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Research

Prospective Study Of Quality Of Life, Drug Use, Clinical Outcome And Side Effects In Patients With Chronic Urticaria At a Tertiary Medical College.

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Abstract

Introduction: Chronic urticaria (CU) is a persistent dermatological condition marked by recurring hives, angioedema, or both, lasting over six weeks. It affects a significant portion of the population, leading to substantial physical, emotional, and functional impairments, including sleep disturbances, fatigue, and irritability, thereby significantly reducing the quality of life.

Materials and Methods: This prospective observational study was conducted over a period of 18 months, including 100 CU patients. The study compared the Urticaria Activity Score (UAS), Total severity scores and Dermatology Life Quality Index (DLQI) at baseline and after 12 weeks of treatment. Patient compliance was assessed using the Morisky Green Levine Scale (MGLS).

Results: Out of the 100 patients, 55% were treated with second-generation antihistamines alone, 32% with a combination of first and second-generation antihistamines, and 13% with a combination of second-generation antihistamines and corticosteroids. Patients treated with the latter combination showed significant improvements: UAS reduced from 6.0 to 1.0, total severity scores from 11.0 to 3.0, and DLQI scores from 25.0 to 8.0 (all p-values < 0.001). Side effects were tolerable, with 26% of patients experiencing somnolence, nausea, dry mouth, or abdominal pain. High treatment compliance was noted in 22% of patients, medium compliance in 49%, and low compliance in 29%.

Conclusion: This present study reaffirms the effectiveness of second-generation antihistamines and corticosteroids in managing chronic urticaria (CU) symptoms, aligning with previous research. However, we found that combining first and second-generation antihistamines improves patient's quality of life compared to second-generation antihistamines alone with minimum side effects.

Keywords: Chronic Urticaria, Angioedema, Antihistamines, Urticaria Activity Score, Quality of Life.

INTRODUCTION

Urticaria is characterized as a dermatological condition marked by transient, localized edema of the skin or mucous membranes (wheal) and an accompanying erythematous area, typically associated with pruritus and resolving within 24 hours.Angioedema involves a similar transient, localized edema of the skin or mucous membranes occurring in deeper tissues, often presenting without pruritus but potentially accompanied by pain or burning sensations.Both wheals and angioedema can co-occur in a patient or manifest independently. While urticaria is referred to as a specific disease entity, angioedema can denote either a disease or an episodic eruption. These conditions can also manifest as symptoms of other diseases, such as anaphylaxis (either wheals or angioedema), autoinflammatory syndromes (wheals), mastocytosis (wheals, known as Darier's sign), or hereditary angioedema (HAE; angioedema).[1]

The international guidelines advocated by the European Academy of Allergy and Clinical Immunology (EAACI), Global Allergy and Asthma European Network (GA^2LEN), European Dermatology Forum (EDF), and World Allergy Organization (WAO) (referred to as the EAACI guideline) define urticaria as a condition characterized by the presence of wheals (hives), angioedema, or both. These guidelines distinguish urticaria as a specific disease from other medical conditions in which wheals, angioedema, or both may appear as symptoms, such as skin prick tests, anaphylaxis, autoinflammatory syndromes, or hereditary angioedema (HAE; bradykinin-mediated angioedema).[1]

Chronic urticaria poses significant challenges regarding its etiology, investigation, and management. Although it can cause considerable distress and persist for years, effective management can often help alleviate symptoms.[2]

Chronic urticaria is a debilitating skin condition that can significantly affect health-related quality of life (HRQOL) and daily functioning. It is often associated with anxiety, depression, sleep disturbances, and difficulties in work and social activities.[3] The underlying pathophysiology of this condition is complex, and the precise triggers for symptoms in patients with chronic spontaneous urticaria (CSU) remain unclear.[4]

Urticaria is marked by the sudden onset of wheals (hives), angioedema, or both. Approximately 30-40% of patients experience only hives, 10-20% only angioedema, and one-third present with both.[5]

