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A COMPARATIVE STUDY ON EFFICACY OF UPDOSING OF BILASTINE V/S FEXOFENADINE IN CHRONIC SPONTANEOUS URTICARIA

Dr. Meghana H N* post graduate, GMC, kadapa*Corresponding Author

ABSTRACT **OBJECTIVES:** Updosing second-generation antihistamines (SGAHs) up to four times is advised in patients who do not respond to the indicated dosages. Even though SGAHs are safe, questions about their safety after updosing persist, and the absence of studies explicitly comparing the updosing of various SGAHs makes it difficult to choose a medication. **MATERIAL ans METHODS:** Bilastine or fexofenadine was administered randomised to 50 patients with chronic spontaneous urticaria (CSU) (25 in each group). For the first two weeks, patients received the recommended dosage of either medication (fexofenadine 180 mg or bilastine 20 mg). Patients who still had symptoms after two weeks (UAS 7) received a double dosage of either fexofenadine (180 mg BD) or bilastine (20 mg BD) for an additional two weeks. UAS score evaluation was used to gauge urticaria control. The CU-Q2oL questionnaire was used to evaluate the patients' quality of life. Analyzing the adverse events (AEs) that patients reported allowed for the evaluation of safety. **RESULTS:** At week 2, 22 patients (UAS 6) had acceptable urticaria control (bilastine, 10; fexofenadine, 13). 26 of the 28 individuals who received high doses of bilastine or fexofenadine at week 4 had acceptable control of their urticaria (bilastine: 15, fexofenadine: 10). When compared to fexofenadine, bilastine was associated with a significant improvement in patient quality of life. Sedation was the most common adverse effect reported by eight patients (2 in the bilastine group and 6 in the fexofenadine group) **CONCLUSION:** Updosing of bilastine provided relief from urticaria symptoms, improved quality of life in the majority of the patients without compromising safety.Bilahist was assosciated with improved quality of life compared to fexofenadine.somnolence or safety.

KEYWORDS : Bilastine,Fexofenadine,Updosing ,Chronic spontaneous urticaria

INTRODUCTION

It is prevalent in every country in the world and has become more common over the past ten years, according to Maurer et alsystematic.'s review and meta-analysis.[3] CU has a significant impact on health-related quality of life , comparable to or greater than moderate-to-severe psoria Effective therapy is therefore of the utmost significance [2]. Second-generation antihistamines are advised as first-line therapy in the management of CU since histamine is a key player in the pathophysiology of urticaria. Many patients in the study stated that unwanted effects were worse than with the standard dose.[11] Bilastine is a novel SGAH with faster and longer duration of action, lowest H1-receptor occupancy in the CNS compared to other SGAHs.[12] In multiple randomized clinical and real-world studies, bilastine was associated with significant improvement in signs and symptoms of urticaria in standard as well as in higher dosage.[13-18] However, the studies directly comparing the effectiveness and safety of bilastine updosing to other SGAH are lacking especially in Indian setup.

MATERIALAND METHODS

Study design

It was a two-arm, single-center, randomised, comparative, open-label trial. All patients gave informed written consent during the recruitment process, which took place between May 2022 and October 2022, and participants were monitored

Study participants

In GMC, Kadapa, this study was conducted. 50 patients between the ages of 18 and 60 who had a clinical history of CSU lasting at least 6 weeks in the previous 3 months without a known aetiology and an urticaria activity score 7 (UAS7) of less than 7 were sought out.

Patients with other forms of urticaria; pregnant or nursing females; patients with immunosuppressive disease or on immunosuppressive drugs; and patients with evidence of cardiac, respiratory, gastrointestinal, and renal disease were excluded from the study.

Patient follow-up

At baseline visit, clinical evaluation of patients was done to assess urticaria activity during the preceding week based on UAS7. Patients' quality of life was assessed using CU-Q2oL questionnaire. Patients were randomized to receive either bilastine 20 mg once daily or fexofenadine 180 mg once daily for a period of 2 weeks. At this visit, patients were given diary to note down UAS (from 0, no itch and no wheals, to 3, itch at its worst with multiple wheals) and adverse events (AEs). Patients were followed at week 2 and week 4.

During the second visit at week 2, patients were again evaluated for their USA7 and CU-Q2oL. Patients were further evaluated regarding urticaria associated discomfort on visual analogue scale (VAS). At this visit, patients with a UAS7 score of 6 and less were considered responsive to drug and were instructed to continue the same treatment. These patients were not considered for further analysis.

The remaining patients with UAS 7 score of 7 and above were given a double dose of bilastine (20 mg twice a day) and fexofenadine (180 mg twice a day).

At visit 3, all evaluations were repeated and patients were asked to report the AEs experience by them during previous 2 weeks. Data were collected using standardized case report forms at baseline; day 14; and day 28.

Study assessment

The primary effectiveness end point was proportion of patients becoming symptom free at weeks 2 and 4. The secondary end points were mean reduction in UAS7 score at week 2 and 3, improvement in quality of life of patients based on CU-Q2oL at weeks 2 and 4, patients' satisfaction with treatment at weeks 2 and 4, and sedation potential of treatment at weeks 2 and 4.

The safety of each treatment regime was analyzed by assessing the proportion of patients showing one or more AE during the study period.

Statistical analysis

Results were presented as mean scores and groups are compared using one-way ANOVA with Tukey HSD test and Fisher's exact test. Data were analyzed using the SPSS software version 2.

