Comparative Study of Bilastine and Fexofenadine in Control of Intermittent Allergic Rhinitis

Bhavya Jolly, Munish K.S, Ajith K.M, Venkatesha B.K

Department of Otorhinolaryngology, S. S. Institute of Medical Sciences and Research Centre, Davanagere, Karnataka, India.

Abstract

Background: Allergic rhinitis (AR) impacts 10-30% of the world affecting the quality of life of many. Hence, the requirement of a treatment targeted at delivering maximum symptom control and has minimum to no side effects.

Objectives: Comparison of efficacy of Bilastine and Fexofenadine in patients suffering from intermittent allergic rhinitis with the help of Total Nasal Symptom Scoring(TNSS) and assessment of side effects- sedation and cardiac toxicity.

Methodology: 60 subjects diagnosed with intermittent allergic rhinitis (IAR) were recruited and divided into groups of 30 each. One group was started on Bilastine 20mg OD and the other on Fexofenadine 120mg OD. TNSS was calculated based on symptom severity at presentation, on 10th day and 30th of antihistamine therapy. AEC values and ECG changes were compared for both groups at day 0, day 30. Measurement of sedation was done at day 10, day 30. Intergroup comparison and intragroup assessment of TNSS and its variables, sedative effects and ECG changes at day 0 and day 30 were done using Un-paired and Paired T-test.

Results: Patients showed reduction in symptoms of AR with both drugs. TNSS and Rhinorrhoea showed significant improvement in Fexofenadine group as compared to Bilastine. AEC values showed significant reduction in both groups. Statistically significant ECG changes were seen after 30 days of Fexofenadine therapy but were clinically insignificant. No sedative effects were noted with both drugs.

Conclusion: Both Bilastine and Fexofenadine were found to be effective in reducing symptoms in patients with IAR. Fexofenadine was more effective than Bilastine in overall symptom control and specifically in controlling rhinorrhoea after one month of therapy. Both the drugs had no sedative effects or cardiac toxicity.

Key words: Allergic Rhinitis(AR), antihistamines, Bilastine, Fexofenadine, Total Nasal Symptom Score(TNSS).

Introduction

Allergic rhinitis (AR) is an inflammatory process of the nasal mucosa, IgE-mediated, elicited by environmental allergens and characterized by the presence of inflammatory cells within the mucosa and submucosa [1]. The symptoms of the same include watery nasal discharge, nasal itching, sneezing and nasal obstruction; which may cause deterioration in the quality of life of an individual[2]. The burden of allergic rhinitis is enormous, constituting about 55% of all allergies. About 20-30% of Indian population suffers from at least one allergic disease. Reported prevalence of allergic rhinitis in India also ranges between 20%-30%[3]. Antihistamines provide very useful symptomatic treatment for both intermittent and persistent allergic rhinitis by antagonizing the effect of histamine at the H1 receptors thereby eliciting major clinical effects related to the same[4]. Second-generation histamine H1 receptor antagonists and newer antihistamines have been developed to reduce or eliminate the sedation and anticholinergic adverse effects that occur with older H1 receptor antagonists in the treatment of intermittent allergic rhinitis. [5]. mines" based on the H1 receptor occupancy[6]. These also show a diversity of pharmacokinetic properties in the body and the parent drugs and metabolites may differ in their biological properties, which in turn have shown to cause cardiac toxicity (arrhythmias) in previous antihistamines [7]. Selection of optimal second-generation antihistamines depends on many

Address for Correspondence:

Dr. Bhavya Jolly

Department of Otorhinolaryngology,
S. S. Institute of Medical Sciences and Research Centre, Davanagere, Karnataka, India.
Email: bhavya28@yahoo.co.in

factors, particularly drug safety and efficacy, impact on psychomotor abilities, and sedation [8]. Hence, for selecting antihistamines for allergic rhinitis, various such modalities should be taken into consideration by a clinician.

This study is determined to compare two antihistamines i.e Fexofenadine and Bilastine with respect to efficacy in symptom reduction in the treatment of intermittent allergic rhinitis along with common side effects associated with the drugs thereby stating the purpose of helping a clinician choose an optimal antihistamine for the treatment of intermittent allergic rhinitis.

Methods And Material

A Prospective comparative study conducted on patients aged 20 years and above, attending outpatient department of ENT in SSIMS & RC, Davangere diagnosed with Intermittent Allergic Rhinitis, who had satisfied inclusion criteria mentioned below during the period of 2 years, i.e. November 2019 to October 2021, were included in the study.

