http://www.jtps.com.pk
Journal of Toxicological & Pharmaceutical Sciences
NEXUS SCIENCE FORUM

ORIGNAL ARTICLE

Comparative study of second generation anti-histamine (Cetrizine) alone v/s antihistamine with leukotriene receptor antagonist (Monstelukast sodium) in the treatment of allergic rhinitis

Fasiha Tariq Qureshi [1], Ali Sharif [*1] and Zaka-ur-Rehman[2]

[1]*Faculty of Pharmacy, The University of Lahore, Pakistan*
[2]*Health Department, Government of Punjab, Lahore, Pakistan*

Abstract

Allergic rhinitis is one of the significant public health problem in which nasal congestion, sneezing, nasal pruritus and rhinorrhea are most common problems faced by patients which not only exacerbate work performance but also their quality of life. Allergic rhinitis prevalence has been increased rapidly in industrialized countries. Present study was carried out among allergic rhinitis patients visiting Lahore General Hospital, Lahore and different clinics of Lahore. Total 200 patients divided into two equal groups (Group-A and Group-B) were included in this study. Group-A was treated with cetirizine alone while Group-B was treated with cetirizine along with montelukast. Results were obtained as relief of symptoms. Data was analyzed by statistical software SPSS (Statistical Package for Social Sciences) version 19.0. Results concluded that combination of cetirizine + montelukast is more beneficial in allergic rhinitis.

Keywords

Allergic rhinitis
Cetirizine
Montelukast sodium
Lahore

To Cite This Article: Qureshi FT, Sharif A and Rehman ZU, 2017. Comparative study of second generation anti-histamine (Cetrizine) alone v/s antihistamine with leukotriene receptor antagonist (Monstelukast sodium) in the treatment of allergic rhinitis. *J Toxicol Pharmaceut Sci*, **1(2),** 96-100.

Introduction

Allergic rhinitis (AR), a nasal mucosal inflammatory disease, is induced by immunoglobulin E (IgE)-mediated reaction in allergen-sensitized individuals (Zhang & Zhang, 2014). AR is considered by sneezing, nasal congestion, rhinorrhea and nasal pruritus, and is often supplemented by ocular pruritus, lacrimation and/or redness in 60-70% of patients (Canonica et al., 2007). Moreover, AR is frequently comorbid with asthma, signifying the close relationship of these conditions and has directed to the notion of 'one airway, one disease'. Indeed, studies have recommended that about 20-50% of allergic rhinitis patients have clinical asthma, while >80% of allergic asthma patients having concomitant symptoms of rhinitis (Peroni et al., 2003; Chen et al., 2008). According to the World Health Organization (WHO) estimates that worldwide distribution of asthma is about 300 million and about 250,000 people die from this every year. Avoidance of allergen exposure and pharmacotherapy are the keystones of allergic rhinitis management. Pharmacotherapy is customized to the patient grounded on symptoms type, their severity and duration, co-morbidities, patient preference and response to prior treatment. Numerous drug classes are used to treat AR including corticosteroids, antihistamines, mast cell stabilizers, anti-cholinergics, decongestants and leukotriene-receptor antagonists (Keith et al., 2012)

Antihistamines (second generation), established in early 1980s, have upgraded H_1 receptor selectivity, no or reduced sedation, longer duration of action, faster onset and less adverse effects (Doepp, 2001; Meltzer,

***Corresponding author:** Email: alisharif.pharmacit@gmail.com

2005). To-date, no clinically noteworthy cardiotoxic effects have been described for loratadine, fexofenadine, desloratadine, cetirizine and levocetirizine. Generally, second generation antihistamines reveal promising pharmacokinetics. They have a relatively fast onset of action, almost complete absorption and widespread distribution to tissue with negligible central nervous system (CNS) penetration unlike first generation antihistamines. The comparatively long half-life permitting for once daily dosing. Several controlled trials of second generation H_1 antihistamines have been published and have shown overall symptoms relief including sneezing, rhinorrhea, pruritus and conjunctival symptoms leading to improved life quality (Golightly & Greos, 2005; Lehman & Blaiss, 2006).

