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Comparative Study of the Effect of Mometasone Fuorate and Levocetrizine in Alleviating the Symptom Triad of Rhinorrhoea, Nasal Obstruction and Sneezing in Patients of Allergic Rhinitis

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Authors' contributions

This work was carried out in collaboration between both authors. Author NKS designed the study, wrote the protocol, and wrote the first draft of the manuscript. Author NKS also managed the literature searches, statistical analyses of the study. Author PSN provided his expert advise and guidance and departmental support. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: The aim of the study is to compare the effect of Mometasone Fuorate and Levocetrizine in alleviating the symptom triad of Rhinorrhoea, Nasal obstruction and Sneezing in patients of Allergic Rhinitis.
Study Design: Prospective cohort study.
Place and Duration of Study: Department of Otolaryngology, Mahatma Gandhi Institute of Medical Sciences (MGIMS), Sevagram, between 1st April 2012 to 31st March 2014.
Methodology: In this study 50 patients were assessed. The diagnosis was made on the basis of 1) Careful detailed history, 2) Clinical examinations, 3) ARIA Classification was used to classify the patients. Patients received, Group A: Mometasone furoate nasal spray 50 µg in each nostril twice daily for the first 7 days followed by once daily upto 8 weeks, Group B: Levocetrizine 5 mg in the night for 8 weeks. In followup period of 12 weeks Patients received Group A: Mometasone furoate nasal spray 50 µg in each nostril once daily for 12 weeks. Group B: Levocetrizine 5 mg in the night for 12 weeks.

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Results: In patients with Intermittent Symptoms, 76% of the participants in the group A were found to be relieved of the nasal discharge as compared to 24% in the group B. This difference was found to be statistically significant (P = .0007). 83% of the participants in the group A were found to be relieved of the nasal obstruction as compared to 17% in the group B. This difference was found to be statistically significant (P = .0022). 61.5% of the participants in the group A were found to be relieved of the sneezing as compared to 48.5% in the group B. This difference was not found to be statistically significant (P=0.8017). In patients with Persistent Symptoms, 84.6% of the participants in the group A were found to be relieved of the nasal discharge as compared to 15.4% in the group B. This difference was found to be statistically significant (P = .0124). 100% of the participants in the group A were found to be relieved of the nasal obstruction as compared to 0% in the group B. This difference was found to be statistically significant (P = .0006). 75% of the participants in the group A were found to be relieved of the sneezing as compared to 25% in the group B. This difference was not found to be statistically significant (P = .5647).
Conclusion: In this study we conclude that both Mometasone Fuorate and Levocetrizine are potent drugs for the management of allergic rhinitis but because of the local action and a high lipophilicity, longer retainability and induction of apoptosis of eosinophills in the nasal mucosa, patients taking Mometasone Fuorate as medication appreciate better relief in symptoms as compared to Levocetrizine.

Keywords: Allergic rhinitis; mometasone; levocetrizine; rhinorrhoea; nasal obstruction; sneezing.

1. INTRODUCTION

The term “Allergy” was coined by Von Pirquet to explain the biologically changed reactivity of the organism exposed to the same antigen. In 1819 John Bostock first described seasonal hay fever as a ‘seasonal catarrh’ suffered by himself and 28 of his patients.

Allergic rhinitis is a global health problem and is increasing in incidence. Recent multinational studies show wide variation in prevalence using simple ‘working definitions’ in standardized questioners. The International Study of Asthma and Allergies in Childhood (1997) noted the prevalence of rhinitis with itchy watery eyes, in 6 to 7 year olds as 0.8 to 14.9% and in 13-14 year old from 1.4 to 39.7 %in different countries throughout the world [1].

Despite the fact that Allergic Rhinitis is not directly associated with a high rate of mortality or hospitalization, it produces a significant morbidity which in turn has a major impact on the quality of life, sleeping habits, academic performance, daily activities, and concentration of sufferers [2].

Pathophysiologically, Allergic Rhinitis is a complex, involving cell mediators, cytokines, chemokines, neuropeptides, and adhesion molecules which cooperate in a complex network to produce the specific symptoms of allergic rhinitis and the nonspecific hyperreactivity [3].

The reaction can be considered in four phases:-

1. Sensitization
2. Subsequent reaction to allergen- Early Phase
3. Late phase reaction
4. Systemic activation

Several different classes of medication have come up for the management of Allergic Rhinitis with different levels of efficacy which include H1-antihistamines (oral and nasal), decongestants (oral and intranasal), mast cell stabilizers (cromones), anticholinergics, antileukotrienes, and Intranasal Corticosteroids [4].

