Evaluation of Bilastine's Efficacy and Safety in Treating Chronic Idiopathic Urticaria in Iraqi Patients

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Abstract

 Background: Many drugs have been found to be effective in treating chronic urticaria, and many others are under investigation. Second-generation antihistamines are the first-line treatment for this condition, as they block peripheral histamine receptors with minimal drowsiness and anticholinergic effects. Therefore, the aim of the current study was to investigate the short-term efficacy and safety of bilastine in Iraqi patients with chronic idiopathic urticaria.

 Methods: This prospective study was conducted at Dermatology Unit/ AL-Diwaniyah Teaching Hospital/ Iraq during the period from January to June 2023. A total of 100 patients, 50 males and 50 females, were enrolled in this study. All these patients were switched over to Bilastine 20 mg/day for one month. The patients were evaluated using the UAS7 scoring system before and one month after bilastine therapy. Statistical analysis was performed using the Statistical Package for Social Sciences, and a paired t-test was used to compare between means. The level of statistical significance was considered at a *P* value < 0.05.

 Results: The mean UAS7 score before Bilastine treatment was 18.91 ±7.18, which was significantly reduced (*P* < 0.001) to 2.38 ±0.72 after one month of treatment with bilastine. Also, before Bilastine treatments, 19 patients (19%) had mild symptoms, 24 patients (24%) had moderate symptoms, and 57 patients (57%) had severe symptoms. However, after treatment, 51 patients (51%) became symptom-free and 49 patients (49%) had well-controlled urticaria.

 Conclusion: Switching over to bilastine 20mg/day resulted in significant improvement in patients with chronic idiopathic urticaria who had no/ or poor response to conventional antihistamines.

Keywords: Antihistamines, Bilastine, Histamine Receptors, Pharmacology, Urticaria

Introduction

The persistence of symptoms for more than six weeks is one of the characteristics that characterize chronic urticaria (1). The latter is classified into chronic idiopathic urticaria (CIU) and chronic inducible urticaria (CINDU). In the former, adults and children experience pruritic, erythematous, and edematous wheals that last for more than six weeks,

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↑*What is "already known" in this topic:*
Second-generation antihistamines are the first-line treatment for chronic idiopathic urticaria. However, only 38.6% of people did respond. Therefore, it is advised to increase the dosage by a factor of four with consequent increase in incidence of adverse effects.

→*What this article adds:*
Data from current study would support existing evidence for switching over to bilastine that would result in significant improvement in patients with chronic idiopathic urticaria who had no/ or poor response to conventional antihistamines without experiencing the adverse effects resulting from increasing the dose of conventional antihistamines.

sometimes along with angioedema. The idiopathic emergence of this subtype is unknown (2-4). In addition, this complaint is a frequent one in dermatological and allergy practices, as about 0.6%-1% of people have CIU (5, 6). However, it may take two years for the appearance of symptoms following the diagnosis of CIU (7, 8). Moreover, CIU is more prevalent in women and carries a heavy burden that impairs patients' quality of life, interferes with everyday activities, and is frequently associated with psychiatric disorders (9, 10).

Though the pathophysiology of CIU is not fully known, it is thought to be caused by autoimmune mechanisms of mast cell activation and the subsequent production of immune mediators like histamine (11). Based on existing data, 3 subtypes of CIU have been identified, including type I (autoallergic), which is largely mediated by immunoglobulin E (IgE); type IIb (autoimmune), which is primarily mediated by IgG autoantibodies, and chronic idiopathic urticaria with uncertain etiology (12). Despite the fact that the clinical profile of these subtypes is still being fully described, evidence points out that patients with type IIb have higher disease activity (13). The specific etiology of this illness remains unknown. However, autoimmunity, food and drug pseudoallergies, pharmaceutical allergies, insect stings, and bites, as well as acute or persistent infections, are possible causes (14).

Regarding the pharmacological treatment of CIU, many drugs have been found to be effective in treating this condition, and others are now under investigation (15). However, second-generation type-1 histamine-receptor blockers (H$_1$-antihistamines) are the first-line treatment for this condition. Compared to first-generation antihistamines, they specifically block peripheral type-1 histamine receptors producing minimal drowsiness and/or anticholinergic effects, as adverse effects (16). Loratadine, desloratadine, cetirizine, and levocetirizine are a few examples of these drugs. In addition, standard dosages of these drugs might not be beneficial for many individuals (approximately 38.6% of people treated with standard doses of these drugs did respond (17). Therefore, it is advised to increase the dose by a factor of four (18).