Need of study: Rhinitis may be one of the following categories according to etiology: IgE-mediated, infectious & idiopathic or autonomic (Small & Kim, 2011). AR, traditionally, has been categorized as seasonal or perennial. However, all patients are not suitable into this classification scheme. For example, few allergens trigger, like pollen, may be seasonal in areas of cooler climates, but persistent in warmer climates. Similarly, patients with multiple "seasonal" allergies may have indications through most of the year. AR, therefore, is now categorized according to symptoms extent (persistent or intermittent) and severity (mild, moderate or severe) (Small et al., 2007; Khaltaev & Bousquet, 2008)

Treatment approaches include allergen immunotherapy and medications. Evasion of clinically related allergens can lead to considerable reduction of symptoms and medication reliance, and is perhaps the most important feature of AR management. Individuals with AR are commonly profound to more than one allergen (Wallace et al., 2008)

The utmost common medications for AR are H_1 antihistamines. These drugs antagonize the histamine action by blocking receptors on target cells. Even though, first-generation antihistamines are effective, they can be allied with performance impairment and drowsiness. Use of 2nd generation antihistamines, which lack the anti-cholinergic characteristics of conventional antihistamines are usually preferred. Over the counter orally available 2nd generation antihistamines include cetirizine, fexofenadine and loratidine. While oral levocetirizine, desloratidine, intranasal olopatadine and azelastine are available by prescription. Intranasal antihistamines are equally or more effective in comparison to oral 2nd generation antihistamines (Wallace et al., 2008).

Montelukast, a common anti-leukotriene in practice, and is the single such agent permitted for pediatric use (Amlani et al., 2011). It has no reported food interactions. Lately an interaction had been reported which exposed an increased plasma concentration of montelukast after intake of grapefruit juice owing to cytochrome P450 (Cingi et al., 2013). Patients showed better compliance with montelukast in comparison to inhaled anti-inflammatory drugs owing to oral and single administration per day (Cingi et al., 2013). Further, it provides an effective and safe anti-inflammatory management for rhinitis, asthma and chronic obstructive pulmonary disease (COPD) (Celik et al., 2005). Even though montelukast is an efficacious drug in allergic rhinitis in order to reduce nasal congestion and inflammation, rhinorrhea, sneezing when designated as monotherapy, but broadly suggested as adjunct to intranasal corticosteroid or antihistamine (Kalpaklioglu & Baccioglu, 2012). These agents mainly help with congestion and are principally valuable in asthmatics where they might have the dual benefit of refining disease of lower airway (Baççioglu et al., 2013).

Allergen immunotherapy involves the incremental administration of inhalant allergens for inducing immune system variations in host reaction with natural coverage to these all combinations of antihistamines and anti-leukotrienes presented a synergistic outcome in seasonal allergic rhinitis treatment. In a research study, participants with seasonal allergic rhinitis showed that neither montelukast nor loratadine conversed any advantage in terms of refining day-time nasal symptoms. The day-time nasal symptoms, however, were pointedly better when these drugs were used in combination (Cox et al., 2011). Similarly, montelukast and cetirizine co-treatment ongoing 6 weeks before induction of pollen season effectively prevented symptoms of allergic rhinitis and diminishes allergic inflammation of nasal mucosa during natural exposure of allergen (Kurowski et al., 2004). In obstinate allergic rhinitis, montelukast, desloratadine, levocetirizine and antihistamine/montelukast combinations significantly enhanced nasal symptoms throughout the initial 24 hours. But then progress by the end of 6 weeks was expressively greater than that accomplished on the first day of treatment in patients treated with either montelukast (alone) or combined with the antihistamine (Ciebiada et al., 2008).

Materials and Methods

It was cross-sectional hospital-based study. Patients with allergic rhinitis visiting Lahore General Hospital Lahore and different clinics of Lahore were study population. Sampling technique was simple random sampling. The sample size of the study was 200 patients. Patients with allergic rhinitis of age 15-60 years were included in the study. Patients suffering from other diseases than allergic rhinitis were excluded from the study. The patients were divided into two equal groups (Group-A and Group-B). Each group

consisted of 100 patients. Among 100 Group-A patients, 55 (55.0%) were males and 45(45.0%) were female patients. Likewise, among 100 Group-B patients, 55 (55.0%) were males and 45(45.0%) were female patients. Group-A was treated with cetirizine alone while Group-B was treated with cetirizine along with montelukast. A semi-structured questionnaire was prepared by researcher and finalized after pre-testing. The patients were interviewed/examined by the researcher herself and results were noted on the questionnaire.