Inclusion criteria: Patients in the age range of 20-60 years.Patients diagnosed with moderate-severe allergic rhinitis of intermittent type on history consistent with allergic symptoms with a TNSS of >/=8/12 (eg. clear rhinorrhoea, pale nasal mucosa, red, watery eyes).

Exclusion criteria: Patients with a nasal pathology other than allergic rhinitis or any nasal anatomical abnormality attributing to nasal obstruction, systemic diseases like systemic hypertension, liver/cardiac disorders, patients who are taking other medications that have drug interactions All patients fulfilling the selection criteria were explained about the nature of the study and a written informed consent was obtained. This study was approved by the Ethical and Research committee, SSIMS & RC, Davangere prior to the commencement. [IERB no : 379-2019]

Methods of Collection of Data:

Patients diagnosed with intermittent allergic rhinitis were enrolled from outpatient department of ENT in SSIMS & RC meeting the inclusion and exclusion criteria. Sample size was 60. Informed and written consent from all the patients were obtained. A detailed history from the patient and an Otorhinolaryngological examination was carried out. Two groups; one was given Fexofenadine (120mg), the other, Bilastine (20mg), per orally, once a day at night time for a month. Proforma for TNSS was filled and was attached to the OPD card. Follow up- Scoring was done on Day-0, Day-10 and Day-30, along with comparison of sedation and cardiac effects. Both drugs were assigned to every patient diagnosed with IAR, on an alternate basis

Total Nasal Symptom Scores (TNSS)[9]: Each symptom (sneezing, nasal congestion, nasal itching, and rhinorrhea) is graded from 0-3

Score Symptoms:

- 0 = None (No symptoms evident)
- 1 = Mild (Symptoms present but easily tolerated)
- 2 = Moderate (Definite awareness of symptoms; bothersome but tolerable)
- 3 = Severe (Symptoms hard to tolerate; interferes with daily activity)

Primary efficacy endpoint: Change in TNSS from day 1 of reporting to OPD to 1 month after usage of drug.

Measurement of Sedation[10].

Score	Characteristics
0	Awake and alert
1	Minimally sedated: tired/sleepy, appropriate response to verbal conversation and/or sound
2	Moderately sedated: somnolent/sleeping, aroused with light tactile stimulation or a verbal command.

Measurement of Cardiac Toxicity[11]**.**

To acquire a standardized heart rate correction formula was made by Bazett to detect long QT intervals (QTc = QT / RR1/2 [sec], where RR is determined in the preceding RR interval). Regarding the 12-lead ECG, "normal" QTc values are generally considered to be between 350 and 440 ms (>450ms in males and >460ms in females is significant), but, this consideration of QTc >440 to <480 ms as indicative of "borderline QT prolongation" [12].

Intervention:

Patients diagnosed with intermittent allergic rhinitis were divided into two groups (Both drugs were assigned to every patient diagnosed with IAR alternatively.); one was given Fexofenadine (120mg), the other, Bilastine (20mg), per orally, once a day at night time for a month. Follow up was done on Day-10 and Day-30 which included comparison of symptom score, measurement of sedation and ECG changes.

Statistical analysis:

Qualitative data represented in the form of frequency and percentage. Association between variables were assessed with Chi Square test. Quantitative data represented using Mean & Standard Deviation. Unpaired t test was used to compare the mean difference between groups. Paired t Test was used

to compare within the group difference. A P value of <0.05 was considered statistically significant. IBM SPSS Version 22.0 for windows was used to do statistical analysis.

Result:

A total of 60 patients were included in this prospective comparative study, out of which 30 patients were enrolled in group 1 (Bilastine 20mg once a day) and 30 patients belonged to group 2 (Fexofenadine 120mg once a day). The mean age in group 1 was 27.33 and that in group 2 was 32.63.

Out of the 30 patients with IAR in group 1, 17(56.7%) cases were males and 13(43.3%) cases were females. Out of the 30 patients with IAR in group 2, 16(53.3%) cases were males and 14(46.7%) cases were females.

Out of the 30 patients with IAR in group 1, 30(100%) cases presented with rhinorrhoea, 25 (83.3%) cases presented with nasal congestion, 30 (100%) cases presented with nasal itching, 30 (100%) cases presented with sneezing. Out of the 30 patients with IAR in group 2, 28 (93.3%) cases presented with rhinorrhoea, 26 (86.7%) cases presented with nasal congestion, 30 (100%) cases presented with nasal itching, 30 (100%) cases presented with sneezing.