Urticarial wheals vary in size from a few millimeters to several centimeters and can be either white or red, sometimes with a red flare. Wheals can last from a few minutes to several hours and may shift shape, appearing as round lesions, rings, map-like patterns, or large patches. These wheals are typically itchy or occasionally cause a burning sensation, and the skin usually returns to its normal state within 1-24 hours, though sometimes wheals resolve even more quickly.[6]

Growing evidence indicates that autoimmunity may play a role in the pathogenesis of chronic urticaria. According to guidelines from leading organizations such as the European Academy of Allergology and Clinical Immunology (EAACI), the EU-funded network of excellence GA^2LEN, the European Dermatology Forum (EDF), and the World Allergy Organization (WAO), second-generation H1 antihistamines are the first-line pharmacological treatment for chronic urticaria.[7]

This study aimed to evaluate the severity of chronic urticaria and its impact on patient's quality of life. Additionally, the study examined the effectiveness of various treatment regimens and assessed patient compliance with these treatments.

MATERIALS AND METHODS

This prospective and observational study was conducted on patients with chronic urticaria in the dermatology outpatient department, with oversight from dermatology supervisors. A total of 100 patients with chronic urticaria were assessed in this study from November 2022 to April 2024 at MMIMSR, Mullana, Ambala.

Case Selection

One hundred cases of both new and existing patients suffering from chronic urticaria of both sexes from an age group of 18 years and older were selected from the outpatient department of Dermatology, MMIMSR, Mullana, Ambala. Individuals with a clinical diagnosis of chronic urticaria (CU) for a duration of at least 6 weeks were included.

The following criteria excluded patients from enrollment in the study: patients with other forms of urticaria, individuals with severe liver or kidney insufficiency, pregnant or breastfeeding females, and those using hormonal contraceptives. The object of the study was fully explained to each patient, and consent was taken from each patient. Baseline symptoms were recorded at the time of presentation, and patients were followed for twelve weeks to assess changes in their symptoms compared to baseline levels.

Parameters used

Urticaria Activity Score (UAS)

It was used to assess the severity and activity of urticaria (hives) over time. It provides a standardized method for evaluating the symptoms experienced by patients with urticaria, particularly chronic urticaria, which is characterized by the presence of hives and/or angioedema lasting for six weeks or more.[8]

Table 1: Wheals and Pruritus summarized Score

Score	Wheals score	Pruritus score
0	None	None
1	Mild (<20 wheals/ 24 h)	Mild (present but not troublesome)
2	Moderate (20-50 wheals/24 h)	Moderate troublesome but does not interfere with sleep
3	Severe (>50 wheals/ 24 h)	Severe (sufficiently troublesome to interfere withnormal daily activity and sleep)

Sum of score:0-6 for each day is summarized over 1 week (Minimum 0, maximum 42)

Total severity score (TSS)

This score was also useful in assessing severity of disease based on frequency and duration of wheals in chronic urticaria patients.

Table 2: Frequency and duration of TSS

0	Clear
1-4	Mild
5-8	Moderate
9-12	Severe

TSS is calculated by adding the above mentioned scores.
Maximum TSS is 12. Based on the TSS value patient's disease severity was graded.
At the end of 12 weeks total severity scores of urticaria were calculated and were compared with the baseline total severity scores.

Quality of life measurement using Dermatology life quality index (DLQI)

The Dermatology Life Quality Index (DLQI) was beused to assess the levels of qualityof lifeimpairment. The DLQI contained six main items: Symptoms and feelings (questions 1 and 2), Daily activities (questions 3 and 4), Leisure (questions 5 and 6), Work and school (question 7), Personal relationships (questions 8 and 9), and Treatment (question 10). All questions were related to the week prior to testing, and response categories include-not at all, a little, a lot, and very much with corresponding scores 0, 1, 2, and 3, respectively; the response "not relevant" was scored as 0. The summing of all responses was given a total index score.[9]

