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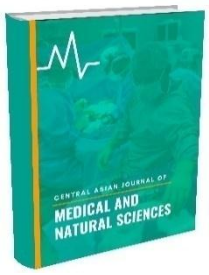

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A Comparative Study to Evaluate the Effects of Fluticasone Nasal Spray with Oral Bilastine Versus Mometasone Nasal Spray with Oral Bilastine in Patients of Moderate to Severe Rhinitis

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Abstract: **Background:** Rhinitis is defined as inflammation of the lining of the nose and is characterized by nasal symptoms including rhinorrhea, sneezing, nasal blockage and itching of the nose. Rhinitis is categorized into three types (a) Allergic rhinitis (b) Non-allergic rhinitis (c) Infectious rhinitis. Rhinitis is a global health problem that causes major illness and disability worldwide. The burden of allergic rhinitis is enormous, estimated to affect about 10-25% of world population. Reported incidence of allergic rhinitis in India also ranges between 20-30%. This study was conducted to compare the safety and efficacy of fluticasone furoate nasal spray with oral bilastine and mometasone furoate nasal spray with oral bilastine in patients of moderate to severe rhinitis.

Methods: The randomized controlled study was conducted in the Department of Pharmacology and Otorhinolaryngology, at BRD Medical College, Gorakhpur over a period of 12 months. 156 patients diagnosed with rhinitis in the Department of Otorhinolaryngology of BRD Medical College were included in the study and divided into two groups of 78 patients .Each patient in the study were subjected to a detailed history and clinical examination. Subjective scoring for rhinitis symptoms, serum IgE level, and the eosinophilic count was done in all patients.

Results: 94 of the 156 patients were women. The age group 26 to 50 made up the majority (57.7%).Majority of patients (60.3%) had allergic rhinitis followed by non-allergic rhinitis (39.7%). Sneezing (97.4%) was the most common symptom among study subjects followed by rhinorrhea (69.2%), nasal congestion (57.7%), and nasal itching (49.4%). In comparison to fluticasone furoate nasal spray, mometasone nasal spray had higher mean TNSS, TOSS and

TSS scores in patients with allergic and non-allergic rhinitis after treatment.

Conclusion: Fluticasone/Bilastine combination was more effective than Mometasone/Bilastine combination. Also, Fluticasone/bilastine combination was more safe and cost-effective as compared to Mometasone/Bilastine combination.

Key words: Allergic rhinitis, Non-allergic rhinitis, Intranasal corticosteroids, total symptom score

Introduction

Rhinitis is defined as inflammation of the lining of the nose and is characterized by nasal symptoms including rhinorrhea, sneezing, nasal blockage and itching of the nose. The most common kind of rhinitis is allergic rhinitis, which is usually triggered by airborne allergens such as pollen and dander.[1] Allergic rhinitis may cause symptoms such as sneezing, nasal itching, coughing, headache, fatigue, malaise and cognitive impairment.[2] The allergens may also affect the eyes, causing watery, reddened or itchy eyes and puffiness around the eyes.

Rhinitis is categorized into three types (a)Allergic-rhinitis-It is the most common form of non-infectious rhinitis. It is induced after allergen exposure by an immunoglobulin E (IgE)-mediated inflammation. It is triggered by mites, animal danders, molds, pollen and other inhaled allergen (b)Non-allergic rhinitis (NAR)-It is the term regrouping all the non-IgE mediated nasal symptoms of rhinitis.[3] It includes vasomotor, idiopathic, hormonal, atrophic, occupational, gustatory rhinitis as well as rhinitis medicamentosa.(c)Infectious rhinitis-Also called rhinosinusitis, is typically regarded as separate entity as it is generally an acute condition due to a virus or bacterial infection.

Rhinitis is a global health problem that causes major illness and disability worldwide. The burden of allergic rhinitis is enormous, estimated to affect about 10-25% of world population (>500 million people). Reported incidence of allergic rhinitis in India also ranges between 20% and 30%.[4]

Studies have shown that prevalence of allergic rhinitis have been increasing in India over past few years.