Bilastine, a more modern non-sedating antihistamine, has been approved for the treatment of patients with chronic urticaria who are older than 12 years at a daily dose of 20mg (19). Also, a previous study conducted in Japan concluded that bilastine is safe and well-tolerated following a 52-week course of therapy in patients with chronic urticaria (20).

On the other hand, for assessment of disease activity and response to treatment, it is highly recommended to use the Urticaria Activity Score (UAS7), which documents disease activity on a daily basis over several consecutive days (21). This scoring system is validated as well as an easy-to-handle tool that should be filled by patients between visits and can be appraised by the patient and his/her dermatologist.

Despite its approval by the Iraqi Ministry of Health for the treatment of chronic urticaria, few data are available regarding the efficacy and safety of Bilastine in Iraqi patients. In addition, currently, available drugs for the treatment of CIU, such as antihistamines, are associated with a number of adverse effects as well as they require dose adjustment from time to time with resultant dose-dependent health hazards. Therefore, the current study was conducted to evaluate the efficacy and safety of Bilastine in Iraqi patients with chronic idiopathic urticaria. Moreover, we hope that data from the current study will provide evidence that would assist dermatologists and practitioners in selecting a suitable treatment for their patients with CIU.

Methods

This prospective type of study was conducted at Dermatology Unit/ AL-Diwaniyah Teaching Hospital/ Iraq during the period from January to June 2023. A total of 100 patients, 50 males and 50 females, were enrolled in this study. Patients included in the study were those aged ≥ 18 years, complaining of chronic idiopathic urticaria for ≥6 months, and with a history of unsatisfactory response to previous antihistamine therapies. However, those having the disease for less than 6 months were excluded from the study together with pregnant or lactating women. All included patients were on 2 antihistamine agents (maximum allowed doses) for 3 months. Unsatisfactory response was defined as recurrence or persistence of symptoms despite regular use of the above-mentioned treatment approach.

Patients were told to stop previous medications at least 48 hours before starting treatment in order to allow for the full elimination of previous drugs from circulation. All recruited patients were switched over to Bilastine 20 mg/day and continued for one month. After that, the patients were assessed using the UAS7 scoring system (21). The two primary urticaria symptoms, wheals, and pruritus, are rated by the UAS on a scale from 0 (no illness activity) to 3 (severe activity). The sum of the values, which vary from 0 (minimum) to 6 (maximum), indicates the severity of the disease. The five score ranges (bands) to which UAS7 values were assigned denoting urticaria disease activity (21). The UAS7 assessment is based on a seven-day nature and was calculated on 5th week (after a full month of treatment).

The treatment outcome was a reduction in wheal and flare. Also, the potential side effects screened in the current study were sedation, headache, and dryness of mouth because these side effects can affect daily life, especially when high levels of attentiveness are necessary. In addition, such adverse effects may compromise patients' compliance with treatment.

Because we were afraid of the lack of compliance of patients for a long duration, one month duration was chosen as a target for the second time assessment. In addition, the study aimed to evaluate the short-term efficacy and safety of Bilastine. Nonetheless, this approach has been employed by several previous studies.

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (IBM, Chicago, USA, version 26). Continuous variables were presented as mean±SD, while categorical variables were presented as numbers and percentages. Comparisons between means were performed using the paired t-test. The level of significance was considered at $P < 0.05$.

Results

General characteristics of patients with idiopathic urticaria are shown in Table 1. The age range of participants was 19-41 years, and the mean age was 31.07±5.39 years. The duration of disease was in the range of 1-3 years and the mean was 1.03 ±0.92 years. However, sub-group analysis of the association between treatment response and characteristics of enrolled patients (Table 2) revealed a non-significant association with age, sex, or duration of symptoms ($P > 0.05$). In addition, results from the current study revealed that at baseline (before starting Bilastine treatment), the mean UAS7 score was 18.91±7.18 which was significantly reduced one month later to become 2.38 ±0.72 ($P < 0.001$; Table 3 and Figure 1). Also, at baseline, 19% of patients were complaining of mild urticaria, 57 % of them were complaining of moderate urticaria and 24 % were complaining of severe urticaria. Following treatment, 51 % of patients expressed complete remission in response to treatment and 49% of them experienced well-controlled disease activity (Table 3).

Discussion

To the best of our knowledge, this is the first Iraqi study that evaluated the efficacy and safety of bilastine in treating chronic idiopathic urticaria.

