

Reviewing Anti-histamines in Urticaria

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CASE 1 – DELAYED EPISODES OF PAINFUL URTICARIAL LESIONS

Case Presentation

An otherwise healthy 37-year-old female, who worked in a grocery store (mostly standing) presented with daily episodes of painful hand and feet swellings for the past 8 months. She also reported difficulty in wearing her shoes. Moreover, she experienced skin lesions on the right side of her body at night as she would sleep leaning on that side.

Medical History

- She reported occasional fever and fatigue along with her skin lesions.
- She also reported difficulty in sleeping and a substantial decrease in her daily work productivity and overall quality of life.
- There were no symptoms of fever, joint involvement, or hearing loss.
- The urticaria was not present during early childhood.
- There was no relevant medical family history.
- There was no history of food/drug allergies or insect bites.
- She was a non-smoker and occasionally consumed alcohol during weekends.

Diagnostic Interventions

General examination

Height	165 cm
Weight	62 kg

BMI	22.77 kg/m ² (normal)
Blood pressure	126/82 mmHg
Temperature	37.5°C (afebrile)

BMI: Body mass index

Physical and clinical examination

Visual examination	All lesions appeared in areas where there was continuous pressure applied
Delayed pressure urticaria testing (2 kg weight and a blood pressure cuff)	Positive test – palpable and visible swelling on the right forearm at the site of pressure at the end of 30 min and at 6 h
Routine hematologic and biochemical screening tests (hemoglobin, white blood cell count and differential, erythrocyte sedimentation rate, liver function tests, and urinalysis)	No abnormal findings

Diagnosis

Based on the clinical history and results of provocative testing, the diagnosis was confirmed as “delayed pressure urticaria (DPU).”

Treatment and Management

- The patient was prescribed levocetirizine (5 mg) plus montelukast (10 mg) once daily along with oral prednisolone for a duration of 2 weeks.
- In addition, she was counseled appropriately about her condition, and was strictly instructed to avoid wearing tight clothing, sitting/sleeping on hard surfaces for prolonged periods, carrying heavy groceries, and other such situations.

Follow-up

- After 2 weeks, there was a notable clinical improvement in the symptoms of the patient.
- The patient strictly adhered to the treatment regimen and suggested instructions.
- The patient also reported a significant improvement in her work productivity and overall quality of life.

Access this article online	
 <p>www.ijss-sn.com</p>	<p>Month of Submission : 12-2020</p> <p>Month of Peer Review : 12-2020</p> <p>Month of Acceptance : 01-2021</p> <p>Month of Publishing : 02-2021</p>

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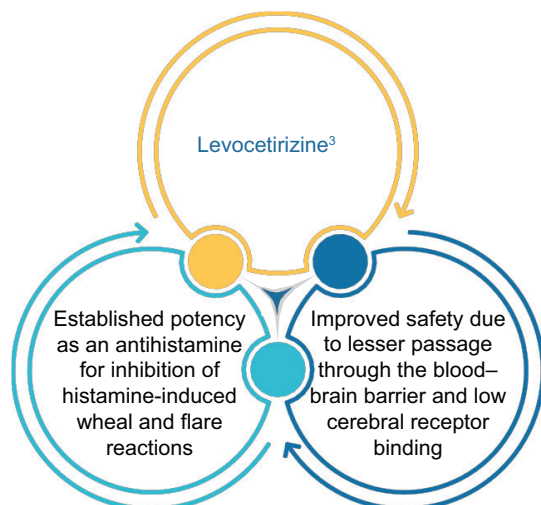


Figure 1: Wheals 6 h after suspension of 7 kg weight over the right shoulder of a patient. (Adapted from Quintero OP et al. J Allergy Clin Immunol Pract. 2017;5:179-80.)

DISCUSSION

DPU is a subtype of chronic inducible urticaria, that is characterized by recurring erythematous and often painful swelling after the skin is exposed to sustained pressure.^[1] It might compose up to 37% of all physical urticarias, which also includes cholinergic urticaria, solar urticaria, and cold urticaria; but rarely as a primary inducible urticaria.^[2] DPU lesions take 4–6 h to manifest and generally last for more than 24 h.^[1] Evidence suggests that the quality of life impairment associated with DPU is significantly higher than that in people with chronic spontaneous urticaria, mostly affecting areas of work/study, leisure, etc.^[2] A representative image of DPU is illustrated in Figure 1.

