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Efficacy of Bilastine in the Management of Urticaria- A Retrospective Study

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Abstract

Background: Urticaria or hives is a common skin condition with a lifetime prevalence of 7.8–22.3%, a point prevalence of 0.5- 1.0%. This study focuses to determine the efficacy of bilastine in combination with other antihistamines or corticosteroids in the treatment and symptomatic relief from Urticaria in Indian patients.

Objective: A retrospective study to evaluate the efficacy of bilastine in the management of Urticaria in an Indian population.

Methods: A retrospective study was carried out on 99 patients (7 children and 92 adults) with urticaria. Bilastine, 20 mg once daily, was given in patients with other antihistamines such as levocetirizine, fexofenadine, and corticosteroids. The treatment outcome was assessed as recovered, unchanged, worsened, change in therapy, or lost to follow-up.

Results: Bilastine was prescribed at 20 mg dose orally either once daily (91 patients) or twice daily (2 patients). About six patients were given bilastine in syrup formulation at a dose of 5 mL (2.5 mg/mL), OD. Out of the 99 patients, most (77/99- 77.78%) reported recovery during the follow-up visit. Seven patients were still on treatment, six patients still had rashes on exposure to the sun, one patient had rashes while swimming, three patients had no recovery, and four were lost to follow-up.

Conclusion: Bilastine (20 mg OD), a new generation non-sedating H1-antihistamine, was highly effective in treating urticaria when given in combination with other second-generation antihistamines.

Introduction

Urticaria or hives is a common skin condition with a lifetime prevalence of 7.8–22.3%, a point prevalence of 0.5-1.0%. It is characterized by the appearance of wheals or pruritis for more than six weeks[1,2]. Sometimes also associated with sudden, pronounced swelling of the lower dermis and subcutis (angioedema) or pain. Urticaria is further subdivided into three different classes. The episodic nature (acute or chronic) or inducible- when included by specific triggers such as temperature, pressure, or cholinergic stimulation[3]. Chronic Urticaria (CU) is the most common formof Urticaria (66 to 93%) of all urticaria cases, followed by physical Urticaria (4 to 33%) and 1-7% of cholinergic Urticaria[2]. On the other hand, acute Urticaria is more prevalent in young ages, induced mainly by Type I hypersensitivity allergic reactions to food, medications, insect sting, viral infections, or transfusion[3]. The pathogenesis of chronic spontaneous Urticaria is still uncertain, although affecting about 15-20% of people once in their lifetime. It is thought to be mediated by an aberrant release of histamines and other inflammatory mediators from mast cells or basophils[4]. However, the exact pathogenesis of Urticaria remains uncertain. The histamine and other mediators, released from activated skin mast cells, bind to H_1 receptors on endothelial cells and sensory neurons. It induces sensory nerve activation, vasodilation, plasma extravasation, and cell recruitment to the urticarial lesion[5,6]. The primary aim of a dermatologist is to provide symptomatic relief from Urticaria by antagonizing the H_1-receptor-mediated actions on wheal (epithelial cells) or pruritus (sensory nerves). The first-generation and second-generation antihistamines (bepotastine, cetirizine, fexofenadine, and olopataltine) have successfully provided relief from urticaria symptoms and are less sedative in nature. Bilastine, (Molecular formula: $C_{28}H_{37}N_3O_3$, 2-[4-[2-[4-[1-(2-ethoxyethyl) benzimidazol-2-yl] piperidin-1-yl] ethyl] phenyl]-2-methylpropionic acid), is a second-generation antihistamine withgreater affinity for H_1-receptors[7]. An in-vitro study using a guinea pig model demonstrated that bilastine had a higher and superior affinity to H_1-receptor than cetirizine by three-folds and fexofenadine by five folds[8]. Bilastine is an orally administered, second-generation antihistamine used in the symptomatic treatment of seasonal or perennial allergic rhino-conjunctivitis and urticaria[9]. In the present two-centric study, we aim to determine the efficacy of bilastine in combination with other antihistamines or corticosteroids in the treatment and symptomatic relief from Urticaria in Indian patients.