In the present study, we evaluated the short-term effects of bilastine in the treatment of Iraqi patients with CIU, and the results revealed that it was effective in controlling the symptoms. However, further research is needed to evaluate the long-term effects of the drug on Iraqi patients.

The current study showed that a hundred patients (equally divided into males and females) with CIU who participated in the current study had an age range of 19-41 years with a mean(SD) age of 31.07(5.39) years as well as the average(SD) duration of having the disease was 1.03(0.92) year (Table 1).

A previous study conducted in India (3) and recruited 49 patients (61.2% males and 38.8% females) with CIU showed that the mean(SD) age of participants was

Table 1. General characteristics of patients with idiopathic urticaria

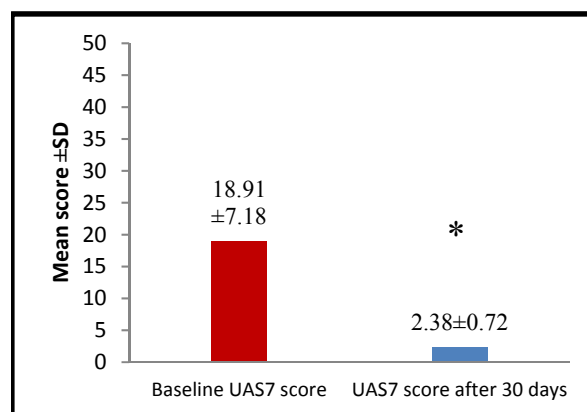| Characteristic	Results
Number of cases	100
Gender	
Male	50 (50.0 %)
Female	50 (50.0 %)
Age (year)	
Range	19-41
Mean ±SD	31.07±5.39
Duration of symptoms (year)	
Range	1-3
Mean ±SD	1.03 ±0.92

SD: standard deviation.

Figure 1. Comparison of mean UAS7 score before and after 30 days of treatment with Bilastine (it is worth mentioning that scores up to 27 are considered moderate).

38.53(14.5) years and the average(SD) duration for having the disease was 10.02(6.78) months. Another study (22) showed that CIU is more prevalent in females than in males. In addition, the study reported that the disease is more prevalent in the 40-59 years age group than in the 10-19 years age group. Moreover, a single-center study in Korea (23) showed that CIU is more prevalent in adults aged 19-59 years, with females being more affected by the disease than males. Further sub-group analysis showed that

Table 2. The association between treatment response and characteristics of enrolled patients

Characteristic	Complete Treatment response (symptom-free) n = 51	Well-controlled urticaria n = 49	P
Sex			
Male	25	25	0.841 C
Female	26	24	
Age (year)			
≤30	20	21	0.711 C
>30	31	28	
Duration of symptoms			
One year	30	31	0.649 C
>1 year	21	18	

C: Chi-squared test.

Table 3. Comparison of the proportion of patients with changes in symptoms before and after Bilastine treatment

Interpretation	At baseline n (%)	One month later n (%)
Complete treatment response (symptom-free)	0 (0.0 %)	51 (51 %)
Well-controlled urticaria	0 (0.0 %)	49 (49 %)
Mild urticaria	19 (19 %)	0 (0.0 %)
Moderate urticaria	24 (24 %)	0 (0.0 %)
Severe urticaria	57 (57 %)	0 (0.0 %)

there was a non-significant association between patients' characteristics and response to treatment ($P > 0.05$; Table 2). Nonetheless, findings from other studies (24-27) also supported these findings.

The higher incidence of CIU among adults than children, reported by current and previous studies, could be attributed to the higher prevalence of autoimmune diseases and other triggering co-morbidities in adults than in children, as it was assumed that this is a common immune-mediated pathway for CIU and those diseases (25, 28). Moreover, the higher prevalence of CIU in females than in males could be attributed to the effects of sex hormones and autoimmunity, as there is a significant association between CIU with a number of autoimmune diseases such as type I diabetes mellitus, systemic lupus erythematosus, rheumatoid arthritis and thyroid dysfunction (29, 25). Moreover, the lack of an association between patients' characteristics and their response to bilastine in the current study could be attributed to the fact that neither the pharmacokinetics nor the pharmacodynamics of bilastine are affected by the gender or age of patients as well as not by the duration of disease (27).

