Comparative Analysis of Treatment of Allergic Rhinitis Utilizing Azelastine and Fluticasone

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ABSTRACT
The present study was conducted to evaluate the efficacy of topical therapy in patients with allergic rhinitis by fluticasone propionate as well as corticosteroid propionate in conjunction with fluticasone propionate alone. The study aims to evaluate the efficacy of topical treatment on people with Allergic Rhinitis (AR). The medicines propionate fluticasone and antihistamine corticosteroids and propionate fluticasone alone were administered to patients with allergic rhinitis. AR was tested. A comparison of the effectiveness of topical treatment with Azelastine of fluticasone propionate and Fluticasone to suppress Allergic Rhinitis symptoms was assessed. Significant disruptions in the quality of living, health as well as function are linked with potentially severe allergic rhinitis. The most prevalent form of recurrent rhinitis is allergic rhinitis, impacting between 10 and 20% of the world population. Statistics show that there is an exponential increase in this condition. The common signs of human rhinorrhea, sneezing, coughing, respiratory inflammation, vomiting and weeping of skin, palatal scratching and ear coughing are considerably higher (* P=.001). The average symptom value (84.14 per cent) was significantly minimised during the test by Fluticasone propionate nasal spray. The intensity of complication decreased substantially by the administration of fluticasone propionate + azelastine hydrochloride nasal spray often functions (91.16 per cent). A mixture of Fluticasone propionate and Azelastine hydrochloride is better than Fluticasone propionate nasal spray to relieve the reactions of Allergic Rhinitis.

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INTRODUCTION
Allergic rhinitis (AR) is an inflammation-induced nasal passage disorder which focuses on deliberately inflammatory medium development with inflammatory cells infiltration. Clinical manifestations include sneezing, nasal congestion, itchy nose as well as rhinorrhea. AR is the most common allergic disease that infects more than 50% of atopic syndrome people in India. AR is a common condition that affects 40% of the population (Sin and Togias, 2011). The term allergic rhinitis (AR) means a seasonal allergy, an unhealthy condition with various nasal and eye symptoms. These symptoms occur as a result of an abnormally increased immunological response to inhalation of the environment - pollen from wood or grass, fur from cats or dogs and mites.

In addition to the allergic reactions, physiological symptoms known to most people, e.g. itching, sneezing, runny nose, stuffy nose, runny eyes as well as headaches. Allergic rhinitis is closely related to a significant emotional burden that negatively impacts
every aspect of a person’s daily life, including work, sports, and social life (Small et al., 2007).

Rhinitis is characterised as broad nasal mucosal inflammation. This inflammation is a common disease impacting up to 40% of the population. Allergic rhinitis has historically been thought to be a severe nasal and throat abnormality. Present reports suggest, however, that the entire airway is associated with a chronic respiratory disease (Dykewicz and Hamilos, 2010).

The upper airways and lower airways are interconnected physiologically, clinically and immuno-logically. The upper airways are the nose, paranasal nasal sinus and the lower respiratory tract are the bronchioles, bronchi, trachea, and lungs. The two paths, for example, involve a ciliary epithelium composed of the cup cells secreting the mucus required to absorb inlet air and to defend airway structures. Submucous frequently contains a blood pump, mucosal layer, supportive cells, muscles, and immune cells in the upper and lower respiratory tract (Bourdin et al., 2009).

In these kinds of allergic conditions, the symptoms not only manifest in the upper respiratory tract but also in the lower respiratory tract. In reality, asthma, as well as rhinitis, sometimes arise together, confirms that. Therefore, a type of infectious disorder is allergic rhinitis, including asthma. The correct prognosis, as well as treatments of allergic rhinitis patients, must be addressed.

Adverse allergic reactions are produced through three stages in the nasal cavity: allergic exposure, severe allergies and persistent allergic inflammation. Currently, oral corticosteroids, antihistamines, oral antihistamines spray, and subcutaneously allergic injections (Tran et al., 2011) provide acute rhinitis therapies.

