

UP TO DATE

Chronic idiopathic urticaria treatment

J.M. Negro-Álvarez*, and J.C. Miralles-López**

* Allergy Section. "Virgen de la Arrixaca" University Hospital. Associated Professor of Allergy. University of Murcia. Murcia. Spain. ** Allergy Section. General University Hospital.

SUMMARY

Chronic idiopathic urticaria (CIU) is a common skin condition that affects 0.1-3% of people in the USA and Europe and accounts for nearly 75% of all chronic urticaria cases. Up to 40% of patients who have chronic urticaria for more than 6 months still have urticarial wheals 10 years later.

The therapeutic management should first be oriented towards palliation of symptoms. A 2% solution of ephedrine as a local spray is very useful for oropharyngeal edema. H₁ antihistamines with a low potential for sedation are the most important first-line treatment.

Combinations of various antihistamines may be useful in suppressing symptomatology. These include: a) First generation H₁ antihistamines; b) Combinations of first and second generations using non-sedating agents in the morning and first generation drugs at night; c) Combinations of second generation antihistamines; d) Combination of doxepin with a first or second generation antihistamine; e) Combination of an H₂ anti-receptor antihistamine (eg, cimetidine or ranitidine) with a first or second generation antihistamine.

Preliminary reports suggest that desloratadine and anti-leukotrienes may be effective in treating some patients with chronic idiopathic urticaria.

Key words: Idiopathic chronic urticaria. Second generation antihistamines. Cetirizine. Desloratadine. Ebastine. Fexofenadine. Hidroxyzine. Loratadine. Mizolastine. Doxepin. Cimetidine. Ranitidine. Anti-leukotrienes.

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INTRODUCTION

Although accurate data on the prevalence of urticaria are unavailable, 15 to 24 percent of the U.S. population may have had this condition (1, 2) which in many cases is prolonged and relapsing. On the basis of published data (3), a similar prevalence in the United Kingdom seems probable. Chronic urticaria is likely to be present at some time in about 25 percent of patients with urticaria. By chronic idiopathic urticaria, I mean the occurrence of widespread wheals daily or almost daily for at least six weeks, in the absence of a causative physical or environmental trigger (4).

Chronic urticaria affects predominantly adults. It is approximately twice as common in woman as in men (5).

Chronic idiopathic urticaria (CIU) is a common skin condition that affects 0,1-3% of people in the USA and Europe (6) and accounts for nearly 75% of all chronic urticaria cases (7). Therefore, the diagnosis of CIU is mainly one of exclusion, and the clinical investigative process can be lengthy. Haematologic, biochemical, immunologic, and endocrine assays are needed to provide direct or indirect evidence of systemic allergic, inflammatory, infectious, or autoimmune processes that may cause chronic urticaria. There after, sensitivity to foods, environmental agents/pollutants, and the presence of chronic infection or occult malignancy must all be excluded before a diagnosis of CIU can be finally established (8).

The duration of CIU varies greatly from patient to patient, with some individuals suffering irritating symptoms such as pruritus for decades. Up to 40% of patients who have chronic urticaria for more than 6 months still have urticarial wheals 10 years later (9). Patients with CIU have measurable decrements in

Table I
Antihistamines

Molecule	Comercial name	Presentation	Dose	Price (euros)	Cost/day (euros)
Cetirizine	Zyrtec	20 comp 10 mg	Once daily	7,75	0,39
Ebastine	Kestine	20 comp 10 mg	Once daily	12,65	0,63
Fexofenadine	Allegra	20 comp 180 mg	Once daily	13,95	0,70
Loratadine	Claritin	20 comp 10 mg	Once daily	7,16	0,36
Mizolastine	Mizolen	20 comp 10 mg	Once daily	10,61	0,53

quality of life, primarily due to recurrent itch, poor sleep, and the physically unappealing nature of the lesions. The activities of daily life and social life are badly affected by CIU. Indeed, the magnitude of this impairment of quality of life approximates that of chronic heart disease (10).

DATA SOURCES

MEDLINE (1966-2001), EMBASE (Excerpta Medica: 1974-2001), and other biomedical and drug directory databases were searched to identify english-language articles (basic science, clinical trial research, and review articles) and abstracts of conference proceeding on antihistamines, chronic urticaria, cetirizine, desloratadine, ebastine, fexofenadine, hidroxicine, loratadine, mizolastine, doxepin, cimetidine, ranitidine, anti-leukotrienes and related terms.

TREATMENT

Is reasonable to define chronic urticaria/angioedema as idiopathic since this is a diagnosis by exclusion of underlying etiologies. If treatment is ineffective up to this point, referral to an allergist or dermatologist might be considered. The therapeutic management should first be oriented towards palliation of symptoms. A 2% solution of ephedrine as a local spray is very useful for oropharyngeal edema. H₁ antihistamines (11) with a low potential for sedation are the most important first-line treatment, however. The pharmacologic actions and use of H₁-receptor antagonists were recently reviewed (12).

