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EFFECTIVENESS AND SAFETY OF TWO DRUG DOSAGE FOR TREATING PATIENTS WITH CHRONIC SPONTANEOUS URTICARIA

Dr. Ramesh Ranganadhula

Assistant Professor, Department of Dermatology, Venerology and Leprosy, Chalmeda Ananda Rao Institute of Medical Sciences, Karimnagar, Telangana

Email id: ranganadhularamesh@gmail.com

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ABSTRACT

Background: The most often diagnosed dermatological disorder reported to doctors is chronic spontaneous urticaria (CSU). Second-generation antihistamines have been shown to be useful in treating the CSU. According to the recommendations, concurrent use of antihistamines is not suggested due to the absence of synergistic effects. Due to the issues presented by CSU, it is critical to investigate appropriate management strategies.

Aim: The current study sought to evaluate the effectiveness and safety of a combination of 5mg levocetirizine and 20mg bilastine to 40mg bilastine up dosage for treating participants with chronic spontaneous urticaria.

Methods: The current study evaluated 124 patients divided into two groups of 62 subjects each. Group I subjects were given a tablet of Bilastine in a dose of 20 mg bd, and Group II subjects were given a combination tablet of Bilastine in a dose of 20 mg and Tablet Levocetirizine in a dose of 5 mg. Urticarial activity score 7 was utilized at both the baseline and follow-up visits after two and six weeks.

Results: The study's findings revealed that both groups had a larger proportion of males aged 20 to 30 years. Angioedema was seen in 15.6% and 23.3% of individuals in Groups I and II, respectively. After 6 weeks, both groups demonstrated substantial improvement in UAS 7 scores ($p<0.05$). In Group I, UAS 7 scores decreased significantly from 19.4% to 0.03% with few adverse effects.

Conclusion: The current study concludes that up-dosing of bilastine is a well-tolerated, safe, and efficient method in comparison to the combined dose of 20 mg Bilastine and 5mg Levocetirizine, demonstrating that up-dosing of Bilastine can be a valuable and efficient addition to the current arsenal of medication with minimal to no side effects.

Keywords: Bilastine, chronic spontaneous urticaria, levocetirizine, up-dosing, UAS-7 scores

INTRODUCTION

Urticaria is characterized by short-lived, recurring, itchy skin wheals that are associated with or without angioedema and last for more than 6 weeks. CSU is a serious healthcare problem that affects 20% of the population and is one of the most often diagnosed dermatological skin disorders in Indian dermatology departments.1

CSU, or chronic spontaneous urticaria, has a global prevalence of 0.5% to 1% in various global populations, which can cause impairment and negatively impact the quality of life (QoL) of afflicted individuals. Modern non-sedating H1 antihistamines are the primary line of treatment being evaluated for persistent spontaneous urticaria.2

The EAACI/GA2LEN/EDF/WAO urticaria recommendations propose increasing histamine doses rather than using combination medications since they have the same mechanism of action and provide no additional benefit. However, antihistamine prescriptions deviate significantly from standards, with combinations of antihistamines being the most typically prescribed medicines. Existing literature data show a substantial variance in antihistamine prescription trends across primary care doctors and dermatologists in terms of antihistamine combination, up-dosing, and antihistamine preference.3

Existing literature evidence on the efficacy and safety of various antihistamine combinations is limited, and further research is required to demonstrate that up-dosing individual antihistamines is safer and more effective than combinations of newly found antihistamines. 4 The current study aims to assess the efficacy and safety of a combination of 5mg levocetirizine and 20mg to 40mg bilastine up dose for the treatment of chronic spontaneous urticaria.

MATERIALS & METHODS

The current prospective randomized comparative clinical trial was designed to evaluate the effectiveness and safety of a combination of 5mg levocetirizine and 20mg bilastine to 40mg bilastine up dosage for the treatment of chronic spontaneous urticaria. The research subjects were from the Institute's Department of Dermatology. All individuals provided verbal and written informed permission before participating in the study.

The research comprised patients aged 18 to 70 years who had a verified diagnosis of CSU and were treated with 20 mg Bilastine for two days but still developed new lesions. The exclusion criteria for the study were subjects on systemic steroids, H1, and H2 anti-histamines except immunosuppressants/Bilastine within 4 weeks, topical corticosteroids, lactating and pregnant females, Hodgkin's disease, systemic autoimmune disorders, atopic dermatitis, collagen vascular disease, drug/food allergy, and/or hereditary angioedema.