Dry mouth and somnolence is an adverse effect commonly found in patients who have had an increased dose of medication for AR. To minimise the extent of allergic rhinitis complications, patients with AR require medications not only that supports them to overcome the complexities, but also that improve their efficacy, and substantive reactions, that can regulate their symptoms. The time has arrived for allergic rhinitis to be treated as a severe illness, needing prompt, robust and adequate symptomatic relief.

Research Objectives

1. To evaluate the efficacy of topical treatment with propionate fluticasone + antihistamine corticosteroids and propionate fluticasone alone in patients with allergic rhinitis (AR) was tested.

2. The aim is to compare the effectiveness of topical treatment just with Azelastine of fluticasone propionate and Fluticasone to suppress allergic rhinitis symptoms.

LITERATURE REVIEW

Historical Aspects

Historically, allergic reactions have been known for over 150 years. Typical symptoms of allergic rhinitis were described as early as 1819 by John Bostock of England. He identified that his own - Summer Catarrh of sneezing, itchy eyes, and nasal congestion occurred only during summer months (Kumar et al., 2012).

In 1928, John Bostock assessed his symptoms of allergic rhinitis with the cutting of hay and deduced his problems were related in some way to substances emanating from hay (Stewart et al., 2004). Thus, he coined the term - Hay fever. The prime target cells of an allergic reaction, mast cells were described in 1877 by Paul Ehrlich. Yet, the significance of degranulation and release of vasoactive amines was not described until the 1940s (Ratner et al., 2008).

In 1865, Blakley performed a scratch test on himself to show his sensitivity to eye grass, and in the early 1900s, Scratch test was commonly used to diagnose the immediate type of allergy (Bousquet et al., 2015).

In 1906, the Austrian paediatrician Clemens von Pirquet coined the word ‘allergy’ for a summary of certain patients with diphtheria having experienced unusual signs in their diagnosis with a horse serum attenuated virus (Sami et al., 2016).

During 1911-1914 – the work of Leonard Noon and John Freeman helped established the basis for immunotherapy or allergy shots (Wallace et al., 2008).

In 1921, Prausnitz and Kristen described passive transfer of a small amount of serum of an individual afflicted with allergic rhinitis to the skin of the non-sensitized individual and discovered that it produced a wheal. This discovery demonstrated an allergic factor within the blood of affected donor (Hoecke et al., 2006).

In the 1960s, Benaich and Johansson of Sweden independently identified a protein component of myeloma protein called-ND protein. In conjunction with L wide, they identified this substance as globulin IgE and established it as a factor responsible for
the production of allergic symptoms (Scadding et al., 2017).

**MATERIALS AND METHODS**

**Study Design**

The current research is a triple-blind retrospective analysis of patients with allergic rhinitis in a tertiary centre on topical therapy using fluticasone propionate corticosteroid + antihistamine in a combination and propionate fluticasone alone.

**Study period:** The present study period was from December 2016 to June 2018.

**Study population:** The study population included patients diagnosed patients of allergic rhinitis were taken up from ENT OPD.

**Sample size:** The survey population contained a minimum specimen number of 220 allergic rhinitis patients.

**Sample size estimation:** The method used to determined the specimen group size was:

\[ n = \frac{(W_{α/2} + W_{β})^2 \times \left\{ (p_1(1 - p_1) + (p_2(1 - p_2)) \right\}}{(p_1 - p_2)^2} \]

where;

- \( W_{β} = \) This depends on power of the test, for 0.84 (80%)
- \( p_1 - p_2 = \) clinically significant difference = 0.20 (20%)
- \( n = \) the sample size needed in each group,
- \( p_1 = \) subjects cured by Drug A = 0.73 (73.4%)
- \( W_{α/2} = \) This depends on level of significance, for 95% this is 1.96
- \( p_2 = \) subjects cured by Drug B = 0.66 (66.0%)

Based on above formula the sample size required per group was 106.

In the study, we took 110 sample size for each group. Hence the total sample size was 220.

