Original Article

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Olopatadine Hydrochloride and Fluticasone Propionate in Topical Treatment of Allergic Rhinitis: A Single Blind Randomised Study

Ear, Nose and Throat Section

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ABSTRACT

Introduction: The use of corticosteroids or antihistaminics in treatment of allergic rhinitis is known and practiced since long. The efficacy of topical use of fluticasone propionate and Olopatadine Hydrochloride (HCL) for symptomatic relief of allergic rhinitis has been studied either individually or with other drugs. But very few studies show comparison between these two drugs.

Aim: To compare the efficacy of topical use of fluticasone propionate and olopatadine hydrochloride for symptomatic relief of allergic rhinitis.

Design: In this single blind, randomized control study, the efficacy of topical use of olopatadine HCL was compared with fluticasone propionate for relieving symptoms of allergic rhinitis.

Materials and Methods: The symptomatic cases were randomized in two groups for treatment using either olopatadine HCL or fluticasone propionate respectively. In each group, the Total Symptom Scores (TSS) and individual symptom scores were recorded before and after treatment with the help of symptom evaluation scale.

Statistical Analysis: Chi-square test, unpaired t-test, Mann Witney U-test, and Wilcoxon signed Rank test were used during analysis. The results of the comparison were noted and analysed.

Results: During four week study period both TSS and individual symptom score were reduced ($p<0.05$) in either groups. The TSS decreased by an average of 85.07% for those treated with olopatadine and by 95.55% for those treated with fluticasone.

Conclusion: Overall fluticasone propionate was superior to olopatadine in relieving symptoms of allergic rhinitis ($p<0.005$).

Keywords: Nasal obstruction, Orbital cellulitis, Pruritus, Rhinorrhea

INTRODUCTION

Globally, allergic rhinitis affects all ages and ethnic groups with an increasing prevalence. It is characterized by one or more symptoms including nasal congestion and nasal block, sneezing, itching (pruritus) and rhinorrhea [1]. Although, not a serious illness but it is clinically relevant as it underlies many complications such as rhino-sinusitis leading to orbital cellulitis and further can spread to cavernous sinus and other intra-cranial areas like meninges, subdural and extradural spaces, brain parenchyma affecting quality of life and productivity at work or school [2]. Many causative agents have been linked to allergic rhinitis including pollens, moulds, dust mites and animal dander [1]. Despite the advanced knowledge of the numerous chemical-mediators of allergy, two major categories of drugs namely antihistamines and corticosteroids [4] are widely used in the management of allergic rhinitis. This study compares the efficacy of topical application of antihistaminic- Olopatadine Hydrochloride (HCL) and corticosteroid-fluticasone propionate in treatment of allergic rhinitis.

MATERIALS AND METHODS

It is time bound parallel prospective single blind randomized control study of 150 cases that presented in ENT Outpatient Department of Krishna Hospital and Medical Research Centre, Karad, Maharashtra, India between October 2012 to December 2014. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee.

Informed consent was obtained from all individual participants included in the study.

Inclusion criteria: The cases presenting with symptoms of nasal obstruction, sneezing, itching sensation in the nose, watery nasal discharge as well the cases with other symptoms like watering of eyes and itching in eyes, palate, ears and showing willingness for single blind clinical trial were included in the study irrespective of age and sex.

Exclusion criteria: The cases presenting with symptoms of nasal obstruction due to structural abnormalities such as grossly deviated nasal septum, extensive nasal polyps, tumour and requiring surgical management as well as those using systemic or oral corticosteroids and/or antihistamines during past 30 days of the entry visit were not taken up for the study as they may confuse the results in the trial. Also, any case with history of surgery or having a disease known to affect the gastrointestinal absorption of drugs, diabetics irrespective of status of its control and women with pregnancy or lactation were not taken up for the study.

All cases were selected as per inclusion and exclusion criterias and investigated by haemoglobin percentage, differential count and Absolute Eosinophil Counts (AEC). All symptomatic cases in the study were divided into group I and group II alternately on first come first serve basis with selection and allocation ratio 1:1 and thus, conforming simple random selection. The prescription drug label was replaced with group specific new label to maintain single blind status of the study. Participants of group I and II were advised to use topical olopatadine and fluticasone propionate respectively on domiciliary basis.