After the final inclusion of the study subjects, detailed history was recorded for all the subjects including demographic data, associated medical disorders, and duration and onset of wheals. A detailed dermatological examination was then done along with routine investigations such as ECG (electrocardiography), TSH (thyroid stimulating hormone), renal function test, liver function test, and complete blood count.

UAS 7 (urticaria activity score 7)[5] was also recorded in all the subjects which is a validated and simple scoring system depending on the once-daily assessment of wheals and pruritus over 7 days which is then summarized with UAS 7 scores in the range of 0 (itch and hive-free) to 42 (maximum symptoms). The illness severity was classified as: ≤6, well managed; 7-15, mild; 16-27, moderate; and 28-42, severe.

All individuals were given a 20 mg Bilastine pill and instructed to record their symptoms before returning for a two-week follow-up. Subjects who were still symptomatic with a daily UAS >3 were evaluated in Group I for up-dosing with Tablet Bilastine (20 mg morning dosage) and 5mg levocetirizine at night. Both groups were examined every two and six weeks. The disease severity was assessed using UAS 7, and drug-related adverse events such as urine retention, constipation, and mouth dryness were documented at baseline and at all follow-up visits of 2, 4, and 6 weeks.

The collected data were statistically evaluated using SPSS. (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk. NY, USA) for assessment of descriptive measures, Student t-test, ANOVA (analysis of variance), and Chi-square test. The results were expressed as mean and standard deviation and frequency and percentages. The p-value of <0.05 was considered statistically significant.

RESULTS

The current study evaluated 124 subjects divided into two groups of 62 subjects each. Group I subjects were given a tablet of Bilastine in a dose of 20 mg bd, and Group II subjects were given a combined tablet of Bilastine in a dose of 20 mg and Tablet Levocetirizine in a dose of 5 mg. The study had 53.2% (n=66) males, with 53.1% (n=34) in Group I and 53.3% (n=32) in Group II, and 46.8% (n=58) females, with 46.9% (n=30) in Group I and 46.7% (n=28) in Group II, which was non-significant with p=1.00. The age difference between two groups at <20, 21-30, 31-40, 41-50, 51-60, and >60 years was not statistically significant (p=0.08) (Table 1).

Type II diabetes was found in 9.4% (n=6) of Group I individuals and 13.3% (n=8) of Group II subjects, for a total of 11.3% (n=14) patients. Hypothyroidism was detected in 4.8% (n=6) of the research patients, with 6.3% (n=4) and 3.3% (n=2) in Groups I and II, respectively. Hypertension was seen in 14.5% (n=18) of the participants, with 9.4% (n=6) and 20% (n=12) in Groups I and II, respectively. There was no comorbidity in 69.4% (n=86) of the participants, including 75% (n=48) from Group

I and 63.3% (n=38) from Group II. The difference in comorbidities between the two groups was statistically insignificant (p=0.55) (Table 2).

At different evaluation dates, Group I UAS 7 scores were 19.42±9.693, 3.89±2.761, 0.73±0.948, and 0.01±0.175. These scores fell substantially from baseline to 2, 4, and 6 weeks (p<0.000). In Group II, mean UAS 7 scores were 23.15±9.379 at baseline, but reduced substantially after 2, 4, and 6 weeks to 8.51±5.442, 4.25±3.003, and 1.05±0.905, respectively, with p<0.000 (Table 3).

The distribution of research individuals based on adverse effects revealed that 87.1% (n=108) had no side effects, compared to 96.9% (n=62) in Group I and 76.7% (n=46) in Group II. Drowsiness was reported by 12.9% (n=16) of the research individuals, with 23.3% (n=14) in Group II compared to 3.1% (n=2) in Group I (p=0.02; Table 4).

DISCUSSION

The current study examined 124 participants, split into two groups of 62 each. Group I patients received a 20 mg bd pill of Bilastine, whereas Group II individuals received a combination tablet of Bilastine (20 mg) and Levocetirizine (5 mg). The research included 53.2% (n=66) men, with 53.1% (n=34) in Group I and 53.3% (n=32) in Group II, and 46.8% (n=58) females, with 46.9% (n=30) in Group I and 46.7% (n=28) in Group II, which was non-significant with p=1.00.

The age difference between two groups at <20, 21-30, 31-40, 41-50, 51-60, and >60 years was not significant (p=0.08). These findings were consistent with earlier investigations by Inui S6 in 2019 and Shah B et al7 in 2020, both of which analysed people with demographic data similar to the current study in CSU. The study findings revealed that type II diabetes was present in 9.4% (n=6) of the study patients in Group I, 13.3% (n=8) in Group II, and 11.3% (n=14) in total. Hypothyroidism was detected in 4.8% (n=6) of research participants, with 6.3% (n=4) and 3.3% (n=2) in Groups I and II, respectively.