Materials and Methods

Patient selection

A total of ninety-nine (n=99) patients (children and adults) with Urticaria with different disease duration were included in the study. The study was conducted at the Dermatology outpatient clinic, Pune, India. At the baseline, patient details such as age, weight, chief complaints, duration of complaints, family history, comorbid conditions (T2M, hypertension, thyroid), history of allergy were procured from the case records.

Treatment details

Bilastine, 20 mg once daily, was given in patients combined with other antihistamines such as levocetirizine- 5 mg OD, fexofenadine-180 mg OD, and corticosteroids (mometasone, calamine, Inj. dexamethasone). The treatment outcome was assessed as recovered, unchanged, worsened, change in therapy, or lost to follow-up.

Statistical analysis

Statistical analysis was done using R studio 2021.09.0 and Microsoft excel 2016. Continuous variables were represented as mean ± standard deviation. For categorical variables, numbers and percentages were used.

Results

Basic details of patients with urticaria

A total of 99 patients, 52 (52.53%) males and 47 (47.47%) females, received bilastine antihistamine therapy for Urticaria at the study centers. Of these, seven patients were children (mean age- 10.14 ± 3.24 years), and 92 were adults (mean age- 36.62 ± 13.57 years).

Table 1: Baseline characteristics of patients with urticaria

Parameters		N=99
Subject Categories		
Children	N (%)	7 (7.07%)
	Mean ± SD (years)	10.14 ± 3.24
Adult	N (%)	92 (92.93%)
	Mean ± SD (years)	36.62 ± 13.57
Overall	N (%)	99 (100.00%)
	Mean ± SD (years)	34.75 ± 14.77
Gender, n (%)		
Female		52 (52.53%)
Male		47 (47.47%)
Height (cm)		
Mean ± SD		60.15 ± 12.4
Duration of Complaints (Months)		
Mean ± SD		5.61 ± 12.10
Treatment History, n (%)		
Antihistamines		32 (32.32%)
Corticosteroids		4 (4.04%)
Antihistamines + Corticosteroids		1 (1.01%)
Family History of Auto Immune Disease, n (%)		
Mother Diabetes		5 (5.05%)
Hair Dye Allergy		1 (1.01%)
Mother Vitiligo		1 (1.01%)
Diagnosis Refined		
Spontaneous Urticaria		75 (75.76%)
Other Urticaria		13 (13.13%)
Physical Urticaria		11 (11.11%)

The mean reported duration of complaints was 5.61± 12.10 months. About 32 patients reported previous treatment with antihistamines. Only seven patients had a family history of allergy or urticaria, which is not significant to the present study. Based on the duration and the induction agents, urticaria patients were subcategorized into three groups: i) spontaneous urticaria (acute and chronic)- 75.76% (75/99) patients, ii) physical urticaria- 11.11% (11/99) patients, and iii) other urticaria (13.13% (13/99) patients.

Table 2 represents the various lifestyle and comorbidities details of urticaria patients. The most-reported lifestyle factors were obesity, diabetes, smoking, drinking, and thyroid.

Table 2: Lifestyle risk factors and comorbidities

Lifestyle Risk factors	N=99 (%)
Diabetes	24 (24.24)
Thyroid	19 (19.19)
Obesity	19 (19.19)
Alcohol intake	23 (23.23)
Smoking	16 (16.16)
Hypothyroidism Diabetes Vitiligo	5 (5.05)
Asthma	2 (2.02)
Psoriasis	1 (1.01)
Renal Failure and Hypertension	1 (1.01)

Chief complaints

The majority of the patients reported rashes with itching 35/99 (35.35%), followed by rashes 21/99 (21.21%) and wheals and itching 17/99 (17.17%). A small subgroup of patients also reported rashes with swelling or wheals with pain. The results are as shown in table 3.