Out of the 30 patients with IAR in group 1, the duration of symptoms was <1 year in 12(40%) of cases, 1-5 years in 12(40%) of cases, 6-10 years in 4(13%) of cases, >10 years in 2(7%) of cases. Out of the 30 patients with IAR in group 2, the duration of symptoms was <1 year in 19(63.3%) of cases, 1-5 years in 10(33.3%) of cases, 6-10 years in 1(3.3%) of cases, >10 years in 0(0%) of cases.

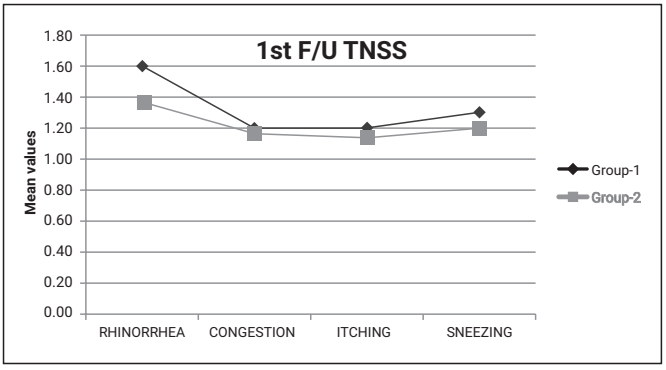
Out of the 30 patients with IAR in group 1, 14(47%) of cases had similar complaints in the past, out of which 7 (46.7%) had used INCS and 6(40%) had used antihistamines in the past 1 year. Out of the 30 patients with IAR in group 2, 7(23.3%) of cases had similar complaints in the past, out of which 6(85.7%) had used INCS and 1(14.2%) had used antihistamines in the past 1 year (graph 5). Chi-square test was applied to compare the treatment taken previously for IAR between the two groups and the test was statistically significant (p<0.005).

Out of the 60 patients with IAR enrolled in the study, none of the patients had family history of allergic rhinitis and 1 patient out of each group had skin allergy.

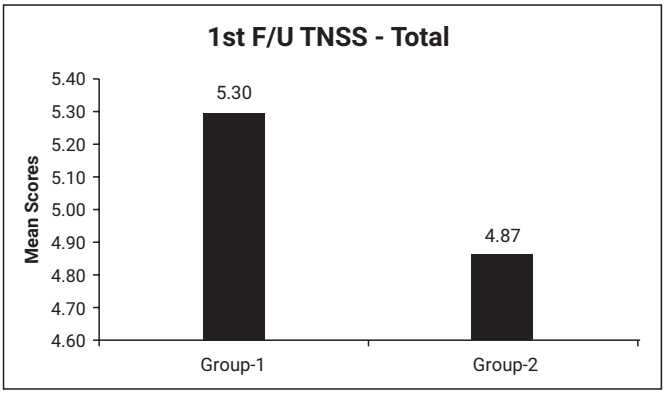
TNSS (tables 1,2; graphs 1.1 to 2.2))

Table 1: Intragroup comparison of the TNSS between 0, 10 and 30 days in group 1.

Group-1							
TNSS	**Day 0**	**Dav 10**	**Day 30**	**Assessment**	**Paired Mean Differences**	**Paired t test**	
Rhinorrhea				Day 0 Vs Day 30	0.6667	0.001	HS
	2.27	16	1.50	Day 0 Vs Day 30	0.7667	0.001	HS
				Day 10 Vs Day 30	0.1000	0.264	HS
Congestion				Day 0 Vs Day 30	0.8667	0.001	HS
	2.07	1.2	0.93	Day 0 Vs Day 30	1.1333	0.001	HS
				Day 10 Vs Day 30	0.2667	0.001	HS
Itching				Day 0 Vs Day 30	1.1333	0.001	HS
	2.33	1.2	0.97	Day 0 Vs Day 30	1.3667	0.001	HS
				Day 10 Vs Day 30	0.2333	0.010	S
Sneezing				Day 0 Vs Day 30	1.1333	0.001	HS
	2.43	1.3	0.93	Day 0 Vs Day 30	1.5000	0.001	HS
				Day 10 Vs Day 30	0.3667	0.001	HS
Total				Day 0 Vs Day 30	3.8000	0.001	HS
	9.1	5.3	4.37	Day 0 Vs Day 30	4.7333	0.001	HS
				Day 10 Vs Day 30	0.9333	0.001	HS