Table 3: Interpretation of DLQI scores

0-1	No effect at all on patient's life
2-5	Small effect on patient's life
6-10	Moderate effect on patient's life
11-20	Very large effect on patient's life
21-30	Extremely large effect on patient's life

Patient's compliance with treatment

In this study Morisky Green Levine Medication Adherence Scale (MGLS) was used for assessment of compliance. MGLS score ranges from 0 – 4 and the developers suggested three levels of medication adherence based on this score: high, medium and low adherence with 0, 1–2, and 3–4 points, respectively.[10]

RESULTS

Table 4: Age & gender distribution

Age	Male (%)	Female(%)	Total(%)
18-29	3 (33.33)	6 (66.67)	9
30-39	9 (32.14)	19 (67.86)	28
40-49	15 (33.33)	30 (66.67)	45
50-59	9 (50.00)	9 (50.00)	18
Total	36 (36.00)	64 (64.00)	100

Age range was from 27 to 58 years.The most frequently affected age group was between 40 and 49 years, comprising 30 female and 15 male patients. The mean age was 42.64 years, with a standard deviation of 7.65 years. In this study, chronic urticaria affected 64% of female patients and 36% of male patients.

Table 5: Precipitating factors

Precipitant	Frequency	Percentage (%)
Food (egg)	3	3.0
Pressure	9	9.0
Heat exposure	8	8.0
Cold exposure	3	3.0
NSAIDS	4	4.0

Regarding precipitating factors, pressure was the most common, accounting for 9% of the cases. This was followed by heat exposure (8%), use of NSAIDs (4%), food allergens such as eggs (3%), and cold exposure (3%). Notably, 73% of the total patients had no specific aggravating or triggering factor for the occurrence of symptoms.

Table 6: Co-morbid factors

Comorbidity	No. of Patients	Percentage (%)
Hypothyroidism	15	15.0
Rheumatoid arthritis	7	7.0
Diabetis Mellitus	2	2.0
Hypertension	1	1.0

Out of the 100 patients, 25% had co-existing systemic conditions.Hypothyroidism was the most common, affecting 15% patients. Rheumatoid arthritis was observed in 7% patients, while diabetes mellitus was present in 2% patients. Additionally, 1% patient had hypertension.

Table 7: Associated angioedema

Angioedema	No. of Patients	Percentage (%)
Lips	14	14.0
Feet	3	3.0
Hands	4	4.0
Eyelid	3	3.0

24% of the patients had associated angioedema, presenting as swelling of the lips, feet, hands, head, or eyelids. Lip swelling was the most common among these cases. The remaining 76% of patients did not experience any associated angioedema.

Table 8: Treatment given

Treatment	No. of Patients	Percentage (%)
2nd gen H1#	55	55.0
1st gen + 2nd gen H1#	32	32.0
2nd gen H1# + CS	13	13.0

Depending on the severity of the disease, out of the 100 patients, 55% were treated with second-generation antihistamines (2nd gen H1#) alone. 32% received a combination of first and second-generation antihistamines (1st gen + 2nd gen H1#), while the remaining 13% were treated with a combination of second-generation antihistamines and corticosteroids (2nd gen H1# + CS).

Table 9: Side effects of the treatment given

Side effects	No. of Patients	Percentage (%)
Somnolence	11	11.0
Nausea	7	7.0
Dry Mouth	5	5.0
Abdominal Pain	3	3.0

In our study, 74% of patients experienced no side effects during treatment. However, 26% of patients reported tolerable side effects, including somnolence (11%), nausea (7%), dry mouth (5%), and abdominal pain (3%). These side effects were predominantly observed in patients who were receiving a combination of first and second-generation antihistamines.

