Comparative evaluation of safety and efficacy of oral Rupatadine with oral Fexofenadine in patients of seasonal allergic rhinitis

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ABSTRACT

Introduction: Allergic rhinitis is a disease of the mucous membranes of the nasal airways. Proinflamatory mediators like histamine, leukotrienes, Platelet activating factor (PAF) play a vital role in pathogenesis. Fexofenadine, an antihistaminic and Rupatadine a H_1 receptor and PAF antagonist are used in the present study and their safety and efficacy were compared.

Objectives: The rationale of this study was to evaluate whether Rupatadine or Fexofenadine was better in the treatment of allergic rhinitis.

Materials & Methods: The present study comprised of a total of 100 patients with typical features of allergic rhinitis. They are divided into 2 groups of 50 patients each,group 1 is treated by Rupatadine and group 2 by Fexofenadine. Patients in the age group of 16-45 years of both sexes were included in the study and the duration of these symptoms had to be of at least one month or more to rule out common cold or other minor infections of the upper respiratory tract.

Results: Rupatadine had a slightly more edge in comparison to Fexofenadine in controlling the symptoms of the allergic rhinitis. Reduction of IgE levels, suppression of Absolute eosinophil count and radiographic evidence of improvement of maxillary sinuses was better with Rupatadine.

Conclusion: Though the results in our study did not show statistically significant difference between the two drugs, clinical efficacy and safety of Rupatadine in allergic rhinitis was clearly outweighing Fexofenadine. Considering all the above factors, Rupatadine appears to be a better choice in the treatment of allergic rhinitis as compared with Fexofenadine.

Keywords: Allergic rhinitis, Fexofenadine, Platelet activating factor, Rupatadine

INTRODUCTION

The earliest record of what might have been an allergic reaction is in the year 3000 B.C. when Slien Nung, emperor of China forbade pregnant women to eat fish, chicken and horse meal. He thought ingestion of these foods was causing ulceration of the skin[1]. The term "ALLERGY" was given by Von Pirquet in 1906[1].

Allergic rhinitis (AR), also known as hay fever, is an IgE mediated hypersensitivity disease of the mucous membranes of the nasal airways[2]. Allergic rhinitis is broadly divided into seasonal and perennial. Seasonal allergic rhinitis (SAR) is also called as Hay fever, found in 10% of the general population. Perennial allergic rhinitis can occur in the patient throughout the year, affecting approximately 10-20% of the population.[2] SAR is normally triggered by various types of pollen, trees, grasses and as well as outdoor mould spores. The major symptoms include sneezing, rhinorrhoea, nasal obstruction and nasal or pharyngeal itching. Epiphora and itching are also common features. Symptoms of Perennial allergic rhinitis (PAR) are similar to those of SAR, although nasal obstruction is generally more pronounced.

Allergic rhinitis has a relevant impact on society because of its high prevalence, association with an impaired quality of life and the presence of co-morbidities such as atopy and asthma[3]. It affects a large percentage of paediatric patients and causes significant number of school days missed per year. Impairment of work in adults also occurs affecting the finances of patients indirectly through lost workdays and directly through healthcare cost spent for the disease[4].

Platelet activating factor (PAF) is an important mediator of allergic rhinitis leading to vasodilation and an increase in vascular permeability that may contribute to the appearance of rhinorrhoea and nasal congestion[5]. Histamine is a mediator of early response, being released from preformed reservoirs in mast cells, whereas PAF, a mediator of late response, is mainly synthesized denovo[6,7]. Further more, each of these mediators is able to promote the release of the other in some tissues and numerous target cells[8].

From the available experimental evidence it could be reasonable to infer that the blockade of both histamine and PAF receptors could be of superior clinical efficacy than the blockade of any one of these receptor types in the treatment of allergic rhinitis.

Rupatadine is a once daily, selective, non sedative, long acting H_1 antihistaminic with antagonistic property to Platelet activating factor through its interaction with specific receptors. Rupatadine has a good safety profile and tolerability at the dose of 10mg/day[9] and is devoid of arrythmogenic effects[10]. Rupatadine is indicated for the relief of symptoms associated with allergic rhinitis in adults and children 12 years of age or older,dose is 10mg once daily. It is contraindicated in patients with a known hypersensitivity to any of its ingredients and side effects include headache, somnolence, dizziness, fatigue, asthenia and dry mouth.