Intranasal Corticosteroids are the most effective treatment option for alleviating the greatest number of Allergic Rhinitis symptoms [4,5].

Corticosteroids affects both mediators and inflammatory cells involved in the allergic process such as prostaglandins, leukotrienes, and mast cells [6]. It inhibits T lymphocytes, particularly TH2 cells, cytokine production and its action and eosinophil recruitment [6,7,8].

The rationale for using topical corticosteroids is that adequate drug concentrations can be achieved at receptor sites in the nasal mucosa. This leads to symptom control and reduces the risk of systemic adverse effects [6,9,10]. considering these effects the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology recommend Intranasal

Corticosteroid (INS) to be used as first-line treatment for allergic rhinitis [11].

Antihistamines are considered a mainstay and standard of treatment for allergic rhinitis with many patients preferring oral medication to intranasal formulations [3,12].

There is evidence suggesting the effectiveness of oral H1 blockers in reducing histamine-mediated symptoms such as rhinorrhea, eye symptoms, sneezing and nasal itching; however, a weaker effect on the relief of nasal congestion was noted [13].

Evidence also suggest that antihistaminic medications are not only capable of reducing the symptomatology of the affected patients, but also have a positive influence on the subjective effectiveness parameters such as quality of life [14,15].

Levocetirizine is an oral, nonsedating H1-antihistamine that proved to be significantly effective in improving symptoms in patients with allergic rhinitis; it presents a good safety profile and, for all these pharmacologic characteristics, is highly indicated as a first-line treatment in subjects with persistent allergic rhinitis [16].

Both Levocetrizine and Mometasone fuorate have proven efficacy in the treatment of allergic rhinitis but there is no comparative study between the two in our literature search from pubmed and google scholar, so through this present study we have tried to compare the two effective medications in alleviating the Symptom Triad of Rhinorrhoea, Nasal Obstruction and Sneezing in patients of Allergic Rhinitis.

2. MATERIALS AND METHODS

After due ethical approval from the Institutional Ethical committee, the patients attending the OPD of Department of Otolaryngology were examined clinically and those found to be having symptom complex of Allergic Rhinitis were further investigated and selected. The study was conducted from 1st April 2012 to 31st March 2014 in which 130 patients were registered but only 50 patients came for regular follow up for 20 weeks of study period.

The clinical diagnosis of the cases was made on the basis of

- Careful detailed history, i.e. patients were particularly asked about other allergic manifestation like asthma, unticaria, eczema etc. and seasonal variations in symptoms their habits and family history. Careful inquiry was also made about different allergens and precipitating factors.
- Clinical examinations – after routine local examinations of ear, nose and throat a complete systemic examination was carried out.
- ARIA Classification of Allergic rhinitis 2010 was used to classify the patients (Fig. 1).

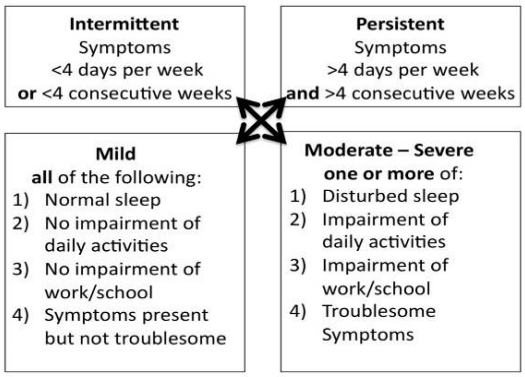

Fig. 1. ARIA classification of allergic rhinitis

2.1 Selection of Patients

For this study patient were selected based on clinical diagnosis, made from the complaints and examinations. Patients were explained about the treatment options and their benefits and side effects. Patients were advised the treatment according to their preference after taking the written informed consent in the vernacular language.

1. Patient having classical symptom complex of allergic rhinitis i.e. sneezing, watery nasal discharge, and nasal obstruction were included.
2. Patients were particularly asked about other allergic manifestations like asthma, urticaria eczema etc. and if found suffering were excluded.
3. Pregnant woman and children below 2 years of age were excluded.
4. Patients with significant Deviated Nasal Septum and nasal polyposis were excluded.

2.2 Treatment Advised

Patients received:-

1. Group A: Intransal spray of corticosteroids in form of Mometasone furoate nasal spray

50 µg in each nostril twice daily for the first 7 days followed by once daily upto 8 weeks
2. Group B: Levocetrizine 5 mg in the night for 8 weeks.

In follow up period of 12 weeks Patients received:-

3. Group A: Intransal spray of corticosteroids in form of Mometasone furoate nasal spray 50 µg in each nostril once daily for 12 weeks.
4. Group B: Levocetrizine 5 mg in the night for 12 weeks.