Table 10: Urticaria activity scores (UAS)

		Baseline		12 weeks		p-value
Treatment	No. of patients	Minimum	Maximum	Minimum	Maximum	
1st gen + 2nd gen H1#	32	4	6	0	2	<.001
2nd gen H1#	55	4	6	0	2	<.001
2nd gen H1# + CS	13	5	6	0	1	<.001

Urticaria activity score among all three treatment groups showed significant reduction during 12th week of assessment compared to baseline (p-value < 0.001).Patients who were treated with 2nd gen H1# + CS experienced a more pronounced decrease in urticaria activity scores, dropping from 6.0 at baseline to 1.0 after 12 weeks of treatment, compared to the other two groups.

Table 11: Total severity scores

		Baseline		12 weeks		p-value
Treatment	No. of patients	Minimum	Maximum	Minimum	Maximum	
1st gen + 2nd gen H1#	32	8	11	0	4	<.001
2nd gen H1#	55	8	11	0	4	<.001
2nd gen H1# + CS	13	10	11	0	3	<.006

Total severity score among all three treatment groups showed significant reduction during 12thweek of assessment compared to baseline (p value <0.001).2nd gen H1# + CS showed a slight better improvement in the total severity score from 11.0 to 3.0 as compared to other two treatment groups which reduced total severity score from 11.0 to 4.0.

Table 12: Dermatology life quality index (DLQI score)

		Baseline		12 weeks		p-value
Treatment	No. of patients	Minimum	Maximum	Minimum	Maximum	
1st gen + 2nd gen H1#	32	17	25	5	8	<.001
2nd gen H1#	55	17	25	5	9	<.001
2nd gen H1# + CS	13	18	25	5	8	<.002

Dermatology life quality index (DLQI) score among all three treatment groups showed significant reduction during 12th week of assessment compared to DLQI scores reduced from 25.0 to 8.0 when patients were treated with 1st gen H1# + 2nd gen H1# and with 2nd gen H1# + CS.However scores reduced from 25.0 to 9.0 when treated with 2nd gen H1# alone (p-value <0.001).

Laboratory findings

When deemed necessary, laboratory investigations such as complete blood count, renal profile, and liver function tests were performed. Among the 65 patients who underwent routine blood investigations, elevated absolute eosinophil counts were observed in 36 patients (55.38%), while remaining 29 (44.62%) had normal absolute eosinophil counts. Other parameters generally remained within normal limits.

Compliance

After calculating patient's adherence to the treatment using the MGLS Scale, it was found that 29% had low compliance, 49% had medium compliance and 22% of the patients had high compliance with the treatment.

DISCUSSION

A cohort of 100 patients with chronic urticaria, who met the specified inclusion and exclusion criteria, were observed and analyzed over an eighteen months period. The findings were compiled based on parameters such as age and gender distribution, disease duration and diurnal variation, precipitating and comorbid factors, and associated angioedema.Laboratory investigations were conducted as necessary.Treatment was administered according to the severity of the condition, and any treatment-related side effects were considered.

Various scoring systems were employed to evaluate disease severity from baseline, with comparisons made after 12 weeks. Given the significant impact of chronic urticaria on patient's quality of life, the Dermatology Life Quality Index (DLQI) was utilized to assess this impact. Additionally, adherence to daily medication was a challenge for many patients; thus, the Morisky-Green-Levine Scale (MGLS) was used to measure treatment compliance.

The age range of participants in our study spanned from 27 to 58 years, with the most commonly affected demographic being those aged 40 to 49 years. The mean age observed was 42.64 years. This finding is consistent with other studies on chronic urticaria patients, where the mean age ranged from 32.8 to 44.4 years.[11,12,13,14]. In our study, 64% of chronic urticaria cases were observed in female patients, while 36% were observed in male patients. This gender distribution is consistent with findings from other studies, which generally report a higher prevalence of chronic urticaria in females.[11,12,13] However, an exception is noted in a study by Naseerudeen N et al., which reported a higher prevalence among males.[14]

Chronic urticaria is defined as a condition lasting longer than six weeks. In our study, the majority of patients presented with symptoms lasting between 3 to 6 months, comprising 15.5% of the total cases. The duration of symptoms ranged from 2 to 24 months. Compared to other studies with larger sample sizes, patients generally presented with symptoms lasting between 3 to 18 months.[11,12,13,14]. Among the 100 patients studied, 22% experienced urticaria onset in the morning, 41% in the evening, and 16% at night.