Fexofenadine hydrochloride is a selective, non-sedating H_1 receptor antagonist[11]. It is an active carboxylic acid metabolite of Terfenadine, which causes QT interval prolongation leading to cardiac arrhythmias[12]. Radiolabeled tissue distribution studies in rats indicated that Fexofenadine does not cross the blood-brain barrier[13]. In adults and children of 12 years and older the recommended dose is 60 mg twice daily or 180 mg once daily. In children of 6 to 11 years of age the recommended dose of Fexofenadine tablets is 30 mg twice daily[14].

In light of these factors the present study was undertaken to evaluate and compare the safety and efficacy of oral Rupatadine with oral Fexofenadine in patients having seasonal allergic rhinitis.

MATERIALS & METHODS

The present study comprised of a total of 100 patients with allergic rhinitis selected from the allergy clinic of the Government E.N.T Hospital, Koti, Hyderabad. A prior written consent was obtained from all the study participants. They were divided into 2 groups of 50 patients each. In the present study we selected patients having the typical features of allergic rhinitis such as sneezing, watery nasal discharge, itching in the nose / throat, and nasal blockade. The duration of these symptoms had to be of at least one month or more to rule out common cold or other minor infections of the upper respiratory tract. Patients in the age group of 16-45 years of both sexes were included in the study because allergic rhinitis is mostly seen in this age group. Secondly in patients above 45years of age, the reactivity to skin test for allergy is reduced and inconsistent.

Patients who were already on medication at the time of the first visit or undergoing desensitization were not included in this study. Similarly patients having features of secondary sinus infection or any major systemic disease like diabetes/ hypertension/ tuberculosis were excluded. Pregnant / lactating women and patients with known history of hypersensitivity to antihistaminics or corticosteroids were also excluded.

After selection of the patient, his/her presenting complaints with duration of symptoms along with history of exposure to any specific agents were noted.

History taking was followed by general, systemic and E.N.T. examination of the patient. Rhinoscopy was done to see the appearance of nasal mucosa, the presence of any nasal discharge, the position of the nasal septum, the condition of the turbinates and any other findings. After examining the patient, investigations were done. X-ray of the Para nasal sinuses was taken to detect any sinusitis and also to see for mucosal thickening which is a feature of allergic sinusitis. Blood samples were taken for investigations like complete blood picture (CBP), absolute eosinophil count and measurement of Immunoglobulin E (IgE) levels. Skin test for allergy was performed on all patients. This helps in strengthening the diagnosis of allergy, finding out the causative allergens in some cases and also to test the ability of the anti-histamines to suppress the skin reaction.

After the investigations, the patients were divided randomly into 2 groups. Patients in Group – I(n=50) received tablets of Rupatadine 10mg tablets (1 tablet / day) for 14 days. Group - II(n=50) received Fexofenadine 180mg tablets (1 tablet / day) for 14 days.

The patients were asked to report at the hospital after 7 days and they were followed up with regard to clinical improvement of symptoms and signs and any adverse effects as reported by the patient. After completion of the total duration of 14 days of treatment the patients again reported at the hospital. They were followed up with regard to clinical improvement, any adverse effects reported and also by repeating all the investigations done before starting of the treatment. Institutional Ethics Committee approval was taken before starting the study.

RESULTS

The present study comprised of 100 patients with allergic rhinitis selected from the allergy clinic of the Government E.N.T Hospital, Koti, Hyderabad. They were divided into 2 groups of 50 patients each treated by the two drugs Rupatadine and Fexofenadine.

Patients in the age group of 16-45 years of both sexes were included in the study, because allergic rhinitis is mostly seen in this age group. In our study maximum number of patients (75%) belonged to the age group between 16 -35 years (Table1). In this study of 100 cases, all the patients (100%) with allergic rhinitis had sneezing followed by watery nasal discharge, which was present in 92 patients (92%). Itching (nose/ conjunctiva / throat) was reported by 44 patients (44%), nasal blocking by 64 patients (64%) and anosmia by 22 patients (22%).

Thus, sneezing and watery nasal discharge were the most common complaints. Anosmia was the least common and usually secondary to nasal blocking. These findings were in accordance with the findings reported by Pfaar et al, who

quoted that sneezing and nasal itching represents main characteristic symptoms besides nasal obstruction and rhinorrhea in allergic rhinitis[15]. When asked about the history of exposure to any specific agent, most of the patients answered in the negative. History of allergic disorders in family members was reported by 18 patients (24%).