Table 3: Chief complaints in patients with urticaria

Chief Complaints	N=99 (%)
Complaints	
Rashes	21 (21.21)
Itching	1 (1.01)
Wheals	10 (10.1)
Swelling	3 (3.03)
Rashes + Itching	35 (35.35)
Wheals + Itching	17 (17.17)
Rashes + Swelling	4 (4.04)
Wheals + Swelling	4 (4.04)
Rashes with pain	2 (2.02)
Wheals + Fever	2 (2.02)

Treatment details

Bilastine was prescribed at 20mg dose orally either once daily (91 patients) or twice daily (2 patients). In addition, about six patients were given bilastine in syrup formulation at a dose of 5 mL (2.5 mg/mL). The treatment details are provided in table 4. The drug used in combination is as listed in table 5.

Table 4: Bilastine treatment details

Duration for BILASTINE prescription (Days)	Bilastine Doses		
	OD(20 mg, Oral)	BD (20 mg, Oral)	OD(5mL, Syrup)
N=99 (%)	91 (91.92%)	2 (2.02%)	6 (6.06%)
Mean ± SD	28.08 ± 19.29	60 ± 42.43	30.00 ± 0.00
Range(Days)	10 - 90	30 - 90	30

Table 5: Bilastine with other drugs

Parameters	N=99 (%)
Antibiotics	12 (12.12)
Corticosteroids	6 (6.06)
Antihistamines	34 (31.31)
Antihistamine and Anti - Helminthics	13 (13.13)
Antihistamines, and anti - inflammatory	3 (3.03)
Antihistamines and Local Anaesthesia	3 (3.03)
Others	10 (10.1)

Treatment outcomes

The treatment outcomes were captured as recovered, unchanged, worsened, change in therapy, or lost to follow-up. Out of the 99 patients, most 77/99 (77.78%) reported recovery during the follow-up visit. However, seven patients were still on treatment, 6/99 (6.06%) patients still had rashes on exposure to the sun, 1/99 (1.01%) patient had rashes while swimming and 4/99 (4.04%) patients were lost to follow-up (Table 6).

Table 6: Treatment outcomes

Recovery Distribution	N (%)
Recovered	77 (77.78)
Still on treatment	7 (7.07)
Still gets rash on sun exposure	6 (6.06)
Still gets rashes while swimming	1 (1.01)
Gets repeated episodes	4 (4.04)
Lost to follow-up	4 (4.04)

Discussion

Urticaria is the most common skin disease characterized by pruritis or wheal with or without angioedema for less than a day. Mast-cell-derived histamines mainly trigger urticaria; hence second-generation H_1-antihistamines play a critical role in treatment. However, most antihistamines have better efficacy but are sedative when given at the prescribed concentration[10]. Therefore, the need for a more efficient second-generation antihistamine with better efficacy, rapid onset of relief, longer duration of action, and a non-sedating nature was considered.

Bilastine, a substrate of the P-glycoprotein efflux transporter, preventing its penetration to the blood-brain barrier, provides high efficacy even at the baseline dose of 20 mg once daily[10,11]. In the present study, Bilastine at a baseline dose of 20 mg, once daily, effectively treated urticaria, with about 77.75% of patients recovering from the initial symptoms. The drug was well tolerated, with none of the patients opting for a change in therapy. Our study results are in accordance with a Japanese open-label, multicentric phase-III conducted on 198 CSU or pruritis patients to evaluate the efficacy and safety of bilastine in a 52-week treatment period.

The study reports that in long-term treatment (52-weeks), bilastine improved the initial condition of the patients and is equally well-tolerated and safe in the Japanese population[12]. In another multicentric, open-label, exploratory study conducted on 115 CSU patients treated with bilastine 20 mg OD for 8-weeks, there was a reduction in the pruritis severity score at the end of the treatment period with improved quality of life[13]. Similar outcomes were obtained in another multicentric, randomized, double-blinded, placebo-controlled phase II/III study conducted on 304 CSU patients (101 patients- 20 mg bilastine; 100 patients- 10 mg bilastine; 103 patients- placebo).

The total symptom score (TSS) was significantly reduced in the 20 mg bilastine group than the placebo in two weeks, with relief in TSS from day 1 of treatment[14]. In clinical trials, bilastine 20 mg OD dose has been demonstrated to be equally effective as Levocetirizine 5mg in controlling pruritis and wheals in urticaria[15]. In the present study, bilastine at 20 mg was effective in terms of recovery from the symptoms.