According to study of International study of asthma and allergies in childhood (ISAAC) phase 1 (1998), in India nasal symptoms alone were present in 12.5% children in 6-7 years age group and 18.6% in 13-14 years age group, while allergic rhino conjunctivitis was observed in 3.3% and 5.6% children, respectively. However, in ISAAC phase 3 (2009) study, prevalence of nasal symptoms increased to 12.9% and 23.6% in 6-7 and 13-14 year age groups, respectively, while that of allergic rhino conjunctivitis increased to 3.9% and 10.4% respectively.

Allergic rhinitis and asthma coexist in 70-80% of Indian patients.[5] Allergic rhinitis have been reported to have a significant adverse impact on health-related quality of life in Indian patients.[6] Evidence indicates that prevalence of allergic rhinitis is high and increasing throughout the world; with 23-30% in Europe, 12-30% in United States and 11.1-17.6% in China.

In the literature, prevalence of allergic rhinitis ranges between 43 and 87%, whereas prevalence of non-allergic rhinitis ranges between 17 and 52%.[7] Regarding mixed rhinitis, the National Rhinitis Classification Task Force has estimated that 43% of individuals with chronic rhinitis have allergic rhinitis, 23% non-allergic rhinitis, and 34% mixed rhinitis.[8]

Rhinitis represents an important economic burden, either in terms of direct (health-care visits, use of medications and hospitalization) or indirect (loss of productivity, absenteeism) costs.[9] There is a lack of information on analyzing rhinitis economic burden in India. Despite an important burden, rhinitis is often trivialized and considered as mild disorder.

Therefore, adverse effects of rhinitis on quality of life are often underestimated. Rhinitis impairs quality of life, has a strong impact on work productivity and school performance [9, 10] and its impact on absenteeism is sometimes greater than that of other chronic diseases such as diabetes, hypertension or asthma.[11]

Rhinitis is also responsible for sleep disturbance, a reduced ability to concentrate, reduced cognitive capacities, and anxiety disorders.[12] Rhinitis may also be responsible of emotional stress and alters social life.[13]

The total burden of this disease lies not only in impaired physical and social functioning but also in a financial burden made greater when considering evidence that allergic rhinitis is a possible causal factor in comorbid diseases such as asthma or sinusitis.[14]

The American Academy of Allergy, Asthma and Immunology and the American College of Allergy, and Immunology recommends intranasal corticosteroid (INCs) to be used as a first-line treatment for allergic rhinitis.[15] Second line therapies include antihistamines, decongestants, cromolyn, leukotriene receptor antagonists and nasal irrigation.[16] Current

available INCs are beclomethasone dipropionate, budesonide, and flunisolide, and the newer INCs known as the second-generation intranasal steroids are triamcinolone acetonide nasal spray (NS), fluticasone propionate NS, mometasone furoate NS, and fluticasone furoate NS.[17]

Fluticasone furoate is a novel corticosteroid molecule that is distinct from mometasone furoate and fluticasone propionate. Fluticasone furoate has several key benefits for treating seasonal allergic rhinitis, including very low systemic bioavailability (0.5%), 24-hour symptom relief with once-daily dosing, thorough coverage of both nasal and ocular symptoms, safety and tolerability with daily use, and availability in a novel, side-actuated delivery device that makes medication administration quick and reliable.

Mometasone furoate, a synthetic glucocorticoid, is a potent and effective treatment for seasonal and perennial allergic rhinitis and nasal polyposis. Mometasone furoate does not reach high systemic concentrations or cause clinically significant adverse effects. The clinical effectiveness of mometasone furoate nasal spray, coupled with its agreeable safety and

tolerability profile, confirms its favourable benefit-risk ratio.

Bilastine, a novel non-sedating second-generation oral antihistamine (OAH) medication, is an H1 receptor antagonist and member of the piperidine class.[18] Bilastine is used to treat allergy problems in people of all ages, including young and old adults, school-age kids, and teenagers.