Of the 100 cases in this study, 82 cases (82%) showed at least one or more signs of allergic rhinitis which include pale nasal mucosa, mucosal edema, and presence of watery discharge, mucosal congestion and hypertrophy of turbinates.

Out of the 100 cases in the study, 12 cases showed mucosal thickening in the maxillary sinuses before starting treatment. Mucosal thickening was detected using X-ray of paranasal sinuses. On blood sample examination, 66 out of 100 patients (66%) showed eosinophil counts above normal levels and 74 out of 100 patients (74%) showed IgE levels above normal, before starting treatment. Positive skin tests were observed in 86 out of 100 patients (86%) before treatment.

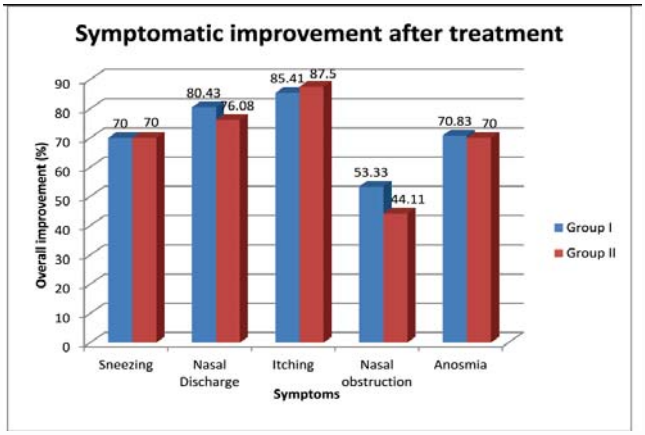
The following results were obtained after treatment. Symptomatic improvement was similar with the two drugs in relation to sneezing. The overall reduction in sneezing was 70% with both the drugs. Nasal discharge was little more effectively reduced by Rupatadine (80%) when compared to Fexofenadine (76%). Relief from itching was more or less similar with both the drugs i.e., 87% with Fexofenadine and 85% with Rupatadine. Nasal obstruction was better relieved by Rupatadine (53%) as compared to Fexofenadine (44%). Anosmia was reduced similarly with both the drugs (70%) (Graph1).

Physical signs of allergic rhinitis as seen by rhinoscopy were improved slightly better with Rupatadine. 47.72% of patients showed normal appearance of nasal cavity after treatment with Rupatadine as compared to 47.36% with Fexofenadine, but the difference is not significant. Rupatadine and Fexofenadine were found to have more or less similar levels of efficacy in controlling the symptoms of the allergic rhinitis, but the results gave Rupatadine slightly more edge.

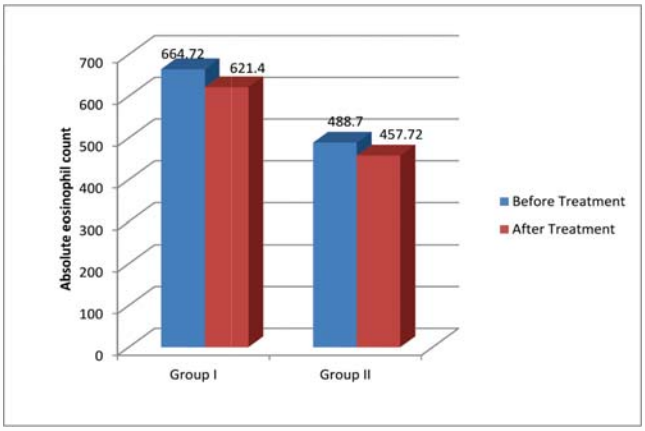
Radiograph of paranasal sinuses was suggestive of allergy in 6 patients in each of the 2 groups. Out of them 6 patients in Rupatadine group and 4 patients in Fexofenadine group had normal radiographic appearance after treatment (Table 2). Mean Absolute eosinophil count in Group I before treatment is 664.72 and after treatment is 621.4 and Mean Absolute eosinophil count in Group II 488.7 before treatment is and after treatment is 457.72 (Graph 2). Rupatadine produced a fall of around 6.3% in the mean absolute eosinophil count whereas Fexofenadine produced minor fall of around 5.8%. Regarding the skin test for allergy, although the skin test result became negative in 81% of patients with Rupatadine and 73% of patients with Fexofenadine, the mean percent reduction of skin reactions were slightly more with Fexofenadine (93%) as compared with that of Rupatadine (92%) (Graph 3). Radiographic evidence of improvement in the maxillary sinuses (mucosal thickening) was better with Rupatadine group compared to Fexofenadine. Rupatadine was more effective in reduction of IgE levels as compared with Fexofenadine (Table 3).