All blinded participants of both groups were assessed before and after the treatment on 4-point symptom scale (0 to 3) for symptoms like nasal blockade, nasal congestion, rhinorrhea, sneezing and nasal itching. In each case, the subjective assessment of symptoms was done to increase the creditability of the symptom scale. The symptoms were assessed as per US department of health and human services, FDA allergic rhinitis criterias [Table/Fig-1]. The symptom scores were recorded in the symptom diary provided to every patient. Effectiveness of treatment was assessed by relief of symptoms periodically during weekly follow-up using 4 point symptom evaluation scale and by repeat differential eosinophil count and AEC.

STATISTICAL METHODS

In this study, Chi-square test was used to find significance of proportion of sex and intermittent or persistent symptoms, whereas unpaired t-test was used to compare the age between group I and group II. Mann Witney U-test was used to find significance of total symptoms score between group I and group II and Wilcoxon signed Rank test used to find the significance of total symptoms score before and after treatment.

RESULTS

All 150 cases enrolled as per eligibility criterions completed four weeks follow-up during the study. All cases were belonging to age ranging from 15 to 50 years (mean age- 32.3 years; SD- 9.43). There were 86 male and 64 female cases. The treatment groups were similar in terms of demographic characteristics [Table/Fig-2] except, due to random selection of the cases in the study the total number of females was more in group I (40) as compared to group II (24).

Total Symptom Score (TSS) Analysis: Both treatment groups had comparable mean TSS at baseline indicating, similar severity of symptoms among all cases at start of study. TSS of group I was 10.89±1.11 and group II was 12.28±1.20. Mean TSS decreased in both the treatment groups after four weeks study period. In group I, TSS reduced to 1.63±1.10 whereas in group II, it reduced to 0.55±0.66 [Table/Fig-3]. The difference in TSS before and after treatment was 9.27±1.07 and 11.73±0.91 in group I and group II. Using Wilcoxon Matched Paired test, the percentage change in symptoms were 85.07% and 95.55% in group I and group II respectively. There was 85.07% change of median total symptom score in group I compared to 95.55% in group II. Both drugs were effective in reducing allergic rhinitis symptom but baseline symptom reduction was more in group II receiving fluticasone propionate.

Individual symptom score analysis: Using symptom evaluation scale, Individual symptom score of each group was noted before and after treatment. Both the groups had more or less equal individual symptom score before treatment [Table/Fig-4]. In both groups, the drugs were effective in reducing Individual symptom score as shown in [Table/Fig-5].

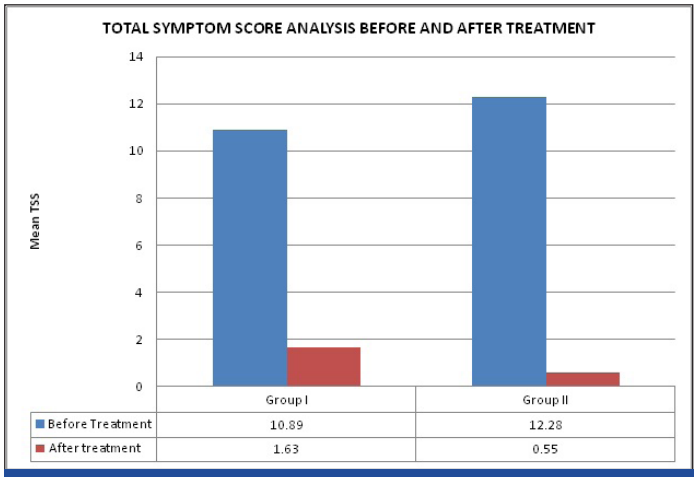
Adverse effects of drugs: Out of 150 cases, 22 experienced adverse drug reactions which were mild in severity and resolved without need for additional therapy and thereby with no interruption in continuation of the study. None of them experienced serious adverse reactions. Amongst these 22 cases, 12 were from group I and 10 belonged to group II. Among the common adverse effects in group-I (Olopatadine) the bitter taste was experienced