DPU is diagnosed based on patient history and the results of skin provocation tests like pressure challenge test.^[1,2] Current treatments for this condition include antihistamines, montelukast, oral steroids, nonsteroidal anti-inflammatory drugs, cyclosporine, omalizumab, and intravenous immunoglobulin.^[2]



A global assessment indicated that levocetirizine 5 mg once daily was an effective agent in patients with chronic idiopathic urticaria.^[3] Its action provides a rapid and satisfactory control of the symptoms and subjective disease measures.^[3]

CONCLUSION

Treatment with levocetirizine in combination with other therapies significantly improved the clinical symptoms and quality of life of the patient.

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CASE 2 – ROLE OF LEVOCETIRIZINE IN CHRONIC SPONTANEOUS URTICARIA

Case Presentation

A 38-year-old married Muslim male Mr. Abdul Ahmed, laborer by occupation and resident of Kota, presented with a complaint of recurrent multiple itchy red raised lesions distributed over the whole body for the past 1 year. Lesions persisted for about 4–6 h, and frequency of appearance of lesions had gradually increased from once weekly initially to 8–10 times weekly at present. Lesions were associated with severe itching that impaired his day-to-day activity and work.

Medical History

- No history of swelling over lips, eyelids, or face.
- No associated difficulty in breathing or abdominal pain.
- He had no significant medical history.
- He reported a history of tobacco chewing for 25 years.
- Personal and medical history was non-contributory.
- He consumed alcohol during weekends.

Diagnostic Interventions

Physical and clinical examination

Physical examination	Patient appeared healthy He had multiple discrete urticarial wheals of varying size from few millimeters to several centimeters over whole body, predominantly over the back
Complete blood count	Normal
Liver and renal functions and urine analysis	Normal
Chest roentgenogram	Normal

Confirmed Diagnosis

Based on the patient history and diagnostic interventions, the diagnosis was confirmed as “chronic spontaneous urticaria.”

Treatment

- The patient was initially started on Tab. Xyzal 5 mg (levocetirizine 5 mg) OD after breakfast for 1 week.
- Dose was gradually escalated to 10 mg BD for 1 week to get desired response and thereafter maintained at the same level with regular follow-up at 4 weeks.

Follow-up

- On follow-up, he gave no history of any new lesions or itching.
- The routine investigations (complete blood count, liver, renal functions, urine analysis and lipid profile) were repeated.
- The observed drug was tolerated well with no side effects or derangement of laboratory parameters.

CONCLUSION

This case report suggested that up dosing of XYZAL was quite effective in chronic spontaneous urticaria with good patient tolerability and compliance.

CASE 3 – COLD URTICARIA: MANAGEMENT WITH LEVOCETIRIZINE

Case Presentation



A 29-year-old healthy female presented with a complaint of intermittent itchy rash after being exposed to cold winds.

Patient History

- She noticed that the rash occurred suddenly after exposure to cold, and the rash resolved on its own within 1–2 h each time it appeared.

- She used to have these symptoms for several years since her adolescence, but they had gradually worsened during her recent vacation trip to a colder destination.
- Her worst symptoms occurred when she was exposed to a cold object, like holding a chilled cold drink in the flexure of her arm while she wore a T-shirt.
- She had experienced severe shortness of breath while exercising in the morning and would get facial swelling after using cold water.
- She was otherwise alright without any significant medical history or any medication use and had no known allergies.

Physical Examination

- Afebrile
- Erythematous pruritic wheals appeared after a cold tuning fork was applied for 2 min to the inner aspect of the forearm (cold stimulus test).

Based on her symptom-based clinical data, the patient was diagnosed with cold urticaria



Treatment and Follow-up

The patient was started on levocetirizine 5 mg once daily for 2 weeks.

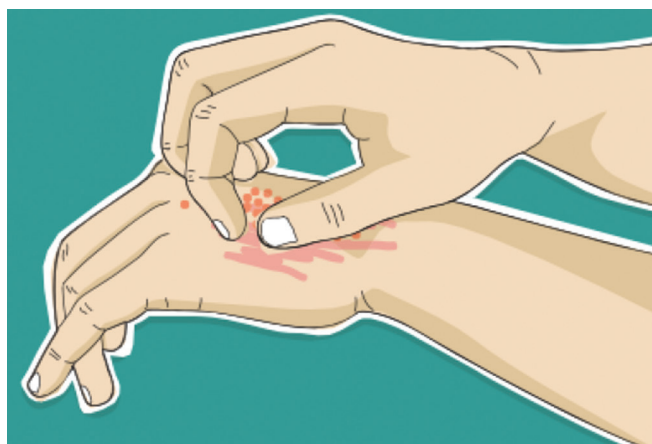


At a follow-up visit 4 weeks after initiation of levocetirizine, the patient reported an improvement in her condition with no significant symptoms following a cold exposure.