Ethical concerns: Formal permission was taken from concerned authority to carry on the study. Verbal consent was taken from participants after explaining the purpose of the study.

Statistical analysis: The data was statistically scrutinized with software Statistical Package for Social Sciences (SPSS) version 19.0. Percentages and frequencies were calculated and data was presented in graphs and tables.

Results and Discussion

Smoking is an ill habit and one of the leading cause of allergic rhinitis and other lung diseases. It was very discouraging that 35.0% Group-A patients and 39.0% Group-B patients were habituated of smoking as shown in table 1.

Table 1: Frequency distribution of patients according to smoking practices

Smoking practices	Group-A		Group-B	
	Frequency	Percentage	Frequency	Percentage
Yes	35	35.0	39	39.0
No	65	65.0	61	61.0
Total	100	100.0	100	100.0

Study highlighted the symptoms of allergic rhinitis among patients and found that 100.0% patients in both groups had runny nose (table 2). A study done by (Kalpaklioglu & Baccioglu, 2012) pointed out that 95.0% patients had runny nose. In our study 64.0% Group-A patients and 85.0% patients of group-B had congested nose (table 2) while the study carried out by (Kalpaklioglu & Baccioglu, 2012) exhibited better scenario than our study results who reported that only 20.0% patients had congested nose (table 2). Study further identified that 92.0% Group-A patients and 89.0% patients of group-B had itchy nose (table 2). (Kalpaklioglu & Baccioglu, 2012) also confirmed in their study that 96.4% patients had itchy nose. Sneezing was also observed among majority of the patients as 77.0% of group-A patients and 94.0% patients of group-B had sneezing (table 2). The findings of our study are comparable with the study undertaken by (Kalpaklioglu & Baccioglu, 2012) who reported that 98.6% patients had sneezing.

Table 2: Frequency distribution of patients according to symptoms

Symptoms	Group-A		Group-B		P value
	Frequency	Percentage	Frequency	Percentage	
Runny nose					
Yes	100	100.0	100	100.0	
No	0	0.0	0	0.0	
Total	100	100.0	100	100.0	
Congested/stuffy nose					
Yes	64	64.0	85	85.0	
No	36	36.0	15	15.0	0.001
Total	100	100.0	100	100.0	
Itchy nose					
Yes	92	92.0	89	89.0	
No	8	8.0	11	11.0	1.000
Total	100	100.0	100	100.0	
Sneezing					
Yes	77	77.0	94	94.0	
No	23	23.0	6	6.0	0.000
Total	100	100.0	100	100.0	
Watering eyes					
Yes	89	89.0	85	85.0	
No	11	11.0	15	15.0	0.285
Total	100	100.0	100	100.0	

Usually, allergic rhinitis is categorized as seasonal or perennial and most of the patients symptoms accrue in (Arlian & Platts-Mills, 2001) also elucidated in their study that symptoms severity grow among patients during pollen season. When the type of allergy was assessed among patients, study revealed that mainstream, 57.0% Group-A and 55.0% Group-B patients had seasonal allergy while remaining proportion in both groups had perennial allergy (table 3).

Table 3: Frequency distribution of patients according to type of allergy

Type of Allergy	Group-A		Group-B		P value
	Frequency	Percentage	Frequency	Percentage	
Seasonal	57	57.0	55	55.0	
Perennial	43	43.0	45	45.0	0.00
Total	100	100.0	100	100.0	

Study further identified that most of Group-A patients had allergy due to dust, followed by pollen, dust/smoke/pollen, dust/smoke, dust/pollen and smoke. Likewise majority of Group-B patients had allergy owing to dust, followed by dust/pollen, smoke, dust/smoke, dust/smoke/pollen, pollen and dust/ perfume/pollen which worsen their symptoms.