Graph 1.1: TNSS 1st follow up (individual symptoms)



Graph 1.2: TNSS 1st follow up

Out of the 30 patients with IAR in group 1, there was a decrease in mean total symptom score both at 1st F/U (first follow-up - 10 days) and at 2nd F/U (second follow-up - 30 days). Paired T-test was applied to compare the total scores between 0, 10 and 30 days and test showed statistically significant results (p=0.001). Similarly, out of the 30 patients with IAR in group 2, there was a decrease in mean symptom score both at 1st F/U and at 2nd F/U. Paired T-test was applied to compare the total scores between 0, 10 and 30 days and test showed statistically significant results (p=0.001). Un-paired T-test was applied to compare the total scores between the two groups at 10 days and the mean difference for TNSS for group 1 was 3.80 (SD 1.52) and that for group 2 was 4.80 (SD 1.81)- the test was statistically significant (p=0.024). Un-paired T-test was applied to compare the total scores between the two groups at 30 days and the mean difference in TNSS for group 1 was 4.73 (SD 1.74) and that for group 2 was 6.20 (SD 2.07)- the test was statistically significant (p=0.002).

Out of the 30 patients with IAR in group 1, there was a decrease in mean score for rhinorrhoea both at 1st F/U and at 2nd F/U but comparing 1st and 2nd F/U for rhinorrhoea the mean difference was not statistically significant. Paired T-test was applied to compare the scores for rhinorrhoea between 0, 10 and 30 days and test showed statistically significant results (p=0.001) while comparing basal to 1st and 2nd F/U scores independently but not statistically significant results (p=0.264) when comparing with each other. While, out of the 30 patients with IAR in group 2, there was a decrease in mean rhinorrhoea score both at 1st F/U and at 2nd F/U. Paired T-test was applied to compare the scores for rhinorrhoea between 0, 10 and 30 days and test showed statistically significant results (p=0.001). Un-paired T-test was applied to compare the scores for rhinorrhoea between the two groups at 10 days and the mean for group 1 was 1.60 (SD 0.56) and that for group 2 was 1.37 (SD 0.61)- the test was not statistically significant (p=0.131). Un-paired T-test was applied to compare the scores for rhinorrhoea between the two groups at 30 days and the mean for group 1 was 1.50 (SD 0.51) and that for group 2 was 0.97 (SD 0.49)- the test was statistically significant (p=0.001).

Out of the 30 patients with IAR in group 1, there was a decrease in mean score for nasal congestion both at 1st F/U and at 2nd F/U. Paired T-test was applied to compare the scores for nasal congestion between 0, 10 and 30 days and test showed statistically significant results (p=0.001). Similarly, out of the 30 patients with IAR in group 2, there was a decrease in mean score for nasal congestion both at 1st F/U and at 2nd F/U. Paired T-test was applied to compare the scores for nasal congestion between 0, 10 and 30 days and test showed statistically significant results (p=0.001). Un-paired T-test was applied to compare the scores for nasal congestion between the two groups at 10 days and the mean for group 1 was 1.20 (SD 0.66) and that for group 2 was 1.17 (SD 0.59)- the test was not statistically significant (p=0.838). Un-paired T-test was applied to compare the scores for nasal congestion between the two groups at 30 days and the mean for group 1 was 0.93 (SD 0.45) and that for group 2 was 0.83 (SD 0.46)- the test was not statistically significant (p=0.399).

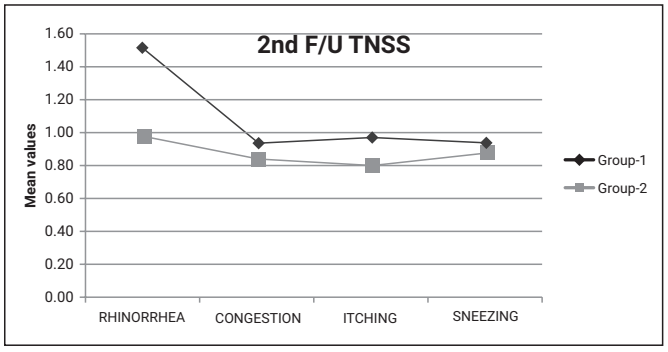
Out of the 30 patients with IAR in group 1, there was a decrease in mean score for nasal itching both at 1st F/U and at 2nd F/U. Paired T-test was applied to compare the scores for nasal itching between 0, 10 and 30 days and test showed statistically significant results (p=0.001, p=0.010). Similarly, out of the 30 patients with IAR in group 2, there was a decrease in mean score for nasal itching both at 1st F/U and at 2nd F/U. Paired T-test was applied to compare the scores for nasal itching between 0, 10 and 30 days and test showed statistically significant results (p=0.001, p=0.002). Un-paired T-test was applied to compare the scores for nasal itching between the two groups at 10 days and the mean for group 1 was 1.20