Evaluation scale	Symptoms	Description of symptoms*
0	Absent	No symptoms
1	Mild	Symptoms present but not troublesome
2	Moderate	Symptoms frequently troublesome but not disturbing daily activity or sleep
3	Severe	Symptoms disturbing daily activity or sleep

[Table/Fig-1]: Symptom evaluation scale.
*US department of health and human services FDA, allergic rhinitis

Variable	Total (n = 150)	Olopatadine HCL 0.6% Group I (n = 75)	Fluticasone propionate Group II (n = 75)	t-value	p-value
AGE (years)					
Mean(SD)	32.3 (9.43)	31.31 (9.90)	33.19 (8.89)	t=2.786	0.4258
Range	15 - 50	15 - 50	15 - 50		
Gender					
Male	86	35	51	χ^2= 6.9771	0.0082
Female	64	40	24		
Symptoms					
Intermittent	87	45	42	χ^2=0.2461	0.6196
Persistent	63	30	33		
Duration of Illness (yrs) Mean (SD)	2.5 (1.3)	2.6 (1.3)	2.5 (1.3)	---	0.6118

[Table/Fig-2]: Comparison in patient baseline characteristics.



[Table/Fig-3]: Graph showing total symptom score analysis before and after treatment of group I and group II.

Variable	Group I (n = 75) Mean (SD)	Group II (n = 75) Mean (SD)	p-value
Sneezing	2.4 (0.7)	2.8 (0.5)	0.0015
Nasal obstruction	2.4 (0.6)	2.4 (0.5)	1.0000
Nasal discharge	2.6 (0.6)	2.4 (0.6)	0.1604
Nasal itching	1.0 (0.8)	1.4 (0.6)	0.0083
Itching of eyes	1.1 (0.6)	1.2 (0.6)	0.6724
Watering of eyes	0.3 (0.5)	0.7 (0.8)	0.0033
Palatal itching	0.7 (0.6)	0.8 (0.8)	0.4987
Itching of ears	0.4 (0.6)	0.5 (0.6)	0.2233

[Table/Fig-4]: Baseline individual symptom score before treatment of each symptom in group I and group II.

Variable	Group I (n = 75) Mean (SD)	Group II (n = 75) Mean (SD)	p-value
Sneezing	0.2 (0.4)	0.2 (0.4)	1.0000
Nasal obstruction	0.4 (0.6)	0.1 (0.3)	0.0028
Nasal discharge	0.72 (0.8)	0.04 (0.2)	0.00001
Nasal itching	0.11 (0.4)	0.04 (0.2)	0.1778
Itching of eyes	0.04 (0.2)	0.07 (0.3)	0.7780
Watering of eyes	0.04 (0.2)	0.04 (0.2)	1.000
Palatal itching	0.07 (0.3)	0.03 (0.2)	0.6724
Itching of ears	0.04 (0.2)	0.01 (0.1)	0.7780

[Table/Fig-5]: Individual symptom score of each symptom after treatment in group I and group II.

in seven, followed by epistaxis in three, somnolence in one and nasal irritation in one. Similarly, the common adverse effect in group II (Fluticasone propionate) headache was experienced in six, followed by sore throat in two and epistaxis in two.

DISCUSSION

In this study, 22 participants experienced mild adverse drug reactions which resolved without any need for additional therapy, thereby, no interruption of the study. None of them experienced serious adverse reactions. The number of symptomatic cases which were not complying the inclusion criterias and those declined to participate etc., was not recorded.

Allergic rhinitis can be classified as either intermittent or persistent with respect to frequency of and duration of symptoms [5]. Accordingly allergic rhinitis is described as:

→ **Intermittent:** if experiencing symptoms for <four days/week or <four consecutive weeks.

→ **Persistent:** if symptoms occurring for more than four days/week and more than four consecutive weeks.

The use of corticosteroids or antihistaminics in allergic rhinitis has been discussed since long. Several studies have been conducted previously by Yanez A et al., Eli O. Meltzer et al., Kaliner M et al., and Ratner P et al., to know the efficacy of topical steroid and anti-histaminic in treatment of allergic rhinitis individually or in comparison with other [4,6-8]. But very few studies have been done on treatment of allergic rhinitis where the efficacies of topical fluticasone propionate and olopatadine hydrochloride are compared. In this study, we compared the efficacy of topical fluticasone propionate and olopatadine hydrochloride nasal spray in treatment of allergic rhinitis.