It is pertinent to mention here that for proper investigation, blood samples of all patients of both groups were drawn for complete blood count (CBC). Ninety four percent group-A patients and 95.0% group-B patients submitted back the report of CBC. Study revealed that none of the patients in both groups had normal eosinophil count hence range was between 7-10%. Immunoglobulin E is most effective method to assess the allergic rhinitis but study showed very

discouraging results that only 10.0% group-A patients and 15.0% group-B patients submitted samples for IgE and their reports were positive. Study further identified that 100.0% Group-A and 90.0% Group-B patients submitted nasal secretion for nasal smear. Among Group-A patients, 90.0% had frequent eosinophils and 10.0% had very frequent eosinophils while among Group-B patients 88.9% had frequent eosinophils and 11.1% had very frequent eosinophils. A similar study undertaken confirmed that 67.2% patients had frequent eosinophils (Montone, 2007).

Home remedy for the treatment of illness is an indigenous practice observed mostly among elderly people since a long time. During study both groups patients were advised to take only prescribed medication and to avoid self-medication/home remedy. It is important to mention that 86.0% Group-A and 100.0% Group-B patients were agreed to avoid home medication/remedy to acquire better results of the treatment.

Study showed very encouraging results that improvement was seen in both groups on revisit but much better results were observed in group-B patients who were treated with cetirizine + montelukast. Before treatment, 100.0% patients in both groups had runny nose but after treatment 79.0% group-A patients (treated with cetirizine alone) and only 15.0% group-B patients had runny nose. Similarly before treatment, 77.0% of group-A and 94.0% group-B patients had sneezing. While after treatment 55.0% group-A patients and none of group-B patients had sneezing showing that combination of cetirizine + montelukast is more efficacious in allergic rhinitis treatment (Kurowski et al., 2004) also elucidated in their study that cetirizine + montelukast are more useful than single use of cetirizine in preventing nasal & eye itching and rhinorrhea.

Study further highlighted that 79.0% group-A patients had sedation with dispensed medicine while among Group-B patients, sedation was observed in only 5.0% patients showing that cetirizine + montelukast are more effective to treat the patients with allergic rhinitis.

Study disclosed that on revisit, blood samples of 85.0% group-A patients and 95.0% group-B patients were drawn for complete blood count. It is significant to mention that on revisit, all patients in both groups had normal eosinophil count i.e. between 1-6%. Likewise 60.0% group-A patients and only 5.0% group-B patients on revisit had rare eosinophils according to nasal smear report which confirmed further efficacy of cetirizine+montelukast. As immunoglobuline E is most effective method to assess the allergic rhinitis, study showed that 10.0% group-A patients and 15.0% group-B patients who submitted samples for IgE had their reports negative on revisit after treatment.

Conclusion: Allergic rhinitis affects patients work performance and quality of life. Before treatment significant majority in both groups had symptoms like runny nose, itchy nose, sneezing and watering eyes. Study concluded that symptoms were reduced in both groups on revisit (after treatment) but much better in group-B patients who were treated with cetirizine+montelukast because before treatment 100.0% patients in both groups had runny nose but after treatment 79.0% group-A patients (treated with cetirizine alone) and only 15.0% Group-B patients had runny nose. After treatment 55.0% group-A patients had sneezing while none of group-B patients had sneezing showing that combination of cetirizine+montelukast is more efficacious in the treatment of allergic rhinitis. After treatment 26.0% group-A and only 5.0% group-B patients had nasal mucosa pale and swollen. Seventy-nine 79.0% group-A patients had sedation with dispensed medicine while only 5.0% group-B patients had sedation showing that cetirizine+montelukast are more effective without sedation. Likewise, on revisit 60.0% Group-A patients and only 5.0% group-B patients had rare eosinophils confirming that combination of cetirizine+montelukast is more beneficial.

References

Amlani S, Nadarajah T and McIvor RA 2011. Montelukast for the treatment of asthma in the adult population. *Expert opinion on pharmacotherapy*, **12**, 2119-2128.

Arlian LG and Platts-Mills TA 2001. The biology of dust mites and the remediation of mite allergens in allergic disease. *Journal of allergy and clinical immunology*, **107**, S406-S413.

Baççioglu A, Yorgancioglu A, Cingi C and Çuhadaroglu Ç 2013. Role of leukotriene antagonists and antihistamines in treatment of allergic rhinitis and asthma comorbidity. *ENT Updates*, **3**, 34.

Canonica G, Bousquet J, Mullol J, Scadding G and Virchow J 2007. A survey of the burden of allergic rhinitis in Europe. *Allergy*, **62**, 17-25.