Regarding precipitating factors, pressure was the most prevalent, contributing to 9% of the cases. Patients reported that wearing tight clothing or sitting on a hard surface often triggered symptoms. This was followed by heat exposure (8%), the use of NSAIDs (4%), food allergens such as eggs (3%), and cold exposure (3%). Notably, 73% of the patients did not identify any specific aggravating or triggering factors for their symptoms. In contrast, a study by Naseerudeen N et al found that food items were the most common aggravating factor for chronic urticaria.[14] In our study, 25% patients had coexisting systemic conditions. Hypothyroidism in 15% rheumatoid arthritis in 7%, diabetes mellitus in 2%, and hypertension in 1%.

The observed association with autoimmune conditions is consistent with findings from other studies.Verneuil et al mentioned hypothyroidism as the most common comorbid factor[15].Rossy Moreira et al observed in their study that the most common comorbidities associated with chronic urticaria were hypertension (35% of patients), thyroid disease (18.8%), gastrointestinal disease (13.8%), diabetes (12.2%), and rheumatic diseases (9.4%).[16]

The urticaria activity score showed a significant reduction in all three treatment groups by the 12th week compared to baseline ($p<0.001$). Patients who were treated with 2nd gen H1# + CS experienced a more pronounced decrease in urticaria activity scores, dropping from 6.0 at baseline to 1.0 after 12 weeks of treatment, compared to the other two groups. Similarly,Godse KV et al found that patients treated with 2nd gen H1# + CS saw their mean UAS decreased from 4.35 at baseline to 0.50 after 12 weeks.[11] Parameters such as the weekly frequency of urticaria and the duration of wheals showed an equal reduction across all three treatment groups by the 12th week of assessment compared to baseline ($p <0.001$).

The total severity score significantly decreased in all three treatment groups by the 12th week of assessment compared to baseline ($p<0.001$). The combination of second-generation antihistamines and corticosteroids showed a slightly greater improvement in the total severity score.There was significant improvement in quality of life in all the three treatment groups more so in 2nd gen H1# + 1st gen H1# and 2nd gen H1# + CS ($p<0.001$).These results were found similar to the study done by Danilycheva I et al on DLQI in patients of chronic Urticaria.[17]

Patients treated with combination of 2nd gen H1# + CS experienced a significant reduction in UAS (urticaria activity scores) and total severity scores. DLQI (dermatology life quality index) scores decreased more in patients treated with 2nd gen H1# + CS and 2nd gen H1# + 1st gen H1# compared to those treated with 2nd gen H1# alone.Only 26% of patients reported tolerable side effects which were predominantly observed in patients who were receiving a combination of first and second-generation antihistamines.

29% had low compliance, 49% had medium compliance and 22% of the patients had high compliance with the treatment. In a study by Heng JK et al., the majority of patients (71.9%) exhibited low adherence to medical therapy 25.2% had medium adherence, while only 2.9% had high adherence scores.[18]

CONCLUSION

In this study, the age group most frequently affected by the condition was individuals between 40-49 years, with a higher prevalence in females. Hypothyroidism was identified as the most common coexisting systemic condition, followed by rheumatoid arthritis. Angioedema was present in 24% of patients, primarily manifesting as lip swelling. Eosinophilia was noted in 36 patients. Although minor side effects occurred during treatment, they did not require therapy discontinuation. A combination of second-generation H1 antihistamines with either first-generation H1 antihistamines or corticosteroids proved more effective than second-generation H1 antihistamines alone. Most patients exhibited low or moderate levels of treatment compliance.

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None

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