2.3 Assessment

It was done by observing subjective relief from symptoms and changes noticed on examination after 8 weeks of treatment and 12 weeks of follow up in each Group. The severity of symptoms was considered according to the ARIA Guidelines 2010 and were divided as follows:

0. Mild Symptoms
1. Any one of moderate to severe symptoms
2. Any two of moderate to severe symptoms
3. Any three of moderate to severe symptoms
4. All four moderate to severe symptoms.

The subjective relief in symptoms, was categorized as:

0 No relief
+1 mild relief
+2 moderate relief
+3 total relief

Statistical analysis was performed EPI Info 7, software available on the W.H.O website.

3. RESULTS AND DISCUSSION

3.1 Results

(Table 1) In patients with Intermittent Symptoms, 76% of the participants in the group A were found to be relieved of the nasal discharge as compared to 24% in the group B. This difference was found to be statistically significant (*P* = .0007). 83% of the participants in the group A were found to be relieved of the nasal obstruction as compared to 17% in the group B. This difference was found to be statistically significant (*P* = .0022). 61.5% of the participants in the group A were found to be relieved of the sneezing as compared to 48.5% in the group B. This difference was not found to be statistically significant (*P*=0.8017).

(Table 2) In patients with Persistent Symptoms, 84.6% of the participants in the group A were found to be relieved of the nasal discharge as compared to 15.4% in the group B. This difference was found to be statistically significant (P = .0124). 100% of the participants in the group A were found to be relieved of the nasal obstruction as compared to 0% in the group B. This difference was found to be statistically significant (P = .0006). 75% of the participants in the group A were found to be relieved of the sneezing as compared to 25% in the group B. This difference was not found to be statistically significant (P = .5647).

Table 1. Comparison of group A and B in patients with intermittent symptoms

Intermittent symptoms		Group A	Group B	Chi-square	P value
Nasal discharge	Relief	19 (76)	6 (24)	11.3	0.0007
	No relief	0	8 (100)		
Nasal	Relief	19 (83)	4 (17)	9.34	0.0022
Obstruction	No relief	0	5 (100)		
Sneezing	Relief	8 (61.5)	5 (48.5)	0.06	0.8017
	No relief	9 (56)	7 (44)		

Table 2. Comparison of group A and B in patients with persistent symptoms

Persistent symptoms		Group A	Group B	Chi-square	P value
Nasal discharge	Relief	11 (84.6)	2 (15.4)	6.24	0.0124
	No relief	0 (0)	4 (100)		
Nasal	Relief	11 (100)	0 (0)	11.68	0.0006
Obstruction	No relief	0 (0)	5 (100)		
Sneezing	Relief	6 (75)	2 (25)	0.3315	0.5647
	No relief	1 (33)	2 (67)		

3.2 DISCUSSION

As per the above results we can assess that Mometasone Furoate Intranasal Spray significantly improves nasal discharge as well as nasal obstruction but there was no statistically significant relief in the symptom of sneezing which is a symptom of early phase of Allergic Rhinitis.

Corticosteroids affects both mediators and inflammatory cells involved in the allergic process such as prostaglandins, leukotrienes, and mast cells [6]. It inhibits T lymphocytes, particularly TH2 cells which decreases cytokine production and its action and eosinophil recruitment [6,7,8].

Topical potency of corticosteroids usually is determined by degree of cutaneous vasoconstrictive activity from a skin model [6]. Potency can also be assessed by glucocorticoid receptor-binding affinity and Lipophilicity which refers to the ability of a chemical compound to dissolve in fats which in turn is an important factor as highly lipophilic agents have a greater degree and faster rate of absorption into the nasal mucosa and therefore enhanced ability to reach the glucocorticoid receptor due to longer retention time in nasal tissue [6,17].

3.2.1 Mometasone fuorate

Mometasone Fuorate has a chemical structure similar to that of cortisol. The presence of a double bond in the 1, 2 position on ring A and of an esterified furoate moiety in the 17α position leads to high glucocorticoid activity and major affinity to the glucocorticoid receptor, respectively. Occupying a lipophilic pocket in the glucocorticoid receptor, the furoate moiety increases receptor binding and activation [17] (Fig. 2).

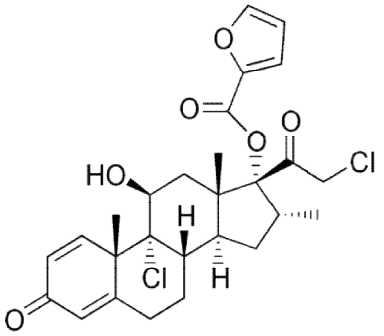

Fig. 2. Molecular structure of mometasone fuorate

The binding between glucocorticoids and the glucocorticoid receptor produces a complex that enters the cell nucleus and regulates the expression of pro- and anti-inflammatory genes.