**Sampling method**

A computer-assisted randomisation table into two groups of 110 patients, each fulfilling inclusion and exclusion criteria.

**Inclusion Criteria**

1. The patients of AR irrespective of the condition they are seasonal or perennial.
2. Willing to participate in the comparative clinical comparative trial by way of informed consent.

**Exclusion Criteria**

1. It is formed of anatomical malformations such as large DNS, nasal obstruction, extensive polyps, tumours as well as requiring surgical management.
2. Many that use chronic or oral antihistamines and corticosteroids for the last 30 days following the initial visits.
3. Diabetes, regardless of its control status.
4. Woman with pregnancy planned pregnancy and lactation.

**Ethical considerations**

The Ethical Committee approved the study of the Medical College.

**Method of collection of data**

Patients presented with sneezing, itching sensation in the nose, watery nasal discharge and sensation of nasal obstruction which are hallmarks of allergic rhinitis and other symptoms like watering of eyes, itching of eyes, palatal itching and itching of ears were carefully evaluated by means of:

1. proper history taking with the help of a proforma
2. Clinical examination and
3. relevant laboratory investigations like absolute eosinophil count. However, nasal smear cytology was not done due to unavailability of the facility.

Efficacy of treatment was assessed by relief of symptoms during periodic weekly follow-up using 4-point symptom evaluation scale, and relevant investigation like absolute eosinophil counts more than 400 cells/mm. The allergic rhinitis patients were assessed on a 4-point scale (0 to 3) for symptoms like nasal blockage, nasal congestion, rhinorrhea, sneezing, nasal itching etc. and their rating was described to every patient. Baseline symptoms scores were recorded in the symptom diary provided to every patient and asked to maintain it along the study period.

The ratings of the symptoms are: 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms, 0 = no symptom. The rating has to be performed by patients themselves to increase the creditability of the subjective scale. The US Department of Health and Human Services suggests
this self-assessment ranking for patients including Allergic Rhinitis and its Impact on Asthma (ARIA), Global Alliance Against Chronic Respiratory Diseases (GARD), World Health Organization (WHO), Food and Drugs Administration: Medication Clinical Research Services (Derendorf et al., 2012).

**Analysis**

With the help of Symptom Evaluation Scale TSS (Total Symptom Score) and individual symptom score were recorded before treatment (see Table 1). Then selected Patients were randomly included in two groups having 110 patients each. Group I and Group II received a nasal spray of 2 puffs/nostril for four weeks from respective drugs.

The drug name was blinded with a sticker in both the groups by non-medical staff. TSS, as well as individual symptom scores before and after treatment, was recorded after four weeks of treatment. In the complete study, drugs were not assigned by the investigator confirming a double-blind, randomised pattern. Those patients with no symptom were considered as symptomatically improved while those with no satisfactory improvement in symptoms were considered as failure.

**Statistical Method**

The measurement of age, combination of sex, length of sickness, sporadic or chronic symptoms and co-morbidity was used to determine a relevant sense of age and category I & GI. The study was used to identify the proportion of symptoms. The overall symptoms between classes of I and II, and the measure for the classification of the classification signed by Wilcoxon used for fig. All data processing was conducted using SPSS for Windows (version 22).

**OBSERVATIONS AND RESULTS**

In the study, both treatment groups had comparable mean total symptoms scores at baseline indicating, similar severity of symptoms among all patients at the beginning of the study. Mean total symptoms scores decreased in both the treatment-groups after four weeks study period. There was 84.14% and 91.16% change in the median of overall symptom score in Group I and Group II with statistical significance.

The mean age of group I and group II were 33.94 and 33.49, respectively. Hence the maximum number of patients belongs to the age group 31-40 years in both study groups. It was statistically insignificant due to no difference among both groups with respect to age (Table 2 and Figure 1). In this study, the total numbers of males were 124 (56.36%), and females were 96 (43.64%). It was statistically insignificant due to no difference among both groups irrespective of sex.

