptoms,8 patients had outdoor symptoms and 35 patients had both indoor and outdoor symptoms. Sixty six patients had symptoms more during morning time, out of which 48 patients were positive for house dust mite (HDM). Analysing the sensitisation pattern of the cohort, 78 patients were polysensitised, 32 were mono-sensitised. Sixty seven patients gave positive sensitisation to dermatophagoides (figure) . Out of 67 patient who came positive for dermatophagoides, 53 patients had perennial symptoms and rest perennial with seasonal exacerbation,47 patients had indoor symptoms more and rest had both indoor and outdoor symptoms. Out of 13 patients who gave positive history for asthma,12 were dermatophagoides positive.

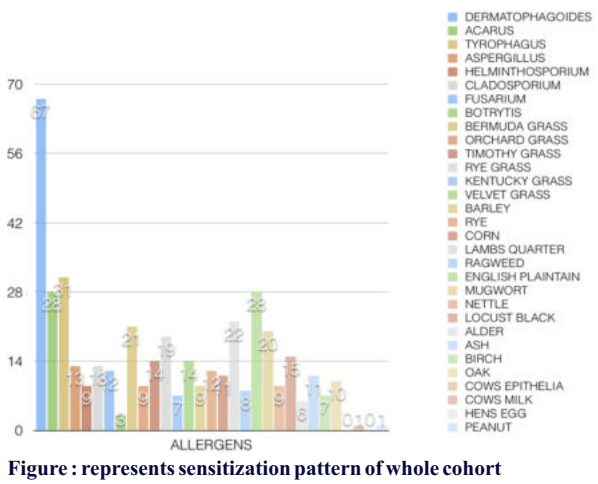

Figure : represents sensitization pattern of whole cohort

The mean total symptom score pretreatment in conventional group was 7.76±3.8 and in immunotherapy group 10.88±2.45. Post treatment mean total symptom score in conventional group was 7.31±3.68 and in immunotherapy group 6.29±3.01. There is significant reduction in total symptom score in both group following 2months of therapy in conventional group(p=0.22) and immunotherapy group(p=0.000) but there is no statistical significance while comparing between post treatment TSS of 2 groups(p=0.197). Mean rescue medication score in conventional group was 0.40±0.22 and immunotherapy was 0.28±0.18. Average rescue medication score when comparing 2 groups after 2 months of treatment appears that patient in immunotherapy group have statistically significant reduction in using rescue medication than that of conventional groups(p=0.017).

Safety

In both the groups the intervention medications were well tolerated. In pharmacotherapy group the only side effects observed among patients was day time sleepiness. In immunotherapy group we observed most AEs were mild local allergic reactions (LAR) such as local pruritis and wheal at the injection site. The majority of these LAR occurred within 1-2 days after administration of each dose of AIT and after each subsequent injection there was increase in wheal size noted among patients. No AEs were reported as systemic allergic reaction in any of the groups.

DISCUSSION

We had different numbers of patients in both the groups but regarding rest of the parameters the two groups were homogenous and statistically comparable as shown in table.

Table 1: comparability of the two groups

	Immunotherapy group	pharmacotherapy group	p value
Age (mean)	30.75	33.49	0.244
Sex (mean)			
Male	14	40	0.196
Female	20	36	
Duration (mean in months)	87	79.24	0.593
Symptoms			
Persistent	31	52	0.007
Intermittent	3	24	
Indoor	21	46	0.653
Outdoor	3	5	
Both	10	25	
Perennial	25	54	0.17
Seasonal	7	12	
Perennial with seasonal exacerbation	2	10	

In this study we used TSS pre and post treatment as one of the criterion to assess the efficacy of the treatment modality. Ideally proper interpretation of symptom score requires proper assessment of timing of relevant allergen exposure since the onset and duration of allergen exposure vary with time especially pollen allergen which was clearly stated in study conducted by O.Pfaar[7] et al. In our study after, the sensitization pattern of cohort after skin prick test, Dermatophagoides came out to be the most common allergen which came positive taking both monosensitized and polysensitized patients in to consideration. Hence assessment during pollen season was less relevant. This was in concordance with the study published by B. Majkowska –Wojciechowska et al[8].