In terms of efficacy of Bilastine in treatment of CIU, data from current study revealed that following 30 days of treatment with 20mg/day of Bilastine, there was a noticeable improvement in urticaria symptoms (measured using the UAS7 score; Figure 1 and Table 2) as 51 patients (out of 100; 51%) reported complete disappearance of symptoms while 49 patients (49%) were quite comfortable and felt that the symptoms are well-controlled with the treatment.

Moreover, the efficacy of Bilastine in the treatment of urticaria is frequently reported by previous studies. For example, two studies conducted in Japan reported significantly rapid as well as prolonged effects of Bilastine on weal and flare indicators of urticaria (30, 31). Another study revealed that treatment for 2 weeks with oral Bilastine (20mg/day) resulted in significant improvement in urticaria symptoms (evaluated using UAS7 score) as well as the quality of life in comparison with placebo (32).

The efficacy of bilastine in the treatment of urticaria, reported in current as well as previous studies, could be explained by its pharmacokinetics and pharmacodynamics as it has a rapid onset of action and considerable bioavailability following oral administration, it's anti-allergic as well as anti-inflammatory properties (3, 33-35).

On the other hand, none of the patients who participated in the current study discontinued the study because of serious adverse effect(s) of the treatment, lack of efficacy, and/or deterioration of symptoms. These findings clearly indicated the safety, efficacy as well as tolerability of Bilastine therapy.

A previous study conducted in India (36) showed that following 4 weeks of treatment, the improvement in CIU symptoms (evaluated by using the UAS7 score) in the Bilastine-treated patients was significantly better than in the groups treated with levocetirizine, fexofenadine or hydroxyzine. Also, treatment with Bilastine was associated with significantly lower levels of unwanted effects, such as somnolence, than levocetirizine, fexofenadine and hydroxyzine. Moreover, Godse and colleagues (3) concluded

that Bilastine is a highly endorsed treatment for CIU that is superior to other histamine-receptor antagonists, as it is more tolerable, safer, and has a rapid onset yet longer duration of action.

The reported tolerability and safety of bilastine in current as well as in previous studies could be attributed to the pharmacological profile of bilastine (3, 33-35). The latter is known as a highly selective histamine-receptor type 1 antagonist and has no, or very weak, affinity for other types of receptors on which other antihistamines may act, such as receptors for 5-hydroxytryptamine, bradykinin, acetylcholine, catecholamines as well as other types of histamine receptors. In addition, Bilastine has limited accessibility for cerebral histamine receptors as the P-glycoprotein-mediated outflow of Bilastine, its poor lipophilicity as well as its high molecular weight limit its ability to cross the blood-brain barrier (BBB), it will not adversely affect psychomotor performance of individuals treated with this medication. Moreover, bilastine is neither being metabolized nor interacting with hepatic drug-metabolizing enzymes so that it will not affect hepatic function and/ or the pharmacology of other drugs, especially those with narrow therapeutic indexes such as benzodiazepines. Furthermore, bilastine does not affect cardiac function (3, 33-35).

Limitations of the current study include: single-center study and short-term follow-up because of difficulties in following up with patients for longer durations because of their poor. Also, although the study is a single-center study, the selection of patients for the study was performed by a specialist dermatologist at a dermatology center in a teaching hospital. Another limitation of the current study was the lack of a control group or comparison to a standard treatment. Therefore, future studies would be conducted to compare the efficacy and safety of more than one treatment for CIU with long-term follow-up of patients at different centers.

Conclusion

In chronic idiopathic urticaria patients who had non-satisfactory responses to commonly available antihistamines, switching over to bilastine resulted in significant improvement of their symptoms.

Authors' Contributions

Study concept and design: F. S., and M.J.; Acquisition of data: F.S., analysis and interpretation of data: F. S., and M. J.; Drafting of the manuscript: F. S., and M.J.; critical revision of the manuscript for important intellectual content: M.J.; statistical analysis: M.J.; administrative, technical, and material support: F. S., M. J.; Study supervision: F. S.

Ethical Considerations

All enrolled subjects provided consent, and the study was approved by the Research Ethics Committee at the College of Medicine/ University of AL-Qadisiyah, AL-Diwaniyah Province (Code No. 4540 on 18-12-2022).

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Conflict of Interests

The authors declare that they have no competing interests.