Total nasal symptom score (TNSS) is a brief questionnaire which evaluate the severity of main symptoms of allergic rhinitis widely used in different countries.[19] The total ocular symptom score (TOSS) is used to indicate allergic conjunctivitis (AC) severity.[20]

Despite the high prevalence of allergic rhinitis (AR) in children and the importance of the use of INCs for the treatment of allergic rhinitis, comparative analyses of alternative treatments in patients, in terms of both cost and effectiveness are lacking. These comparative analyses are important because differences in cost of acquisition, efficacy, side effects, and therapeutic adherence between alternative treatments for allergic rhinitis could have a considerable impact on the control and the tremendous economic burden of the disease. Therefore, the primary objective of this study was to compare the

safety and efficacy of fluticasone furoate nasal spray with oral Bilastine and mometasone furoate nasal spray with oral Bilastine in patients of moderate to severe rhinitis.

Material and methods

The study was conducted in the Department of Pharmacology and Otorhinolaryngology, at BRD Medical College, Gorakhpur over a period of 12 months starting from February 2022 (Nine months of data collection and three months of analysis and writing) after obtaining informed consent from the patients and ethical clearance from the institutional ethics committee. Clinically diagnosed subjects of rhinitis reporting to the Department of Otorhinolaryngology were recruited in the study.

Study Design Type of Study: Randomized controlled trial.

Sample Size: 156 Patients diagnosed with rhinitis in the Department of Otorhinolaryngology of BRD Medical College from February 2022 to 2023 were included in the study.

Inclusion criteria:

1. All patients with symptoms and signs of allergic rhinitis and non–allergic rhinitis.
2. All patients above 18 years irrespective of sex and providing consent for participation in the study.

Exclusion criteria:

1. Pregnant and lactating women
2. Paediatric allergic rhinitis
3. Systemic disease such as hypertension and diabetes mellitus

Study Protocol:

All patients with rhinitis who met the inclusion criteria and did not fall within the exclusion criteria were included in the study. Study participants were divided into two groups of 78 patients. Group 1 receives Bilastine one tablet per day (20mg) + Mometasone furoate two spray actuation (50 micrograms per spray actuation) in each nostril once daily (total daily dose, 200 micrograms) and Group 2 receives Bilastine one tablet per day (20mg)+ Fluticasone furoate two spray actuation (27.5 micrograms/actuation) in each nostril once daily (total dose 110 micrograms).

Each patient in the study were subjected to a detailed history and clinical examination. Subjective scoring for rhinitis symptoms, serum IgE level, and the eosinophilic count was done in all the patients.

Efficacy was assessed by mean change in total symptom score (TSS) which is the sum of total nasal symptom score (TNSS) and total ocular symptom score (TOSS) at the end of 3 months from the baseline.

History of medication taken for rhinitis was noted.

Examination:

Nasal examination usually included physical examination of external nose, vestibule, anterior rhinoscopy, posterior rhinoscopy.

Data Management & Statistical Analysis:

The data were collected and entered in MS excel 2010. Different statistical analyses were performed using SPSS software version 22. Normally distributed data were analyzed using parametric tests and non-Normally distributed data were analyzed using non-parametric tests. Descriptive statistics were calculated for quantitative categorical variables. Graphical representation of the variable has been shown to understand the results clearly and the categorical data were analyzed using the Chi-Square test.

If $p<0.05$, then the hypothesis is said to be statistically significant, and if$p>0.05$, then the hypothesis is said to be statistically insignificant.

Results

Table 1:Distribution of patients according to type of allergy

Types of allergy	Mometasone + Bilastine (Group A)	Fluticasone + Bilastine (Group B)	Frequency	Percent
Allergic-rhinitis	48	46	94	60.3
Non-allergic rhinitis	30	32	62	39.7

Table 1 shows that the majority of patients (60.3%) had allergic rhinitis, followed by non-allergic rhinitis (39.7%). Allergic rhinitis patients were more in group A while non-allergic were more in Group B.