Sneezing was present in most of the subjects which were included in both groups (Table 3). Fluticasone nasal spray was effective in reducing sneezing by 91.35% as compared to 95.8% by Azelastine + Fluticasone propionate nasal spray. Therefore Azelastine + Fluticasone propionate nasal spray and fluticasone propionate nasal spray were effective in subsiding this symptom, but Azelastine + Fluticasone nasal spray was better.

The study comprised of 68 patients (61.82%) in group I had intermittent symptoms compared to 73 patients (66.36%) in Group II. Forty-two patients (38.18%) in group I had persistent symptoms compared to 37 patients (33.64%) in Group II (see Table 4 and Table 5). It was statistically insignificant due to no difference in both groups with respect to symptoms.

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Moreover, Fluticasone nasal spray reduced nasal obstruction by 74.15% as compared to 88.79% by Fluticasone + Azelastine nasal spray. Therefore Fluticasone propionate + Azelastine nasal spray, as well as Fluticasone propionate nasal spray, were effective in subsiding this symptom but Fluticasone propionate + Azelastine nasal spray was better (Table 6).

Additionally, it was observed that Fluticasone nasal spray reduced eye-watering by 88.89% as compared to 96.29% by Fluticasone propionate + Azelastine hydrochloride nasal spray (see Table 7). Therefore...
### Table 1: Evaluation of Total Symptom Score (TSS)

| Symptom Evaluation Scale | Description                          | Definition                                                                 |
|--------------------------|--------------------------------------|-----------------------------------------------------------------------------|
| 0                        | Absent                               | No Signs                                                                   |
| 1                        | Mild                                 | No signs yet symptoms sometimes alarming                                   |
| 2                        | Moderate                              | Disrupting or sleep disorders and other symptoms                           |
| 3                        | Severe                               | Symptoms disturbing daily activities and normal sleep                        |

### Table 2: Distribution according to age group in two groups

| Age group (Years) | Group I (%) | Group II (%) | Total (%)  |
|-------------------|-------------|--------------|------------|
| ≤20               | 19 (17.27)  | 22 (20.00)   | 41 (18.64) |
| 21-30             | 34 (30.91)  | 36 (32.72)   | 70 (31.82) |
| 31-40             | 27 (24.55)  | 23 (20.91)   | 50 (22.72) |
| 41-50             | 14 (12.73)  | 15 (13.64)   | 29 (13.18) |
| 51-60             | 10 (09.09)  | 09 (08.64)   | 19 (08.64) |
| >60               | 06 (05.45)  | 05 (04.55)   | 11 (05.00) |
| Total             | 110 (100)   | 110 (100)    | 220 (100)  |

Mean age: 33.94 ± 13.45

*P=0.79

(*P<0.05 statistically not significant value; calculated by Unpaired ‘t’ test)

### Table 3: Distribution according to sex in two groups

| Sex     | Group I (%) | Group II (%) | Total (%)  |
|---------|-------------|--------------|------------|
| Male    | 61 (55.45)  | 63 (57.27)   | 124 (56.36) |
| Female  | 49 (44.55)  | 47 (42.73)   | 96 (43.64)  |
| Total   | 110 (100)   | 110 (100)    | 220 (100)   |

### Table 4: Distribution according to intermittent/persistent symptoms in two groups

| Symptoms     | Group I (%) | Group II (%) | Total (%)  |
|--------------|-------------|--------------|------------|
| Intermittent | 68 (61.82)  | 73 (66.36)   | 141 (64.09) |
| Persistent   | 42 (38.18)  | 37 (33.64)   | 79 (35.91)  |
| Total        | 110 (100)   | 110 (100)    | 220 (100)   |

(X2 =0.49; *P=0.48; *P>0.05 statistically not significant; calculated by chisquare test)

### Table 5: Pre-treatment and post-treatment Comparison of Sneezing symptom score in both groups

| Groups       | Group I | Group II | *P value |
|--------------|---------|----------|----------|
| Pre-treatment| 2.44 ± 0.71 | 2.61 ± 0.79 | 0.061    |
| Post-treatment| 0.21 ± 0.36 | 0.11 ± 0.41 | 0.041    |