In this study, olopatadine nasal spray was effective in reducing the total symptom scores significantly (p=0.00001) in 85.07 % of cases. This result compared favourably with Eli O. Meltzer et al., (p< 0.001), Kaliner M et al., (p<0.05) [6,7]. Olopatadine nasal spray in this study was effective in relieving individual symptom of allergic rhinitis like sneezing, nasal obstruction, nasal discharge, nasal itching, itching of eyes, watering of eyes, palatal itching, and itching of ears suggesting extremely significant p-value = 0.00001. Olopatadine nasal spray was effective in relieving individual symptoms of sneezing (91.01%), watering of eyes (87.50%) and itching of eyes (96.43%) which is also in accordance with study conducted by Eli O. Meltzer et al., and Kaliner M et al., [6,7].

In this study, fluticasone propionate nasal spray was also effective in reducing the total symptom scores significantly (p=0.00001) by 95.55 %. This result is in accordance with study by Dykewicz MS et al., (2003) which say that patients treated with fluticasone nasal spray had a significantly greater reduction from baseline in total symptom score compared with placebo (p< 0.001), representing a 91% greater improvement with fluticasone than placebo [9]. Thereby, suggesting that treatment with fluticasone propionate was also extremely significant in reduction of symptoms of allergic rhinitis. Fluticasone group also had a significantly greater mean reduction in individual symptom of rhinorrhea, sneezing, nasal itching, nasal congestion, watering of eyes, itching of eyes, palatal itching and itching of ears (p=0.0001). Also, the fluticasone propionate nasal spray was effective in relieving all nasal symptoms which goes in accordance with study done by Ratner P et al., and Dykewicz MS et al. [8,9].

In this four week study, topical treatment with olopatadine nasal and fluticasone propionate provided relief from symptoms of allergic rhinitis. But there was a significant difference between the magnitudes of reduction of some symptom in all cases. Both the drugs were equally effective in reduction of sneezing symptom, 91.01% by olopatadine and 91.30% by fluticasone propionate, which is in accordance with the study performed by Kaliner M et al., where efficacy of olopatadine and fluticasone propionate is compared and in that also, there is no significant difference in reduction of sneezing symptom [7]. Similarly, there was no significant difference between these two drugs in relieving other symptoms like itching and watering of eyes, palatal itching and itching of ears which is in accordance with the study by Kaliner M et al., [7]. However, fluticasone propionate was more effective (96.72%) in relieving nasal obstruction symptom than olopatadine hydrochloride (83.61%) which is in accordance with the study performed by Wallace et al., and Bosquet J et al., which concluded that nasal steroid was better than antihistaminic in relieving nasal obstruction symptom [10,11]. However, this is in contrast with the study done by Kaliner M et al., where no significant difference was found in relieving nasal obstruction symptom between both drugs [7]. Also, fluticasone propionate was better (98.36 %) than olopatadine (71.88%) in treating nasal itching symptom of allergic rhinitis, it is in accordance with study done by Ratner P et al., [8].

Fluticasone propionate reduced mean TSS by 95.55% as compared to 85.07% by olopatadine hydrochloride nasal spray with p=0.00001 suggesting that difference between them was very much significant which is in accordance with the study performed by Yanez et al., [4]. However, this is in contrast with the study done by Kaliner M et al., which suggests that both drugs are equally effective in relieving allergic rhinitis symptom [7].

CONCLUSION

In allergic rhinitis, both antihistaminic-Olopatadine HCL and corticosteroid, Fluticasone propionate used topically were equally effective in relieving symptoms like sneezing, watering and itching of eyes, itching of ear and palate. Olopatadine HCL was significantly effective in reduction of all baseline symptoms except nasal obstruction and rhinorrhea. Fluticasone propionate was superior in relieving most of the symptoms including distressing nasal obstruction, rhinorrhoea, and nasal pruritus. The adverse drug reactions though mild and comparable between the groups, were marginally higher in group I. Overall; fluticasone propionate was superior to olopatadine HCL in relieving symptoms of allergic rhinitis.

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