Few patients from both the groups reported with mild adverse or undesirable effects. Dryness of mouth was reported by 6 patients using Rupatadine and 5 patients using Fexofenadine. Drowsiness was reported by 2 patients on Rupatadine and 1 patient on Fexofenadine. Among the patients using Fexofenadine; headache was reported by 2 and vomiting was reported by 1 patient. All these adverse effects were subsided by themselves with continued treatment. So adverse effects were found to be slightly more with Fexofenadine than the other drug (Table 4).

Graph 1: Symptomatic improvement after treatment in both the groups



Graph 2: Changes in Mean Absolute eosinophil count values with the two drugs



Graph 3: Overall suppression of skin test reactions after treatment

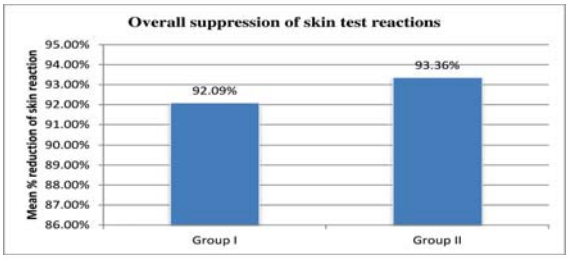


Table 1: Age distribution of patients among 2 groups

Age Groups	Group-I		Group-II	
	No. of Patients	Percentage (%)	No. of Patients	Percentage (%)
16 – 25	21	42	19	38
26 – 35	17	34	18	36
36 – 45	12	24	13	26

No significant difference was noted in the age distribution of the two study groups.

Table 2: Radiograph [Occipito Mental View or Water's View] of Para Nasal Sinuses (Mucosal thickening)

Groups	Before treatment	After treatment Number of cases showing		
		Complete Improvement	Partial Improvement	No Improvement
Group-I	6	6	0	0
Group-II	6	4	2	0

Table 3: Comparative % reduction of IgE values with the treatment by the two drugs

	% reduction with Rupatadine	% reduction with Fexofenadine
Mean	11.36	9.99
± SD	11.99	5.91
± SE	1.69	0.83

p>0.05 (p = 0.23) not significant

Table 4: Adverse effects reported during treatment by both group drugs

Drug	No of patients who reported with adverse effects	Dryness of mouth / throat	Drowsiness	Others
Group-I	8	6	2	Nil
Group-II	9	5	1	Headache (2) Vomiting (1)

DISCUSSION

There are several studies conducted comparing the efficacy of Rupatadine with Cetirizine[16], Levocetirizine[17], Olopatadine hydrochloride[18], Loratadine[19], Ebastine[20] in Allergic rhinitis. Similarly studies were also performed comparing Fexofenadine with Cetirizine[21], Loratadine[22], Desloratadine[23], Terfenadine[12] in patients with Allergic rhinitis. But there are hardly any available studies comparing Rupatadine with Fexofenadine in treatment of Allergic rhinitis.

Though the results in our study did not show statistically significant difference between the two drugs, clinical efficacy and safety of Rupatadine in allergic rhinitis was clearly outweighing Fexofenadine. Considering all the above factors, Rupatadine appears to be a better choice in the treatment of allergic rhinitis as compared with Fexofenadine. However, further studies with an increased sample size should be carried out to understand the significant difference in the clinical efficacy and safety of Rupatadine with Fexofenadine in patients suffering with Allergic rhinitis.

CONCLUSION

The two drugs, Rupatadine and Fexofenadine were found to have more or less similar levels of efficacy in controlling the symptoms of the allergic rhinitis, but the results gave Rupatadine slightly more edge. Nasal obstruction was effectively relieved by Rupatadine.

Radiographic evidence of improvement in the maxillary sinuses (mucosal thickening) and reduction in IgE levels and suppression of Absolute eosinophil count was better with Rupatadine group compared to Fexofenadine. Adverse effects were found to be slightly more with Fexofenadine than the other drug. Considering all the above factors, Rupatadine appears to be a better choice in the treatment of allergic rhinitis as compared with Fexofenadine. However, further studies with an increased sample size should be carried out to understand the significant difference in the clinical efficacy and safety of Rupatadine with Fexofenadine in patients suffering with Allergic rhinitis.

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