It has been documented that in vitro, Mometasone Fuorate is the most steroid potent inhibitor of IL-4 and IL-5 which are released from T-helper cell type 2 (Th2) and regulate mast cell activation and degranulation, eosinophil differentiation, and IgE production. INF-gamma is a T-helper cell type 1 (Th1)-secreted cytokine that downregulates the effects of the Th2 cytokines. Mometasone Fuorate acts by reversing the exaggerated Th2 response that contributes to the pathophysiology of allergic disease [18] and it also enhances eosinophil apoptosis [19].

Lastly it inhibits the adhesion-molecule system, activation of which is crucial in the pathogenesis of inflammatory cell infiltration in the nasal mucosa and hence protects against cell injury due to inflammation [20].

3.2.2 Levocetrizine

Levocetirizine (R-cetirizine), or (R)-[2-[4-[(4-chlorophenyl)phenylmethyl]- 1-piperazinyl] ethoxy]acetic acid dihydrochloride is the pharmacologically active enantiomer of cetirizine [21] (Fig. 3).

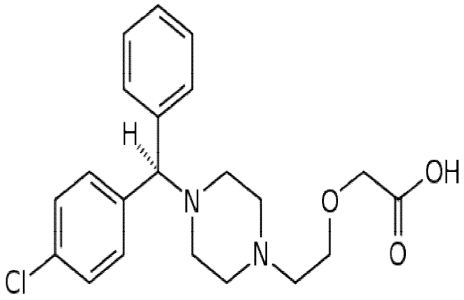

Fig. 3. Molecular structure of levocetrizine

Cetirizine consists of a racemic mixture of R- and S-cetirizine. The two enantiomers differ as to pharmacological activity, bond affinity to the H-1 receptor, and dissociation constant. Various studies agree in attributing all pharmacological activity, higher bond affinity, and longer dissociation half-life to R-cetirizine [22]. These characteristics make levocetirizine an excellent pseudo-irreversible antagonist of the H-1 receptor [23]. Antagonism of histamine causes

inhibition of the increase in vascular permeability and vasodilation. Inhibition of edema formation and mucus secretion.

T lymphocytes, dendritic cells and lung macrophages have histamine H-1 receptor on their cell surface which causes the expression of activation molecules and the synthesis of cytokines and chemokines with proinflammatory effects when activated, are limited by Levocetrizine [24].

In terms of its pharmacological profile levocetirizine exhibits rapid absorption and high bioavailability giving a fast onset and long duration of antihistaminic effect.

Hence considering the pharmacological properties of the two drugs we can Mometasone Fuorate Nasal Spray affects both mediators and inflammatory cells involved in the allergic process such as prostaglandins, leukotrienes, and mast cells and also inhibits T lymphocytes, particularly TH2 cells, which decreases cytokine production and its action and eosinophil recruitment and because of its vasoconstrictive ability it cause significant improvement in the symptoms of Rhinorrhoea and Nasal obstruction. Levocetirizine on the other hand is an pseudo-irreversible antagonist of the H-1 receptor and hence produce relief in symptoms which are in the acute phase because of release of histamine but does not inhibit T Lymphocytes which are recruited through other cascades hence it controls the symptom of acute phase i.e sneezing but is not as effective as Mometasone Fuorate nasal spray in controlling persistent symptoms as well as nasal obstruction.

4. CONCLUSION

In this study we conclude that both Mometasone Fuorate nasal spray and Levocetrizine are potent drugs but patients taking Mometasone Fuorate nasal spray as medication appreciate better relief in symptoms as compared to Levocetrizine.

5. LIMITATIONS

1. The sample for study is small because of the over the counter availability of these formulations patients seek self-medication and did not turn up for follow up.
2. The study does not consider ocular, pharyngeal and laryngeal symptoms and also asthma.

6. FUTURE PROSPECTS

- Future studies can be planned taking into consideration more variables and symptom complex associated with Allergic Rhinitis.
- Patient should be contacted by other means for follow up and should be motivated for OPD visits rather than self-medication.
- Combination therapy of the studied medication can be looked into for the synergistic action.

CONSENT

All authors declare that 'written informed consent was obtained from the patients (or other approved parties) for participation in the study publication of this study.

ETHICAL APPROVAL

All authors hereby declare that the study titled "Comparative study of the effect of Mometasone Fuorate and Levocetrizine in alleviating the Symptom Triad of Rhinorrhoea, Nasal Obstruction and Sneezing in patients of Allergic Rhinitis" has been approved by the institutional ethical committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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