Thirteen patients gave history of asthma and out of that 12 patient were HDM (house dust mite) sensitive on SPT. A study conducted by Gidey et al[9] in Ethiopian asthmatic patients had house dust mites as the commonest sensitizers. In our study group 78 patients were polysensitised, there is an increasing trend of polysensitization with increase in age. Kim et al[10], in their study concluded that with increasing age, prevalence of polysensitization to inhalant allergens increase. Polysensitization increases with increase in duration of symptoms, Pascal Demoly et al[11] conducted a study where in 60-80% of patients diagnosed to have allergic rhinitis were polysensitized. Study also says that polysensitisation is a risk factor for subsequent devolepment of allergic asthma.

BSACI guidelines published in 2007-8 mentioned that immunotherapy to be continued for 3-5 years for better results. No study till date have assessed and compared the results after 2 months. We assessed our patient 2 months following initiation of treatment. Results helped us to conclude that immunotherapy is at least as

effective as pharmacotherapy in controlling the symptoms in patients. Paolo Maria Matricardi et al[12] conducted a study wherein they said INCS, OAH, and other drugs are normally considered as a "first-line" and used for fast-acting anti-symptomatic treatment for allergic rhinitis. In contrast immunotherapy is usually considered a "second-line" treatment, but the latter has got the ability to modify the natural history of disease.

Out of 34 patients in immunotherapy group, 27 patients were undergoing dustmite immunotherapy, 5 patients were on grass pollen immunotherapy and 2 patient was given immunotherapy against mugwort. In our study we tried to control those factors that can influence the efficacy, such as screening of patients, allergen choice, quality of extract, and compliance of patients etc.There was a statistically significant reduction in the rescue medication score in this group, thereby giving a persistently stable control.

This study showed that pharmacotherapy and immunotherapy both are well tolerated and efficacious in decreasing symptoms of allergic rhinitis by decreasing the total symptom score in both the cases but more reduction in immunotherapy group. Rak et al[13] compared efficacy of immunotherapy and nasal corticosteroids, they found that nasal symptoms decreased significantly in the nasal steroid treated patients when compared to SIT-treated patients . A study conducted by Giovannini [14] et al also compared between Drug treatment and immunotherapy.. After one year 12 of 15 patients treated with SIT had less symptoms and reduced rescue medications, to none in drug treated group and after three years 15 of 15 were improved in immunotherapy group compared to one of 15 in pharmacotherapy group. The results of our study were almost similar, but we did analysis after 2 months of therapy.

There are not many studies comparing medication scores between pharmacotherapy and immunotherapy, but studies are there comparing those two with placebo. Our study is unique wherein the two groups are being compared. Matricardi et al[12] conducted similar study comparing both pharmacotherapy and immunotherapy wherein they compared their 2 groups only with total symptom score and not with medication score. Interestingly till date there is debate on effectiveness of single AIT in polysensitized patients. In our study significant effect is also seen in patients in immunotherapy group regardless of their sensitization status which is in concordance with another study conducted by demoly et al[11].

CONCLUSION

Both pharmacotherapy and immunotherapy is efficacious and safe in treating patients with AR based on TSS, but the magnitude of reduction in TSS is more in immunotherapy group. Reduction in ARMS is seen more in immunotherapy group and was statistically significant . Majority of patients in the study group were polysensitized, but the effectiveness of single AIT in treating polysensitized patients, showed a good response irrespective of their polysensitisation. Allergen immunotherapy can be used as anti symptomatic treatment and is as effective as pharmacotherapy with added advantage of changing the course of disease. The effect on asthma is yet to be seen and requires a longer follow up but preliminary results look promising.

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