(SD 0.48) and that for group 2 was 1.13 (SD 0.51)- the test was not statistically significant (p=0.605). Un-paired T-test was applied to compare the scores for nasal itching between the two groups at 30 days and the mean for group 1 was 0.97 (SD 0.32) and that for group 2 was 0.80 (SD 0.48)- the test was not statistically significant (p=0.121).

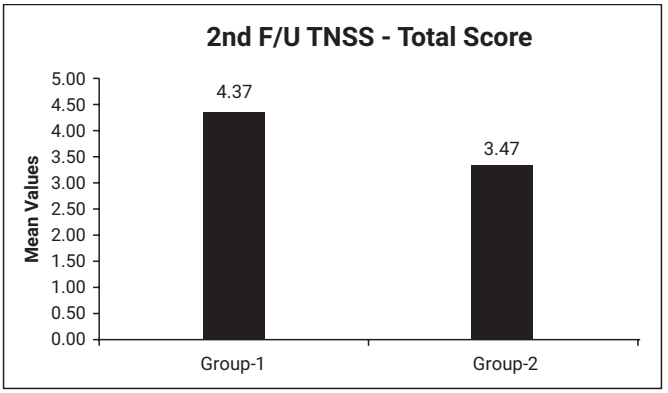
Out of the 30 patients with IAR in group 1, there was a decrease in mean score for sneezing both at 1st F/U and at 2nd F/U. Paired T-test was applied to compare the scores for sneezing between 0, 10 and 30 days and test showed statistically significant results (p=0.001). Similarly, out of the 30 patients with IAR in group 2, there was a decrease in mean score for sneezing both at 1st F/U and at 2nd F/U. Paired T-test was applied to compare the scores for sneezing between 0, 10 and 30 days and test showed statistically significant results (p=0.001, p=0.002). Un-paired T-test was applied to compare the scores for sneezing between the two groups at 10 days and the mean for group 1 was 1.30 (SD 0.47) and that for group 2 was 1.20 (SD 0.48)- the test was not statistically significant (p=0.418). Un-paired T-test was applied to compare the scores for sneezing between the two groups at 30 days and the mean for group 1 was 0.93 (SD 0.45) and that for group 2 was 0.87 (SD 0.43)- the test was not statistically significant (p=0.561).

Table 2: Intragroup comparison of the TNSS between 0, 10 and 30 days in group

Group-2							
TNSS	**Day 0**	**Dav 10**	**Day 30**	**Assessment**	**Paired Mean Differences**	**Paired t test**	
Rhinorrhea				Day 0 Vs Day 30	0.96667	0.001	HS
	2.33	1.37	0.97	Day 0 Vs Day 30	1.36667	0.001	HS
				Day 10 Vs Day 30	0.40000	0.001	HS
Congestion				Day 0 Vs Day 30	1.1000	0.001	HS
	2.27	1.17	0.83	Day 0 Vs Day 30	1.4333	0.001	HS
				Day 10 Vs Day 30	0.3333	0.001	HS
Itching				Day 0 Vs Day 30	1.3667	0.001	HS
	2.50	1.13	0.80	Day 0 Vs Day 30	1.7000	0.001	HS
				Day 10 Vs Day 30	0.3333	0.002	HS
Sneezing				Day 0 Vs Day 30	1.3667	0.001	HS
	2.57	1.2	0.87	Day 0 Vs Day 30	1.7000	0.001	HS
				Day 10 Vs Day 30	0.3333	0.002	HS
Total				Day 0 Vs Day 30	4.8000	0.001	HS
	9.67	4.87	3.47	Day 0 Vs Day 30	6.2000	0.001	HS
				Day 10 Vs Day 30	1.4000	0.001	HS



Graph 2.1: TNSS 2nd follow up (individual symptoms)



Graph 2.2: TNSS 2nd follow up

Basal investigation readings taken at day 0 - mean AEC for group 1 was 442.53 (SD 271.48) and that for group 2 was 543.10 (SD 314.27). Unpaired t-test was done to compare the basal AEC values between

the two groups and the result were found to be not significant (p=0.19). Mean QTc for group 1 was 417.10 (SD 17.57) and that for group 2 was 420.07 (SD 13.02). Unpaired t-test was done to compare the basal QTc values between the two groups and the result were found to be not significant (p=0.461).