References

1. Ghazanfar MN, Kibsgaard L, Thomsen SF, Vestergaard C. Risk of comorbidities in patients diagnosed with chronic urticaria: A nationwide registry-study. World Allergy Organ J. 2020;13(1).
2. Song WJ, Choi M, Lee DH, Kwon JW, Kim GW, Kim MH, et al. The KAAACI/KDA Evidence-Based Practice Guidelines for Chronic Spontaneous Urticaria in Korean Adults and Children: Part 1. Definition, Methodology and First-line Management. Allergy Asthma Immunol Res. 2020;12(4):563-578.
3. De A, Godse K, Dhoot D, Sarda A. Real-Life Experience of Efficacy and Safety of Bilastine in the Refractory Cases of Chronic Spontaneous Urticaria and its Effect on the Quality of Life of Patients. Indian J Dermatol. 2021;66(2):159-164.
4. Sánchez-Borges M, Ansotegui IJ, Baiardini I, Bernstein J, Canonica GW, Ebisawa M, et al. The challenges of chronic urticaria part 1: Epidemiology, immunopathogenesis, comorbidities, quality of life, and management. World Allergy Organ J. 2021;14(6):100533.
5. Zuberbier T, Abdul Latiff AH, Abuzakouk M, Aquilina S, Asero R, Baker D, et al. The international EAACI/GA2LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2022; 77:734–766.
6. Katelaris CH, Lima H, Marsland A, Weller K, Shah A, Waserman S. How to measure disease activity, impact, and control in patients with recurrent wheals, angioedema, or both. J Allergy Clin Immunol Pract. 2021;9:2151–2157.
7. Maurer M, Abuzakouk M, Bérard F, Canonica W, Oude Elberink H, Giménez-Arnau A, et al. The burden of chronic spontaneous urticaria is substantial: real-world evidence from ASSURE-CSU. Allergy. 2017;72:2005–2016.
8. Metz M, Altrichter S, Buttgereit T, Fluhr JW, Fok JS, Hawro T, et al. The diagnostic workup in chronic spontaneous urticaria - what to test and why. J Allergy Clin Immunol Pract. 2021;9:2274–2283.
9. Kolkhir P, Altrichter S, Asero R, Daschner A, Ferrer M, Giménez-Arnau A, et al. Autoimmune diseases are linked to type IIb autoimmune chronic spontaneous urticaria. Allergy Asthma Immunol Res. 2021;13:545–559.
10. Schoepke N, Asero R, Ellrich A, Ferrer M, Gimenez-Arnau A, Grattan CEH, et al. Biomarkers and clinical characteristics of autoimmune chronic spontaneous urticaria: results of the PURIST study. Allergy. 2019;74:2427–2436.
11. Maheshwari A, Garg T, Chander R, Debnath E. Chronic Spontaneous Urticaria: An Etiopathogenic Study. Indian J Dermatol. 2022;67(1):92.
12. Zuberbier T, Bernstein JA, Maurer M. Chronic spontaneous urticaria guidelines: what is new? J Allergy Clin Immunol. 2022;150(6):1249–1255.
13. He L, Yi W, Huang X, Long H, Lu Q. Chronic urticaria: advances in understanding of the disease and clinical management. Clin Rev Allergy Immunol. 2021;1–25.
14. Guillen-Aguinaga S, Jáuregui Presa I, Aguinaga-Ontoso E, Guillen-Grima F, Ferrer M. Updosing nonsedating antihistamines in patients with chronic spontaneous urticaria: a systematic review and meta-analysis. Br J Dermatol. 2016;175(6):1153–1165.
15. Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, et al. The EAACI/GA (2) LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: The 2013 revision and update. Allergy. 2014; 69:868–87.
16. Yagami A, Furue M, Togawa M, Saito A, Hide M. One-year safety and efficacy study of bilastine treatment in Japanese patients with chronic spontaneous urticaria or pruritus associated with skin diseases. J Dermatol. 2017; 44:375–85.
17. Hide M, Yagami A, Togawa M, Saito A, Furue M. Efficacy and safety of bilastine in Japanese patients with chronic spontaneous urticaria: A multicenter, randomized, double blind, placebo-controlled, parallel-group phase II/III study. Allergol Int. 2017; 66:317–25.
18. Weller K, Zuberbier T and Maurer M. Chronic urticaria: tools to aid the diagnosis and assessment of disease status in daily practice. J Eur Acad Dermatol Venereol. 2015;29:38-44.
19. Yagami A, Furue M, Togawa M, Saito A, Hide M. One-year safety and efficacy study of bilastine treatment in Japanese patients with chronic spontaneous urticaria or pruritus associated with skin diseases. J Dermatol. 2017;44:375–85.