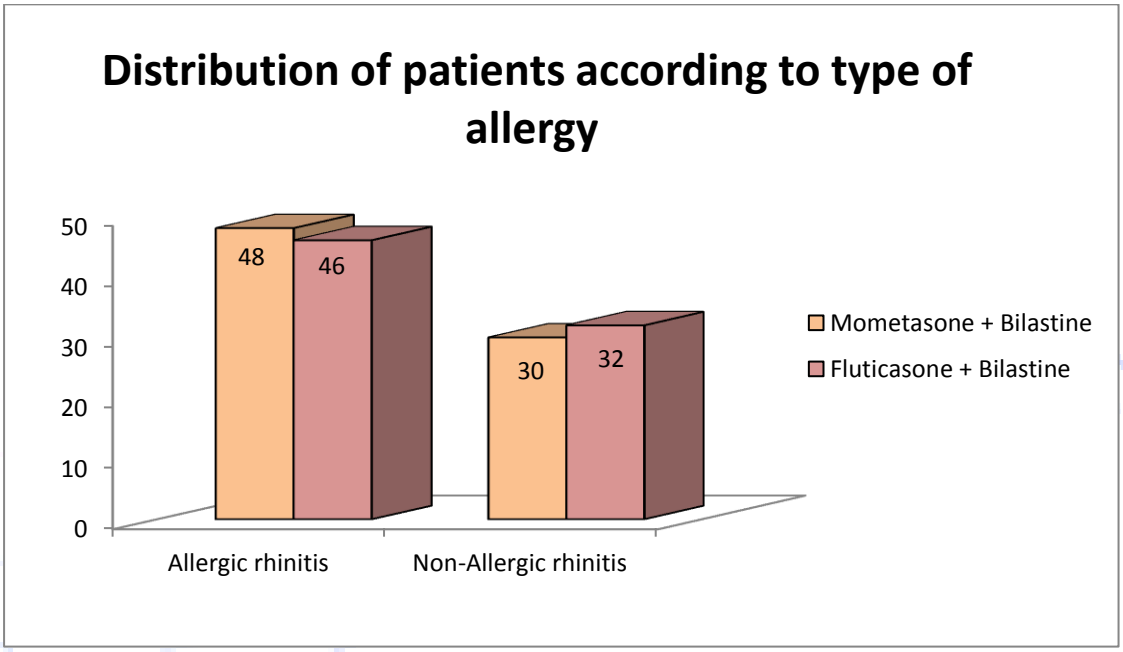

Table 2: Distribution of Symptoms among patients

Symptoms	Mometasone + Bilastine	Fluticasone + Bilastine	Frequency	Percent
Sneezing	78	74	152	97.4
Nasal itching	41	36	77	49.4
Nasal discharge	5	15	20	12.8
Nasal congestion	37	53	90	57.7
Tearing/Itching/Redness in eyes	20	32	52	33.3
Rhinorrhea	62	46	108	69.2
Smelling disorder	8	24	32	20.5
Headache /Heaviness in head	37	28	65	41.7
Fever	5	19	24	15.4
Post-nasal drip	5	23	28	17.9
Epistaxis	10	14	24	15.4
Ear discharge / itching	10	14	24	15.4
Recurrent cold	23	32	55	35.3
Throat itching	9	11	20	12.8
Cough	9	11	20	12.8
Breathlessness	10	18	28	17.9

Table 2 shows that sneezing (97.4%) was the most common symptom among study subjects, followed by rhinorrhea (69.2%), nasal congestion (57.7%), nasal itching (49.4%), headache/heaviness in the head (41.7%), recurrent cold (35.3%), smelling disorder (20.5%), post-nasal drip (17.9%), epistaxis (15.4%), nasal discharge and cough (12.8%).