Combinations of various antihistamines may be useful in suppressing symptomatology. These include:

1. *First generation H₁ antihistamines.* Sedation from first generation antihistamines may reduce the

discomfort of pruritus associated with urticaria; however, first generation antihistamines may cause undesirable and potentially dangerous side effects (9) related to sedation, including driving impairment and risk for fatal automobile accidents, decreased workplace productivity, increase risk for occupational accidents, and impaired learning and academic performance. Doses of antihistamines that can sedate the patient, including 25 mg of hydroxyzine, are useful at bedtime.

2. *Combinations of first and second generations using non-sedating agents* (table I). In the morning and first generation drugs at night (13). All the new generation of H₁-antihistamines have been shown to be significantly more effective than placebo in chronic urticaria (9). Several studies show the new antihistamines to be as effective as, or sometimes more effective than traditional sedating antihistamines. Second generation antihistamines, at recommended doses do not have a sedative effect. Cetirizine may have a sedative effect in a small percentage of patients (14).

3. *Combinations of second generation antihistamines* (9).

4. Doxepin, a tricyclic antidepressant drug with marked H₁ antihistaminic activity, is particularly valuable when severe urticaria is associated with anxiety and depression. Doxepin possesses more potent H₁ antihistamine properties than some first generation classical antihistamines, although side effects such as dry mouth may limit their tolerability. This drug can be given at a dosage of 25 mg orally twice daily or as a single 25-mg dose at bedtime. Doxepin should not be given concurrently with monoamine oxidase inhibitors or terfenadine.

5. *Combination of an H₂ anti-receptor antihistamine* (15) (eg, cimetidine or ranitidine) with a first or second generation antihistamine.

Antihistamines may not be entirely effective in controlling urticaria because other capillary permeability inducing mediators are released (eg, leukotrienes; prostaglandin D₂; kinins; platelet

activating factor, etc.). Glucocorticosteroid treatment may be appropriate when antihistamines are not effective (16). These agents are helpful in controlling the inflammatory cell influx that can potentiate the urticaria by secondary release of histamine releasing factors and cytokines. Managing physicians should explain the potential side effects associated with glucocorticosteroids. In some clinical situations, the managing physician or patient may request more evidence to justify the initiation of glucocorticosteroid therapy. A skin biopsy with perivascular predominant-polymorphonuclear cell urticaria may justify initiation and continuation of glucocorticosteroid treatment (17). In adults, these medications are best administered daily as a single oral dose of 30 mg of prednisolone or prednisone early in the morning (18). The dose should be tapered when the urticaria subsides. The course should be completed within three weeks. Prolonged use of corticosteroids is almost invariably associated with reduced efficacy and toxic side effects. As soon as possible, glucocorticosteroid therapy should be discontinued or reduced to minimal requirements such as an every other day regimen to reduce potential side effects. On rare occasions, chronic urticaria/angioedema may not respond to prednisone. Some of these patients may respond to methylprednisolone (19).

A double-blind, placebo-controlled multicenter trial (n = 190) of desloratadine in moderate-severe CIU has recently been compared (20). Clinical experience in CIU has so far shown desloratadine to be a safe and effective treatment, providing rapid onset of action and long duration of symptoms relief.

Preliminary reports suggest that anti-leukotrienes may be effective in treating some patients with chronic idiopathic urticaria (21, 22). There are reports that oral cyclosporine (23), colchicine, or dapsone (24) may be helpful in selected cases of severe refractory chronic urticaria/angioedema.

Repeated plasmapheresis over a 2-month period may be effective in controlling refractory chronic urticaria especially in patients with circulating IgG autoantibody to IgE or the high affinity IgE receptor (25, 26).

A report described the efficacy of intravenous immunoglobulin therapy in patients with severe chronic urticaria caused by circulating autoantibodies (27).

Glossopharyngeal and laryngeal angioedema deserve special attention as they may become life threatening or present as manifestations of anaphylaxis. Patients may present with other symptoms of anaphylaxis that may require emergency treatment. The mainstay of treatment

for this emergency is epinephrine in doses dependent on the patient's age (28). Intramuscular administration of epinephrine in children has been shown to produce a faster time of action than subcutaneous administration (29).

RESUMEN

La urticaria crónica idiopática (UCI) es una afección común que afecta entre el 0,1 y el 3% de la población de EE.UU. y Europa. La duración varía mucho entre pacientes, sufriendola algunos durante décadas.

La primera línea de tratamiento son los antihistamínicos no sedantes de segunda generación, aunque en algunos casos con importante componente de ansiedad puede ser beneficioso asociar un antihistamínico de primera generación por su efecto sedante sobre el paciente.

En algunos casos, refractarios a los antihistamínicos, se pueden utilizar glucocorticoides, aunque sus efectos secundarios limitan su uso, debiendo ser prescritos el menor tiempo posible y a las menores dosis posibles. Los antileucotrienos pueden ser útiles en el tratamiento de algunos pacientes. También se han utilizado en algunos casos ciclosporina, colchicina, dapsona, así como plasmaféresis e inmunoglobulinas intravenosas.

Correspondence:

J.M.ª Negro Álvarez
Residencial La Paloma. Dúplex A-1
Valle, 7. El Palmar. 30120 Murcia
Tel.: 968-369500/968-885786
Fax: 968-369778/968-885786
E-mail: jnegroa@meditex.es

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