(*P<0.05 statistically significant by Mann Whitney U test)

### Table 6: Pre-treatment and post-treatment comparison of nasal obstruction symptom score in both groups

| Groups       | Group I (M ± SD) | Group II (M ± SD) | *P value |
|--------------|------------------|-------------------|----------|
| Pre-treatment| 2.36 ± 0.66      | 2.41 ± 0.61       | 0.561    |
| Post-treatment| 0.61 ± 0.21    | 0.27 ± 0.13       | <0.0001  |

(*p<0.05 statistically significant; calculated by Mann Whitney U test
M=mean, SD= standard deviation.)
Table 7: Pre-treatment and post-treatment comparison of watering of eyes symptom score in both groups

| Groups    | Group I (Mean ±SD) | Group II (Mean ±SD) | *P value |
|-----------|--------------------|---------------------|----------|
| Pre-treatment | 0.45 ±0.51         | 0.63 ± 0.23         | 0.061    |
| Post-treatment | 0.04 ±0.11         | 0.04 ± 0.13         | 0.781    |

(*p<0.05 statistically significant; calculated by Mann Whitney U test)

Fluticasone + Azelastine nasal spray, as well as Fluticasone propionate nasal spray both, were effective in subsiding this symptom with statistical insignificance.

Identifying Side Effects

Out of the 220 participants in this sample, only 12 reported a moderate and managed side effect of the medication that did not involve additional treatment. It did not impede the continuity of a trial. However, none of the patients reported any significant side effect. Amongst 12 patients, five patients (4.54%) belonged to Group I (Fluticasone propionate) and seven patients (6.36%) to Group II (Fluticasone propionate + Azelastine). In Fluticasone propionate group most common side effect experienced by patients was nasal bleeding (2 patients) followed by nasal discomfort (1 patient), throat irritation (1 patient) and headache (1 patient). It was statistically insignificant due to no difference among both groups with respect to side effects (see Table 8).

DISCUSSION

Allergic rhinitis is a highly distressing condition, and it tends to recur several times. Allergic rhinitis patients need medication that can adequately control their symptoms, more specifically with greater efficacy and faster substantial response. It is time for allergic rhinitis to be recognised as significant morbid condition, requiring effective symptomatic relief promptly and in an uncomplicated way. There is a paucity of comparisons with steroid alone and in combination with antihistaminic in treatment of allergic rhinitis (Dykewicz et al., 2003).

The study was carried out in the Department of ENT from December 2016 to June 2018. A total sample size of 220 patients with allergic rhinitis regardless of the seasonal or perennial type presented to OPD was included in the study. No diabetic Mellitus irrespective of management and abortion, planned breastfeeding and lactation, is identified in the nasal obstruction cases, such as gross DNA, severe polyps, tumours and the individual with systemic or oral corticosteroids or antihistamine over the past 30 days. In Group I and Group II, patients were divided randomly into two groups, with 110 patients in each category.

In this study, the total numbers of males were 124 (56.36%), and females were 96 (43.64%). It was statistically insignificant due to no difference in both groups with respect to sex. (*P=0.78) The findings were similar to the present study in Berger et al. (2016) and Derendorf et al. (2012) studies males were more compared to females with no statistical difference. The findings were in contrast to the present study Ratner et al. (2008) and Scadding et al. (2017) were female outnumbered males but without any statistical difference.

In appearance and clinical path, however, allergic rhinitis per se may not vary as per age. The mean illness duration of group I (Fluticasone propionate) was 3.15 years, and Group II (Azelastine + Fluticasone Propionate) 3.49 years. Duration of illness is statistically similar between both groups with (*P = 0.18). In the study, 68 patients (61.81%) in group I had intermittent symptoms compared to 73 patients (66.36%) in Group II. Forty-two patients (38.18%) in group I had persistent symptoms compared to 37 patients (33.64%) in Group II. It was statistically insignificant due to no difference in both groups with respect to symptoms. (*P=0.48) (Berger et al., 2016).