Treatment Rationale

- The EAACI/GA²LEN/EDF/WAO guideline recommends 2nd generation H1-antihistamines (AHs) to be taken regularly by the patients with chronic urticaria.^[1]
- The CSACI, therefore, recommends in agreement with other international bodies, that only less sedating newer generation AHs should be first-line treatment regimen, and should be preferred over older AHs and that the use of first-generation AHs should be significantly curtailed in chronic urticaria.^[2]

EAACI/GA²LEN/EDF/WAO: European Academy of Allergology and Clinical Immunology, EU founded network of excellence, the Global Allergy and Asthma European Network, European Dermatology Forum and World allergy organization. CSACI: Canadian Society of Allergy and Clinical Immunology.



DISCUSSION

- Cold-induced urticaria is a form of chronic urticaria with a duration of symptoms of at least 6 weeks.^[3]
- It is the second most common type of chronic inducible urticarial.^[3]
- It is more common in younger individuals and more likely to affect females as opposed to males.^[3]
- Non-sedating AHs, used up to 4 times the standard dose for non-responders to the standard dose, have found to be effective in controlling the frequency and severity of symptoms associated with cold-induced urticaria, regardless of the cause.^[3]

Studies on Levocetirizine

- Levocetirizine reduces the discomfort caused by urticaria symptoms in approximately 75% of patients without affecting sleep or safety.^[4]

- Levocetirizine in chronic urticaria doubled the effectiveness in the course of treatment at higher doses.^[4]
- It improved the quality of life of the patient.^[4]

CONCLUSION

Levocetirizine 5 mg once daily is recommended for patients with urticaria induced by cold.

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CASE 4 – A CASE REPORT OF PHYSICAL URTICARIA

Case Presentation

A 39-year-old female presented with a complaint of bilateral areas on her legs, which had been subjected to laser treatment for removal of unwanted hair. The pruritus worsened over time and she experienced a diffuse and substantial wheal and flare reaction.

Medical History

- The patient had a similar but less intensive reaction during her first laser treatment procedure 5 weeks earlier.
- The reaction included initial follicular papules worsening over hours into diffuse urticaria of the lower extremities.
- There was no relevant personal or family history of atopy.
- She denied oral/pharyngeal swelling and shortness of breath.
- She denied history of any pruritic eruptions following exposure to cold, heat, pressure, emotional stress, exercise, or spicy food.
- There was no history of any medication allergies as well.

- She reported being a social drinker and consuming alcohol occasionally.

Diagnostic Interventions

On physical examination	No abnormal findings detected
Dermographism	Negative
Blood pressure	130/84 mmHg
Temperature	37.5°C (afebrile)
Complete blood count	Normal

Diagnosis

Based on the patient history and diagnostics, the diagnosis was confirmed to be “**laser-induced urticaria.**”

Treatment

- The patient was prescribed 5 mg levocetirizine once daily for alleviation of symptoms for a week.
- She was also prescribed desoximetasone cream to be applied twice a day to the treatment site.

Follow-up

- No urticarial lesions were noted after a week of continuous treatment.
- At the 1-month follow-up, the patient denied having any more symptoms.
- The patient decided to undergo a third laser hair removal treatment several weeks later.
- The patient did not develop urticaria after prophylactic levocetirizine 5 mg tablet was taken 2 h before the session.

DISCUSSION

Urticarial responses are commonly seen after laser hair reduction procedures.^[1] After laser treatment, an urticarial papule develops around each treated follicle that contained a pigmented hair shaft.^[1] This urticarial response is usually



Figure 1: Development of urticaria after using long-pulse duration alexandrite laser

limited to the immediate area surrounding the hair shaft, with a more subtle urticarial response occurring at the entire treatment site.^[1] A representative image of laser-induced urticaria is illustrated in Figure 1.^[1]

In accordance to clinical evidence, levocetirizine 5 mg/day has been effective in reducing symptoms of chronic idiopathic urticaria and improving quality of life, with an acceptable tolerability profile.^[2]

CONCLUSION

Levocetirizine provided symptomatic relief and enabled the patient to complete her laser treatments without trouble.