Celik P, Sakar A, Havlucu Y, Yuksel H, Turkdogan P and Yorgancioglu A 2005. Short-term effects of montelukast in stable patients with moderate to severe COPD. *Respiratory medicine*, **99**, 444-450.

Chen J, Kong W, Xiang J, Shu H, Shi Q, Tan H and Zhou Y 2008. Age features of the allergens in allergic rhinitis patients of different age in Hubei area. *Lin chuang er bi yan hou tou jing wai ke za zhi= Journal of clinical otorhinolaryngology, head, and neck surgery*, **22**, 683-685, 694.

Ciebiada M, Ciebiada MG, Kmiecik T, DuBuske L and Gorski P 2008. Quality of life in patients with

persistent allergic rhinitis treated with montelukast alone or in combination with levocetirizine or desloratadine. *J Investig Allergol Clin Immunol*, **18**, 343-349.

Cingi C, Toros SZ, Gürbüz MK, Ince I, Cakli H, Erdogmus N, Karasulu E and Kaya E 2013. Effect of grapefruit juice on bioavailability of montelukast. *The Laryngoscope*, **123**, 816-819.

Cox L, Nelson H, Lockey R, Calabria C, Chacko T, Finegold I, Nelson M, Weber R, Bernstein DI and Blessing-Moore J 2011. Allergen immunotherapy: a practice parameter third update. *Journal of allergy and clinical immunology*, **127**, S1-S55.

Doepp M 2001. Literatur nicht beachtet. *Clin Endocrinol Metab*, **86**, 1868-1870.

Golightly LK and Greos LS 2005. Second-generation antihistamines. *Drugs*, **65**, 341-384.

Kalpaklioglu F and Baccioglu A 2012. Efficacy and safety of H1-antihistamines: an update. *Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Inflammatory and Anti-Allergy Agents)*, **11**, 230-237.

Keith PK, Desrosiers M, Laister T, Schellenberg RR and Waserman S 2012. The burden of allergic rhinitis (AR) in Canada: perspectives of physicians and patients. *Allergy, Asthma & Clinical Immunology*, **8**, 7.

Khaltaev N and Bousquet J 2008. Allergic Rhinitis and its Impact on Asthma Update (ARIA 2008) The Perspective From Spain. *J Investig Allergol Clin Immunol*, **18**, 327-334.

Kurowski M, Kuna P and Gorski P 2004. Montelukast plus cetirizine in the prophylactic treatment of seasonal allergic rhinitis: influence on clinical symptoms and nasal allergic inflammation. *Allergy*, **59**, 280-288.

Lehman JM and Blaiss MS 2006. Selecting the optimal oral antihistamine for patients with allergic rhinitis. *Drugs*, **66**, 2309-2319.

Meltzer EO 2005. Evaluation of the optimal oral antihistamine for patients with allergic rhinitis. conference date, congerence title, Place of conference.

Montone KT 2007. Infectious diseases of the head and neck: a review. *American journal of clinical pathology*, **128**, 35-67.

Peroni D, Piacentini G, Alfonsi L, Zerman L, Di Blasi P, Visona G, Nottegar F and Boner A 2003. Rhinitis in pre-school children: prevalence, association with allergic diseases and risk factors. *Clinical & Experimental Allergy*, **33**, 1349-1354.

Small P, Frenkiel S, Becker A, Boisvert P, Bouchard J, Carr S, Cockcroft D, Denburg J, Desrosiers M and Gall R 2007. Rhinitis: A Practical and Comprehensive Approach to Assessment and Therapy. *Journal of otolaryngology*, **36**.

Small P and Kim H 2011. Allergic rhinitis. *Allergy, Asthma & Clinical Immunology*, **7**, S3.

Wallace DV, Dykewicz MS, Bernstein DI, Blessing-Moore J, Cox L, Khan DA, Lang DM, Nicklas RA, Oppenheimer J and Portnoy JM 2008. The diagnosis and management of rhinitis: an updated practice parameter. *Journal of allergy and clinical immunology*, **122**, S1-S84.

Zhang Y and Zhang L 2014. Prevalence of allergic rhinitis in china. *Allergy, asthma & immunology research*, **6**, 105-113.