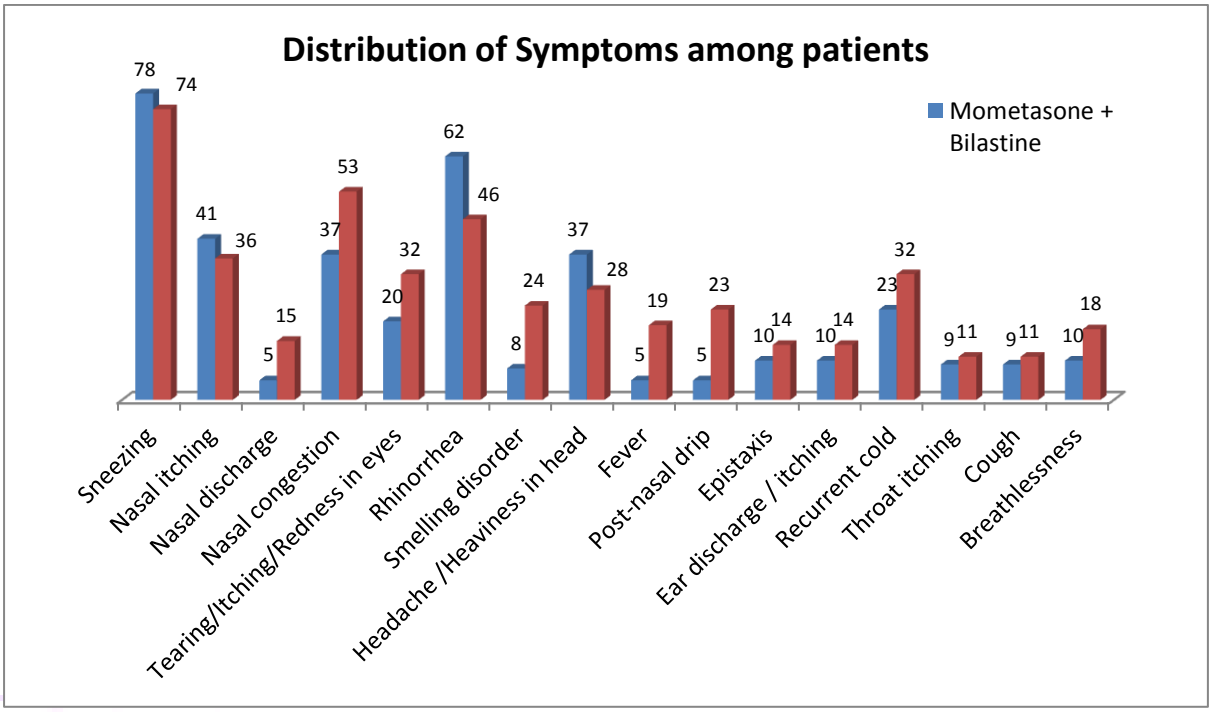

Table 3: Comparison of symptom scores and clinical characteristics for treatment at baseline and after three months

Treatment		Mometasone + Bilastine	Fluticasone + Bilastine	p value*
TNSS	Baseline	8.65±2.6	8.22±2.8	<0.001
	After 3 months	3.36 ± 0.1	2.83 ± 1.1	<0.001
TOSS	Baseline	3.46±3.5	2.97±3.0	<0.001
	After 3 months	1.01 ± 1.1	0.50 ± 0.8	<0.001
TSS	Baseline	12.12±4.9	11.35±4.7	<0.001
	After 3 months	4.37±1.6	3.33 ±1.7	<0.001
Absolute Eosinophilic count	Baseline	605.53±273.3	592.29±207.7	<0.001
	After 3 months	451.52 ± 251.2	439.30 ± 147.3	<0.001
IgE_level	Baseline	528.80±377.54	715.07±636.64	<0.001
	After 3 months	425.59 ± 337.69	480.42 ± 298.43	<0.001

Table 3 demonstrates significant baseline and post-treatment differences in the mean nasal symptom score, ocular symptom score, total symptom score, eosinophilic count, and IgE level between group A and group B. ($p < 0.05$)

Table 4: Association of Adverse effects with treatment among patients withallergic rhinitis

Side Effects	Treatment	
	Mometasone + Bilastine	Fluticasone + Bilastine
Total	**78**	**78**
Dryness of nose	5(6.41%)	3(3.84)%
Nose Irritation	0(0%)	4(5.12%)
Sore throat	8(10.25%)	3(3.84%)
Headache	4(5.12%)	0
Nausea	4(5.12%)	4(5.12%)
Fatigue / tiredness	0	0
Epistaxis	0	0

Table 4 shows that mometasone-furoate had more adverse effects than fluticasone-furoate. No person shows any signs of fatigue, tiredness or bleeding nose.