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CASE 5 – ROLE OF LEVOCETIRIZINE IN CHRONIC SPONTANEOUS URTICARIA

Case Presentation



A 24-year-old male presented to his general practitioner with a complaint of severe itching and relapsing rash.

Patient History

- His symptoms began in the last few months and then became severe in the past 4 weeks.
- The rash was present all over his body without an identifiable trigger with occasional swelling on lips and eyes.
- His symptoms worsened at night and also while wearing tight clothes.

- His symptoms lasted for 6–12 h and troubled him on majority of the days in a week.
- He did not have any previous allergic episodes.
- He looked anxious and depressed while he came to the clinic.
- He only took over-the-counter medications for his itch, which did not give him relief.
- Since he was having persistent symptoms affecting his daily schedule, he needed medical help.

Physical Examination

- Afebrile.
- Presence of wheals and angioedema.
- Review of symptoms was unremarkable.

Laboratory Tests

- Results of routine screening laboratory tests for complete blood count and erythrocyte sedimentation rate were normal



- Based on symptom-based clinical data, the patient was diagnosed with chronic spontaneous urticaria (CSU).

Treatment and Follow-up



- The patient was prescribed levocetirizine 5 mg once daily for 2 weeks.
- At a follow-up visit 4 weeks after initiation of levocetirizine, the patient reported reduction in the number and size of wheals along with a significant improvement in itching.

Treatment Rationale

- The EAACI/GA²LEN/EDF/WAO guideline suggests 2nd generation H1-antihistamines (AHs) to be

taken regularly by the patients suffering from chronic urticarial.^[1]

- The CSACI, therefore, recommends in agreement with other international bodies, that only less sedating newer generation AHs should be first-line the treatment regimen, and should be preferred over older AHs and that the use of first generation AHs should be significantly curtailed.^[2]

DISCUSSION

- Chronic spontaneous urticaria (CSU), previously termed as chronic idiopathic urticaria (CIU),^[3] is defined as spontaneous appearance of wheals, angioedema, or both for more than 6 weeks due to known or unknown causes.^[1]
- Approximately 40% of patients with CSU report episodes of angioedema or deeper swelling of dermal or mucosal tissues, whereas only 10% show angioedema as their primary manifestation.^[3]
- In majority of the cases, it is a self-limiting disorder, persisting for 2–5 years, although 20% of them suffer for more than 5 years.^[3]
- New-generation antihistamines taken once daily are effective and well tolerated in the treatment of CSU symptoms and in improving the patient's quality of life (QoL).^[4]

Study on Levocetirizine in CSU^[4]

- In a study conducted by Nettis *et al.*, levocetirizine was found to be superior in reducing the mean total symptom score as well as individual symptoms, number of daily episodes and number of wheals, and QoL compared to placebo.
- Beneficial effects of levocetirizine appeared during the first 3 weeks and lasted throughout the duration of the active trial and were found to be effective in controlling CSU.
- It concluded that levocetirizine 5 mg once daily is an effective agent in patients with CSU/CIU compared to placebo.

EAACI/GA²LEN/EDF/WAO: European Academy of Allergology and Clinical Immunology, EU founded network of excellence, the Global Allergy and Asthma European Network, European Dermatology Forum and World allergy organization. CSACI: Canadian Society of Allergy and Clinical Immunology.

CONCLUSION

Thus, levocetirizine 5 mg once daily is a favorable treatment choice for patients with chronic spontaneous urticaria.

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CASE 6 – A CASE OF EFFECTIVE TREATMENT OF CHRONIC URTICARIA

Case Presentation

A 25-year-old male, college student by occupation, resident of Jodhpur (Rajasthan), presented with chronic spontaneous urticaria, with a complaint of recurrent multiple itchy, red, raised, wheal, and flare lesions distributed over whole body, predominantly over trunk for 6 months. Wheal and flare lesions appeared 3–4 times/week and persisted for about 12 h.

Medical History

- Wheals and flares were 5–10 cm in size and were associated with severe itching, which impaired his academic performance and led to social pressure.
- No history of swelling over lips, eyelids, or face.
- No associated difficulty in breathing or abdominal pain.
- There was no significant history.
- Personal and medical histories were non-contributory.

Diagnostic Interventions

Physical examination	Patient appeared healthy with multiple discrete urticarial wheals of size varying from 5–10 mm over whole body, predominantly over trunk region
Complete blood count	Normal
Liver and renal functions	Normal
Lipid profile and urine analysis	Normal

Diagnosis

Based on the patient history and diagnostic interventions, the diagnosis was confirmed as “Chronic Spontaneous Urticaria.”