Investigation readings taken at day 30 (2nd follow up)- mean AEC for group 1 was 344.33 (SD 186.56) and that for group 2 was 360.07 (SD 218.17). Unpaired t-test was done to compare the basal AEC values between the two groups and the result were found to be not significant (p=0.765). Mean QTc for group 1 was 420.73 (SD 16.97) and that for group 2 was 425.50 (SD 16.33). Unpaired t-test was done to compare the basal QTc values between the two groups and the result were found to be not significant (p=0.272).

Paired t-test was done to compare the basal and 2nd follow up AEC values in group 1 and the result were found to be significant (p=0.003). Similarly, paired t-test was done to compare the basal and 2nd follow up AEC values in group 2 and the result were found to be significant (p=0.001).

Paired t-test was done to compare the basal and 2nd follow up QTc values in group 1 and the result were found to be not significant (p=0.07). On the other hand, paired t-test was done to compare the basal and 2nd follow up QTc values in group 2 and the result were found to be significant (p=0.04).

None of the patients in both the groups complained of sedation at 1st F/U and 2nd F/U.

Discussion

In this study, the presenting age group was 20 to 60 years with mean age of 27.33 ± 9.97 years in group 1 and mean age of 32.63 ± 13.92 years in group 2. Both the groups tested had patients ranging from similar age group, with no gender preponderance. Navarro A. et al in 2005, the average age of the patients with the diagnosis of allergic rhinitis was 30 ± 15 years which is similar to this study [13]. In a study by Canonica G. W et al in 2021 in Europe, the patients with AR were seen to be gender balanced [14]. It was also noted that the patients treated with Bilastine had significantly more number of patients with history of previous treatment taken for allergic rhinitis. In a study by Randall K.L in 2018, it was noted that there is a widespread belief in the community that taking long-term antihistamines makes them less effective and that it is better to swap between different types of antihistamines for the best effect. Though there is no compelling evidence that tachyphylaxis occurs with the newer H1 antihistamines[15].

TNSS showed statistically significant improvement in the quality of life of all the patients with IAR treated with both the drugs. There were better scores of improvement in rhinorrhoea in patients treated with Fexofenadine over 30 days (mean value 0.97) over those treated with Bilastine (mean value 1.50). Similarly, there was more improvement perceived in the TNSS in patients treated with Fexofenadine over 30 days (mean value 3.47) over those treated with Bilastine (mean value 4.37); concluding that Fexofenadine had more effective symptom control as compared to Bilastine. None of the patients showed worsening of symptoms during the treatment period with any of the drugs. Church MK in a literature review concluded that bilastine was as effective as fexofenadine at reducing symptoms in patients with allergic rhinitis[16]. Similarly, in a study by Corcóstegui R et al, they noted that Bilastine has also been shown to possess anti-inflammatory activity similar to and fexofenadine[17].

After 30 days of treatment with both the drugs, none of the patients had complaints of sedation or altered psychomotor activity.

Two patients treated with Fexofenadine had borderline QTc prolongation but clinically significant ECG changes were not seen in either of the two groups. In a study by Renwick AG in 1999, it as seen that fexofenadine undergoes limited metabolism and is not associated with cardiac effects[17]. This was in accordance to the study although borderline QTc prolongation for two patients couldn't be explained. No other side effects were reported by any patient during the course of the study.

This study demonstrates the comparison of efficacy in symptom control of IAR by Bilastine or Fexofenadine without potential side effects, thus, targeting individual symptom along with an aggregate of all symptoms of allergic rhinitis in tailoring treatment according to patient's requirements.

Limitations of the study:

Even though this study showed significant improvement in patient symptom score in control of IAR, further study with larger population and longer duration is required to know the recurrence/ persistence of symptoms and long term side effects of Bilastine and Fexofenadine. There was no randomisation/blinding done. Patients with previous anti-allergic treatment were not excluded from the study which showed significant intergroup variation. The occupation of the patients was not taken into account in this study.

Conclusion

Both Bilastine and Fexofenadine were effective in

reduction of symptoms, and thus improving the quality of life in patients with Intermittent Allergic Rhinitis, although Fexofenadine was more effective than Bilastine in overall symptom control and in specifically controlling rhinorrhoea. Both the drugs had no sedative effects or cardiac toxicity in terms of QT prolongation.

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