20. Hide M, Yagami A, Togawa M, Saito A, Furue M. Efficacy and safety of bilastine in Japanese patients with chronic spontaneous urticaria: A multicenter, randomized, double blind, placebo-controlled, parallel-group phase II/III study. Allergol Int. 2017;66:317–25.
21. Weller, K., Zuberbier, T. and Maurer, M. Chronic urticaria: tools to aid the diagnosis and assessment of disease status in daily practice. J Eur Acad Dermatol Venereol 2015;29:38-44.
22. Seo JH, Kwon JW. Epidemiology of urticaria including physical urticaria and angioedema in Korea. Korean J Intern Med. 2019 Mar;34(2):418-425.
23. Jo YH, Yoo HW, Kim SH, Kim YM, Kim HY. Clinical characteristics and treatment response of chronic spontaneous urticaria according to age: A single-center Korean study. Asian Pac J Allergy Immunol. 2022 Dec;40(4):374-378.
24. Wertenteil S, Strunk A, Garg A. Prevalence estimates for chronic urticaria in the United States: A sex- and age-adjusted population analysis. J Am Acad Dermatol. 2019 Jul;81(1):152-156.
25. Barzilai A, Baum A, Ben-Shoshan M, Tzanani I, Hakroush R, Coster D, et al. Epidemiological and Clinical Characteristics of Adult and Pediatric Patients with Chronic Spontaneous Urticaria. Journal of Clinical Medicine. 2023;12(23):7482.
26. Thomsen SF, Pritzier EC, Anderson CD. Chronic urticaria in the real-life clinical practice setting in Sweden, Norway and Denmark: baseline results from the non-interventional multicentre AWARE study. J Eur Acad Dermatol Venereol. 2017;31:1048–1055.
27. Church MK, Tiongco-Recto M, Ridolo E & Novák Z. Bilastine: a lifetime companion for the treatment of allergies. Current Medical Research and Opinion. 2019;36(3):445–454.
28. Najafipour M, Zareizadeh M, Najafipour F. Relationship between Chronic urticaria and autoimmune thyroid disease. J Adv Pharm Technol Res. 2018;9:158–161.
29. Kim YS, Park SH, Han K, Lee JH, Kim NI, Roh JY, et al. Clinical course of chronic spontaneous urticaria in the Korean adult population. Allergy Asthma Immunol Res. 2018;10(1):83-7.
30. Togawa M, Yamava H, Rodriguez M, Nagashima H. Pharmacokinetics, pharmacodynamics and population pharmacokinetic/pharmacodynamic modelling of bilastine, a second-generation antihistamine, in healthy Japanese subjects. Clin Drug Investig. 2016;36:1011–1032.
31. Yagami A, Furue M, Togawa M, Saito A, Hide M. One-year safety and efficacy study of bilastine treatment in Japanese patients with chronic spontaneous urticaria or pruritus associated with skin diseases. J Dermatol. 2017;44:375–85.
32. Togawa YA, Saito M, Furue AM. Efficacy and safety of bilastine in Japanese patients with chronic spontaneous urticaria: A multicenter, randomized, double-blind, placebo-controlled, parallel-group phase II/III study. Allergol Int. 2017;66:317–342.
33. Scaglione F. Safety profile of bilastine: 2nd generation H1-antihistamines. Eur Rev Med Pharmacol Sci. 2012 Dec;16(14):1999-2005. PMID: 23242729.
34. Podder I, Dhabal A, Chakraborty SS. Efficacy and Safety of Up-dosed Second-generation Antihistamines in Uncontrolled Chronic Spontaneous Urticaria: A Review. J Clin Aesthet Dermatol. 2023 Mar;16(3):44-50.
35. Wai C, Ch'ng A, Chung C, Gabriel G, Godse M, Mitthamsiri K, et al. Experience with bilastine in the management of urticaria: Original Real-world cases of Bilastine In Treatment (ORBIT) in Asia. Drugs in Context. 2022; 11: 1-11. 10.7573/dic.2021-12-2.
36. Shah B, Dhoot D, Choudhary A, Jangid N, Mistry D, Shah S, et al. A Comparative, Three-Arm, Randomized Clinical Trial to Evaluate the Effectiveness and Tolerability of Bilastine vs Fexofenadine vs Levocetirizine at the Standard Dose and Bilastine vs Fexofenadine at Higher Than the Standard Dose (Up-Dosing) vs Levocetirizine and Hydroxyzine (in Combination) in Patients with Chronic Spontaneous Urticaria. Clin Cosmet Investig Dermatol. 2022;15:261-270.