In the analysis, the mean baseline ratings for all care classes showed a comparable frequency of symptoms in both participants at the beginning of the research. In both cases, three main signs were present before therapy: allergic rhinitis, sneezing, nasal congestion as well as nasal discharge. It was observed that Fluticasone nasal propionate was more successful in alleviating all symptoms close to the studies by Havle et al. (2016) and Ratner et al. (2008). Table 9 and Table 10 represents the supplementary researches of previous authors.

The Fluticasone propionate nasal spray was also efficacious in dramatically lowering overall symptoms of AR (P=0.001). This result is comparable to Ratner et al. (2013) research that observed a drop in baseline in the TSS (Total statistical score)(* P=0.001) of Fluticasone Propionate + Azelastine Hydrochloride nasal spray indicating an increase of 96%. Therefore, it is proposed that Fluticasone Pro-
Table 8: Distribution according to Side effects in two groups

| Side effects       | Group I (n=110) | Group II (n=110) | Total (n=220) | *P Value |
|--------------------|----------------|-----------------|---------------|----------|
| Nasal discomfort   | 01 (0.91)      | 01 (0.91)       | 02 (0.91)     | 1.00     |
| Nasal bleeding     | 02 (1.81)      | 03 (2.73)       | 05 (2.72)     | 1.00     |
| Throat irritation  | 01 (0.91)      | 02 (1.81)       | 03 (1.36)     | 1.00     |
| Headache           | 01 (0.91)      | 01 (0.91)       | 02 (0.91)     | 1.00     |
| Total              | 05 (4.54)      | 07 (6.36)       | 12 (5.45)     | 0.76     |

Table 9: Efficiency Fluticasone potency Propionate in supplementary research

| Studies                       | TSS (% change) |
|-------------------------------|----------------|
| (Ratner et al., 2008)         | 27.1%          |
| (Dykewicz and Hamilos, 2010)  | 91%            |
| (Havle et al., 2016)          | 95.55%         |
| (Carr et al., 2012)           | 49%            |
| (Berger et al., 2016)         | 66%            |
| Present study                 | 84.14%         |

Table 10: Efficiency of Fluticasone Propionate compared to other studies

| Studies                      | Current study |
|------------------------------|---------------|
| (Ratner et al., 2008)        | (Dykewicz and Hamilos, 2010) |
| (Havle et al., 2016)         | (Berger et al., 2016)         |
| Nasal obstruction            | 21.1 %         | 92 %           | 96.74 % | 74.15 % |
| Nasal discharge              | 23 %           | 90.01 %        | 98.42 % | 69.60 % |
| Sneezing                     | 31.8 %         | 85.10 %        | 91.83 % | 91.35 % |

Fluticasone + Azelastine Hydrochloride nasal spraying was of significant significance in reducing allergic rhinitis symptoms as well.

CONCLUSION

The result of allergic patients with rhinitis has demonstrated that Fluticasone Propionate nasal spray has been positive and efficient. In the first category, the median illness duration (Propionate Fluticasone) was 3.15 years, and in the second, 3.49 years (Propionate Fluticasone + Azelastine). Statistically comparable duration of disease for both the two classes(* P= 0.18). In this analysis, 68 patients in group I (61.81%), along with 73 patients (66.36%) in Group II, had sporadic symptoms. 42 (38.18%) of Group I patients have recurring symptoms as contrasted to 37 of Group II patients (3 3.64%) because of no variations between their symptoms observed within the two classes (statistically irrelevant S=1.32). In comparison, Fluticasone propionate + Azelastine hydrochloride nasal spray is more effective to relieve rhinitis than fluticasone propionate spray alone for AR impact. The outcomes of this research demonstrate that Azelastine nasal sprays with a spray of Fluticasone might have significant clinical effects in subjects with allergic rhinitis compared with fluticasone propionate alone.

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Conflict of Interest
I hereby declare that there is no conflict of interest related to this manuscript.

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