Treatment

- The patient was started on Tab. Xyzal 10 mg (levocetirizine 10 mg) B.D. after breakfast for 1 week.

- He was also asked to focus on increasing intake of fruits, vegetables, grains, and low-fat dairy products.

Follow-up

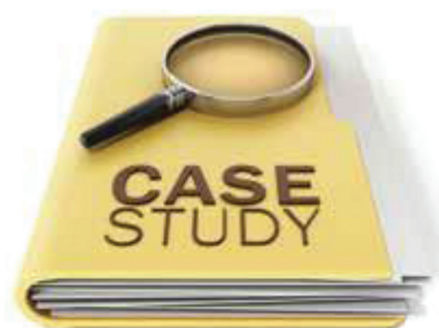
- On follow-up after 2 weeks, there was no complaint of appearance of new wheals and flares.
- There was no itching and urticaria was alleviated.
- He was maintained on the same regimen with regular follow-up at 4 weeks.
- On the next follow-up after 4 weeks, there was no history of any itching or lesions.
- He was advised to come for regular follow-ups in 4 weeks.
- It was observed that the drug was well tolerated, with no side effects.
- Due to twice a day dosing, compliance was good.

CONCLUSION

This case report suggested that up dosing of XYZAL was quite effective in chronic spontaneous urticaria with good patient tolerability and compliance.

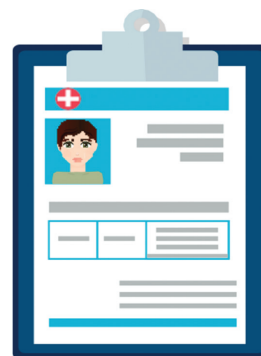
CASE 7 - ROLE OF LEVOCETIRIZINE IN AQUAGENIC URTICARIA

Case Presentation



A 42-year-old woman was referred to the dermatology department due to recurrent episodes of urticarial.

Patient History



- She presented with a 2-year history of pinpoint sized wheals affecting the shoulders, arms, trunk, abdomen, and back, when she took a bath or shower.
- These symptoms appeared within 10–20 min after contact with water and provoked intense pruritus. Each episode lasted for 20–40 min and spontaneously resolved.
- The patient did not complain of angioedema, wheezing, or dyspnea with these episodes.
- She had no personal history of allergies or drug allergy and no family history of urticaria.
- She had no treatment history before visiting clinic.



Figure 1: Urticaria after wet compression (Representative image)

Investigations	
Clinical investigations	
Immunoglobulin E	1965 IU/mL (normal, 0–170)
Alkaline phosphatase	349 U/L (normal, 106–322)
Eosinophil count	Normal
Immunological study	Within normal ranges
Water provocation tests	
Room temperature wet compress to the upper body for 30 min	Pin head to match head sized wheal surrounded by erythema on the shoulder [Figure 1]
Cold water and hot water compress were also applied for 30 min	Induction of pinpoint wheals at the site of compresses application
Water challenge test with tap water, distilled water, and normal saline	Similar results
Pressure test	
A 6000 g weight was applied to the skin for a period of 20 min	After 8 h, no lesions had appeared
Exercise test	
Running	Lesions were not reproduced after running
Ice cube test	
An ice cube filled plastic bag was applied to the patient's forearm for 20 min	No lesions were noted on the forearm after removal of cold stimulation

Diagnosis

Based on the findings, the patient was diagnosed with aquagenic urticaria.

Treatment

Levocetirizine was prescribed initially at a dose of 5 mg daily for symptom relief.

Follow-up

- After 2 weeks, no lesions had developed on contact with water.
- Once the symptoms were relieved, the dose was reduced to 5 mg every other day.
- The patient was still symptom free at the 1-year follow-up.

DISCUSSION

Aquagenic urticaria (AU) is a type of physical urticaria produced by contact with water. Urticaria is produced

irrespective of water temperature, pH, or psychogenic factors. Incidence of AU is slightly greater in women than in men.^[1] There is lack of a clear pathogenesis for AU, which has contributed to difficulty in proposing evidence-based treatments for affected patients.^[2]

Patients with AU usually present with characteristic 1–3 mm folliculocentric wheals and surrounding 1–3 cm erythematous flares within 20–30 min following skin contact with water. They can also experience associated symptoms, including pruritus, burning, and uncomfortable prickling. Diagnosis of AU is largely based on a history of recurrent urticaria after exposure to water combined with a water challenge test.^[2]