However, a TSS score, pruritis severity score would have given a better understanding of the treatment efficacy. Further, a larger sample and longer follow-up duration with a comparator arm (or placebo) will help understand the efficacy and tolerability of the drug.

Conclusion

Bilastine is a new generation non-sedating H_1-antihistamine which is highly effective in treatment of urticaria when combined with other second-generation antihistamines, and corticosteroids.

Ethical Approval: N/A

Conflict of Interest: Nil

Financial Disclosure: None

References

1. Gaig P, Olona M, Muñoz Lejarazu D, Caballero MT, Domínguez FJ, Echechipia S, et al. Epidemiology of urticaria in Spain. *J Investig Allergol Clin Imm*unol 2004;14:214-20.
2. Hellgren L. The prevalence of Urticaria in the total population. Acta Allergol 1972;27:236-40.
3. Godse K, De A, Zawar V, Shah B, Girdhar M, Rajagopalan M, et al. Consensus statement for the diagnosis and treatment of Urticaria: A 2017 update. *Indian J Dermatol* 2018;63:2-15.
4. Zuberbier T, Asero R, Bindslev-Jensen C, Walter Canonica G, Church MK, Giménez-Arnau A, et al. EAACI/GA(2)LEN/EDF/ WAO guideline: Definition, classification and diagnosis of urticaria. *Allergy* 2009;64:1417-26.
5. Fukunaga A, Oda Y, Washio K. Efficacy of switching to bilastine, a histamine H1 receptor antagonist, in patients with chronic spontaneous Urticaria (H1-SWITCH): study protocol for a randomized controlled trial. *Trials*. 2020;21(1):23.
6. Saini SS, Kaplan AP. Chronic Spontaneous Urticaria: The Devil's Itch. *J Allergy Clin Immunol Pract*. 2018;6:1097-1106.
7. Jáuregui I, Ferrer M, Bartra J, et al. Bilastine for the treatment of urticaria. *Expert Opin Pharmacother*. 2013;14:1537-44.
8. Corcóstegui R, Labeaga L, Innerarity A et al. Preclinical pharmacology of bilastine, a new selective histamine H1 receptor antagonist. Receptor selectivity and in vitro antihistaminic activity. Drugs RD 2005;6:371-84.
9. Wang XY, Lim-Jurado M, Prepageran N, Tantilipikorn P, Wang de Y. Treatment of allergic rhinitis and Urticaria: a review of the newest antihistamine drug bilastine. *Ther Clin Risk Manag*. 2016;12:585-97.

10. Church MK, Labeaga L. Bilastine: a new H1-antihistamine with an optimal profile for updosing in Urticaria. *J Eur Acad Dermatol Venereol*. 2017;31:1447-52.
11. Leceta A, Sologuren A, Valiente R, Campo C, Labeaga L. Bilastine in allergic rhinoconjunctivitis and Urticaria: a practical approach to treatment decisions based on queries received by the medical information department. *Drugs Context*. 2017;6:212500.
12. Yagami A, Furue M, Togawa M, Saito A, Hide M. One-year safety and efficacy study of bilastine treatmentin Japanese patients with chronic spontaneous Urticaria or pruritus associated with skin diseases. *J Dermatol*.2017;44:375-85.
13. Serra E, Campo C, Novák Z. Efficacy and safety of bilastine in reducing pruritus in patients with chronic spontaneous Urticaria and other skin diseases: an exploratory study. *J Dermatolog Treat* 2020;31:270-8.
14. Hide M, Yagami A, Togawa M, Saito A, Furue M. Efficacy and safety of bilastine in Japanese patients withchronic spontaneous Urticaria: A multicenter, randomized, double-blind, placebo-controlled, parallel-groupphase II/III study. *Allergol Int* 2017;66:317-25.
15. Product Monograph Including Patient Medication Information. Blexten®. Available from: https://www.aralez.com/wp-content/ uploads/2016/12/BLEXTEN-Product-Monography-English.pdf.