RESULTS

A total of 50 patients were randomized to receive either bilastine (n = 25) or fexofenadine (n = 25).

Control of urticaria

After 2 weeks of treatment, 40% (n = 10) of patients in bilastine group while 44% (n = 11) of patients in fexofenadine were having adequate control of urticaria. The difference in response rate was not statistically significant in both the groups (P = 0.54)

15 and 12 patients were non-responder to standard dose of bilastine and fexofenadine, respectively. These patients were updosed to bilastine (20 mg BD) and fexofenadine (180 mg BD) for the next 2 weeks, respectively. At the end of 4 weeks, 15/15 patients in the bilastine group and 12/14 patients in the fexofenadine group achieved adequate control of urticaria . The difference in improvement was not statistically significant (P = 0.5).

Improvement in mean UAS7 score

At baseline, the mean UAS7 score in the bilastine and fexofenadine group was 17.66 ± 3.97 and 18.34 ± 3.94, respectively. Following treatment with either bilastine or fexofenadine for 2 weeks, the mean UAS7 score fell to 7.85 ± 4.50 and 7.80 ± 3.76 in the bilastine group and fexofenadine group, respectively. Similar reduction in mean UAS score was observed at week 4 in both the groups (5.88 ± 4.22 vs. 5.69 ± 1.82). This improvement in UAS7 score from baseline in both the groups was statistically significant ($P < 0.0001$); however, the difference between the treatment groups was not significant ($P = 0.96$)

Bilastine was associated with a significant improvement quality of life of patients compared to fexofenadine. At baseline, the mean CU-Q2oL score in the bilastine and fexofenadine group was 42 ± 6.53 and 48.2 ± 7.82, respectively. At week 2, bilastine was associated with a significant reduction in mean CU-Q2oL score compared to fexofenadine (31 ± 6.1 vs. 43.2 ± 6.05; $P < 0.005$).

Urticaria-associated discomfort during the preceding week was measured using a VAS. In terms of VAS, there was a statistical difference between bilastine and fexofenadine at both visits.It suggests that bilastine is well accepted as a non-sedating antihistamine as compared to other by patients.

A major concern with increasing doses of H1-antihistamines is that of somnolence. Sleepiness with the drug was measured by VAS. On day 14, fexofenadine had a higher sedation score than bilastine. The somnolence score of bilastine and fexofenadine did not increase when their dose was increased . Bilastine was statistically better ($P < 0.05$) than the fexofenadine as a non-sedating antihistamine.

DISCUSSION

More than 50% of patients do not respond adequately to licensed dosage of SGAHs.[5-10] In such patients', various guidelines recommend updosing of SGAHs.[1-4] However, studies directly comparing effectiveness and safety of SGAHs are limited, especially in Indian setup. This study compares the effectiveness and tolerability of bilastine and fexofenadine at a standard dose for 14 days followed by updosing of bilastine and fexofenadine in patients not responding to standard dosage either drugs. This study provides evidence that in patients with difficult to treat CU, increasing the daily dose of two SGAHs, bilastine and fexofenadine, to up to 2 times their conventionally prescribed doses increase the control of urticaria symptoms without compromising patient safety.

In our study, there was a significant improvement in UAS7 score in both the treatment groups with 59.6% and 54.2% of patients achieving adequate control of urticaria in the bilastine and fexofenadine group, respectively, at standard dosage. These results are in accordance with the previous published studies for individual drugs.[13-16,19-22]

In their retrospective analysis, Weller et al. showed that updosing of bilastine was a successful treatment for the majority of patients with CSU.[17] Likewise, Krause et al. came to the same conclusion that updosing of bilastine was linked to greater effectiveness .[18]

In their study, Magen et al. found a substantial effect from increasing the dosage of fexofenadine in CSU patients to 2-3 tablets.[23] Godse et al. found that most patients with urticaria responded to fexofenadine at higher doses .[24]

When compared to fexofenadine in our trial, bilastine was linked to a significant improvement in patients' quality of life as measured by CU-Q2oL. There are no comparison studies to compare how well bilastine and fexofenadine improve quality of life. However, both medications were linked to a rise in patients' quality of life who had urticaria[13,16,26,27]

This suggests that both bilastine and fexofenadine are highly efficacious in the management of urticaria as suggested in the previous studies.

About 54.25% of patients in the bilastine group and 49.05% in the fexofenadine group achieved adequate control of urticaria after doubling the dose of respective drug. This clearly suggests that, in patients with difficult to treat urticaria, updosing of SGAHs is associated with increase in control of urticaria. These results are in accordance with the previous studies.[17,18,23-25]

The discovery that patients did not suffer increased somnolence after increasing their daily dose, as opposed to an anticipated rise in somnolence based on claims that all second-generation H1-antihistamines may cause a mild degree of drowsiness, was perhaps the study's most important finding.

One of the most frequently reported adverse effects of antihistamines is somnolence, which is well documented. Patients using bilastine did not, however, experience increased somnolence when their daily dose was doubled in our trial. Patients in the bilastine group also experienced less somnolence than those on fexofenadine on both visits—days 14 and 28. It might be because of a resistance to somnolence that might arise after taking H1-antihistamines for four days straight.

CONCLUSION

This study provides proof that bilastine, a second-generation non-sedating antihistamine, is more efficacious, well-tolerated, and less sedating than fexofenadine when given in higher doses to CSU patients. Bilastine updosing (raising the daily dose) reduced urticaria symptoms and improved quality of life in most individuals without impairing sleep or safety.

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