The urticarial symptoms, such as wheal formation and pruritus, are thought to be mediated, at least partially, by the effects of histamine on the H1 receptor. Therefore, the first-line therapy for AU generally consists of oral H1 antihistamines. The second-generation H1 antihistamines with lesser central nervous system depression, but greater duration of action are preferred in the treatment of urticaria.^[2]

Levocetirizine has been shown in observational studies as an effective and satisfactory therapy for patients with allergic respiratory and skin disease. Levocetirizine markedly improves the symptoms of urticaria. In the study by Fang *et al.*, it was shown that 60–80% of urticaria patients, treated with levocetirizine, reported complete or marked improvements in individual symptoms.^[3]

CONCLUSION

Second-generation H1-antihistamine such as levocetirizine is effective in resolving symptoms of aquagenic urticaria.

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CASE 8 – A CASE OF CHRONIC SPONTANEOUS URTICARIA

Case Presentation

A 33-year-old man presented to the dermatology clinic with multiple relapsing erythematous edematous wheals primarily on his limbs and trunk region for the past 7 months. The wheals were itchy with a stinging sensation. They appeared recurrently for varying duration (till a few hours) at one site along with new wheals appearing at other sites.

Medical History

- Initially, small, recurrent eruptions occurred on the trunk at the interval of several weeks.
- Gradually, the condition became much worse and involved all four limbs in addition to the trunk with a much higher recurrence, that is, multiple times in a day.
- The patient reported that the wheals aggravated mainly at night and got slightly relieved by the application of warm water provided a slight relief.
- There was no relevant family or personal history.
- The patient also reported residing in a damp environment and having an aversion to open air, even during summers.
- He had a history of complete vaccination with normal response to it.
- There was no relevant history of food or drug allergies.

Diagnostics

Physical and clinical examination

Physical examination	<ul style="list-style-type: none"> Multiple edematous, itchy wheals on trunk and limbs with concurrent burning and stinging sensations The eruptions were widespread and variable in intensity
Laboratory investigation	<ul style="list-style-type: none"> High level of IgE (480 IU/mL) High level of absolute eosinophil count (1000/mm³)
CU-QoL	• 78
VAS	• 9

IgE: Immunoglobulin E, CU-QoL: Chronic urticaria quality of life questionnaire, VAS: Visual analog scale

Confirmed Diagnosis

- Based on the symptoms, patient history, and clinical examination, the diagnosis was confirmed as “**chronic spontaneous urticaria (CSU).**”

Treatment and Follow-up

- The patient was initially started on **levocetirizine 5 mg once daily** for a duration of 2 weeks.
- After 2 weeks, there was a visible reduction in the number and size of wheals and substantial improvement in itching.
- However, to achieve complete resolution of the lesions, dose of levocetirizine was increased to 10 mg BD and he was maintained on the same for 4 weeks subsequently.
- At the next follow-up visit after 4 weeks, there was complete resolution of the symptoms and lesions.
- The patient reported significant and gradual improvement in his quality of life.

DISCUSSION

Representative image: Case of urticarial wheals



CSU is a mast cell-mediated condition characterized by spontaneous occurrence of wheals and/or angioedema for a total duration of 6 weeks or more.^[1] The global prevalence of CSU is estimated to be between 0.23% and 1.8%.^[1]

Women are affected twice as often as men.^[1] Both children and adults are affected, although the prevalence is highest in the 40-60 years age group.

The management of CSU is aimed at avoiding exacerbating factors and controlling symptoms as long as CSU persists.^[1] The second-generation H1-antihistamines taken regularly, are the first-line pharmacological treatment.^[1] If symptoms persist at 2–4 week intervals, the dose can be up-titrated to 4 times the standard dose.^[1]

In accordance to recent evidence, the second-generation H1-antihistamine, levocetirizine demonstrated superior therapeutic efficacy to placebo for the treatment of patients with CSU.^[2]

Compared with placebo, levocetirizine had significantly reduced wheal scores with small to medium effect sizes.^[2]

CONCLUSION

As established by the current case report, levocetirizine is an effective and well-tolerated pharmacotherapy for CSU.

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How to cite this article: Arora J, Jain S, Sharma J, Singh JK, Kapoor S, Singhi MK, Keshari M, Pudukadan D. Reviewing Anti-Histamines in Urticaria. *Int J Sci Stud* 2021;8(11):10-19.

Source of Support: Nil, **Conflicts of Interest:** None declared.