Table 5: Comparison of cost-effectiveness of Group A (Mometasone +Bilastine combination) with Group B (Fluticasone + Bilastine combination)

	Cost per bottle (Mometasone/Fluticasone)	Cost of a strip of bilastine tablets	Total cost of three months treatment
Group A	333.20	107.95	1971.15
Group B	312.88	107.95	1910.19

	Change in total symptom score (effectiveness)	Cost/effectiveness
Group A	7.75	254.34
Group B	8.02	238.17

Group B (Fluticasone + Bilastine) was found to be more cost-effective than Group A(Mometasone + Bilastine).

Discussion

The present study recruited a total of 156 study subjects, divided into two groups of 78 patients. The majority of cases were observed in the age group 26- 50 years, accounting for 57.7% of total study subjects, according to the age wise distribution of the study subjects. However, the least number of the study subjects (9.6%) were recorded in the age group >50 years. Of the total study subjects 60.3% were female. Majority (57.7%) of the patients were unemployed followed by belonging to hazardous occupation. Majority of the patients (39.7%) came from lower-middle class families. A thorough history and clinical assessment was performed on each participant in the study. All patients received subjective assessment for their eosinophilic count, serum IgE level, and rhinitis symptoms.

Sneezing (97.4%) was the most prevalent symptom among study participants, followed by rhinorrhea (69.2%), nasal congestion (57.7%), nasal itching (49.4%), headache/heaviness in the head (41.7%), recurrent cold (35.3%), smelling disorder (20.5%), post-nasal drip (17.9%), epistaxis (15.4%), nasal discharge and cough (12.8 %).

After three months, there was statistically significant difference in the nasal symptom score and the ocular symptom score between treatment group A (Mometasone+Bilastine) and B(Fluticasone+Bilastine). (p=0.002, 0.001).Therefore, Fluticasone furoate +Bilastine was more effective in reducing the nasal and ocular symptoms of rhinitis as compared to Mometasone + Bilastine. After three months, the differences in Eosinophilic count and IgE level between treatment

groups A (Mometasone +Bilastine) and B (Fluticasone+Bilastine) were found to be statistically insignificant.

As found in the current study, the most common adverse events were sore throat, dryness of nose, headache and nausea. Although the adverse effects were insignificantly associated with treatment received by both groups, fluticasone furoate and bilastine combination appears to be safer than mometasone furoate and bilastine. The cost-effectiveness of each study medication was descriptively evaluated as medication cost per treatment success.

In comparison to fluticasone furoate and Bilastine nasal sprays, the average cost of mometasone furoate and Bilastine nasal sprays was about 3.14% higher. The cost-effectiveness ratio was calculated to be Rs 238.17 for fluticasone furoate and bilastine combination and it was Rs 254.34 for mometasone furoate and bilastine combination. Therefore, the study shows that Fluticasone + Bilastine combination is more cost-effective.

Conclusion

A total of 156 research volunteers were recruited for this Randomized controlled trial, with 62 males and 94 females. Of the total study subjects (N=156), n=78 allocated to Intervention Group A (Mometasone + Bilastine) and n=78 to Group B (Fluticasone + Bilastine).Follow up was done after 3 months.

The majority (61.5%) were not having a family history of allergy. About 60.3% had allergic rhinitis while the rest had non-allergic rhinitis. The majority (43.6%) of patients had rhinitis due to house dust, dusty winds, smokes and fumes, wood dust and pollen dust. From the findings of my present study, it is clear that Fluticasone/Bilastine combination was more effective than Mometasone/Bilastine combination. Also, Fluticasone furoate was more safer and cost-effective as compared to Mometasone/Bilastine combination.

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