Hypertension was seen in 14.5% (n=18) of the participants, with 9.4% (n=6) and 20% (n=12) in Groups I and II, respectively. There was no comorbidity in 69.4% (n=86) of the participants, including 75% (n=48) from Group I and 63.3% (n=38) from Group II. The difference in comorbidities between the two groups was not statistically significant (p=0.55). These findings were congruent with those of De A et al8 in 2021 and Weller K et al9 in 2018, who found no change in comorbidities in urticaria patients treated with bilastine or levocetirizine, as shown in the current study.

At successive testing dates, two sets of research participants had mean UAS 7 scores of 19.42±9.693, 3.89±2.761, 0.73±0.948, and 0.01±0.175, respectively. These scores fell substantially from baseline to 2, 4, and 6 weeks (p<0.000). after baseline, Group II had a mean UAS 7 score of 23.15±9.379, which substantially dropped after 2, 4, and 6 weeks to 8.51±5.442, 4.25±3.003, and 1.05±0.905, respectively (p<0.000). These findings were consistent with the findings of Podder I et al10 in 2023 and Cataldi M et al11 in 2018, who, like the current investigation, showed a substantial drop in UAS 7 scores with the administration of Bilastine and levocetirizine in respective studies.

The study results also showed that for the distribution of study subjects based on the adverse effects, no side-effects were seen in 87.1% (n=108) subjects with 96.9% (n=62) subjects from Group I and 76.7% (n=46) subjects from Group II. Drowsiness was seen in 12.9% (n=16) of the research individuals, which was substantially greater in Group II subjects with 23.3% (n=14) compared to 3.1% (n=2) in Group I (p=0.02). These findings were consistent with those of Serra E et al12 and Hide M et al13 in 2017, who observed more side effects with bilastine and levocetirizine than with bilastine alone, as evidenced in the results of the current investigation.

CONCLUSIONS

Within its limitations, the current study concludes that up-dosing of bilastine is a well-tolerated, safe, and efficient method in comparison to the combined dose of 20 mg Bilastine and 5mg Levocetirizine, demonstrating that up-dosing of Bilastine can be a valuable and efficient addition to the current arsenal of medication with minimal to no side effects.

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S. No	Characteristics	Group I		Group II		Total		p-value
		n	%	n	%	N	%	
1.	**Gender**							
a)	Males	34	53.1	32	53.3	66	53.2	1.00
b)	Females	30	46.9	28	46.7	58	46.8	
c)	Total	64	100	60	100	124	100	
2.	**Age (years)**							
a)	<20	16	25	12	20	28	22.6	0.08
b)	21-30	20	31.3	20	33.3	40	32.3	
c)	31-40	18	28.1	4	6.7	22	17.7	
d)	41-50	8	12.5	16	26.7	24	19.4	
e)	51-60	0	0	6	10	6	4.8	
f)	>60	2	3.1	2	3.3	4	3.2	
g)	Total	64	100	60	100	124	100	

Table 1: Distribution of study subjects based on their gender and age range

Characteristics	Group I		Group II		Total		p-value
	n	%	n	%	n	%	
T2 diabetes mellitus	6	9.4	8	13.3	14	11.3	0.55
Hypothyroidism	4	6.3	2	3.3	6	4.8	
Hypertension	6	9.4	12	20	18	14.5	
None	48	75	38	63.3	86	69.4	
Total	64	100	60	100	124	100	

Table 2: Distribution of study subjects depending on the comorbidities

	Number (n)	Mean ± S. D	p-value
Group I; UAS7 scores			
Baseline	64	19.42±9.693	**<0.000**
2 weeks	64	3.89±2.761	
4 weeks	64	0.73±0.948	
6 weeks	64	0.01±0.175	
Group II; UAS7 scores			
Baseline	64	23.15±9.379	**<0.000**
2 weeks	64	8.51±5.442	
4 weeks	64	4.25±3.003	
6 weeks	64	1.05±0.905	

Table 3: UAS 7 scores in two groups of study subjects at different assessment times

S. No	Side effects	Group I		Group II		Total		p-value
		n	%	n	%	n	%	
1.	**None**	62	96.9	46	76.7	108	87.1	**0.02**
2.	**Drowsiness**	2	3.1	14	23.3	16	12.9	
3.	**Total**	64	100	60	100	124	100	

Table 4: Distribution of study subjects based on the adverse effects