Treatment of Chronic Urticaria

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KEYWORDS

• Chronic urticaria • Therapy • Antihistamines • Corticosteroids • Ciclosporin • Omalizumab

KEY POINTS

- Second-generation antihistamines are unquestionably the first-line treatment for chronic urticaria and can be used at higher than licensed doses if normal doses fail to control the disease.
- A short course of oral corticosteroids should be considered for patients not responding to antihistamines before trying other immunosuppressive drugs.
- Ciclosporin is effective in most antihistamine-resistant patients who require long-term corticosteroid treatments to control their disease.
- Omalizumab is effective in most subsets of chronic urticaria who do not respond to other treatments but its high cost represents a limitation to its widespread use.

INTRODUCTION

Chronic urticaria (CU) is a skin disorder characterized by the recurrent eruption of short-lived wheals accompanied by redness and itching for at least 6 weeks.[1] CU has an estimated prevalence of 0.5% to 1%, a female predominance (female/male ratio: 2/1),[1,2] and a heavy impact on the quality of life.[3] Recent advances in the knowledge of CU pathophysiology have led to a rethinking of therapeutic strategies. The demonstration of histamine-releasing autoantibodies[4–6] and of increased inflammation and coagulation biomarkers[7,8] has provided the rationale for the use of immunomodulatory and anti-inflammatory drugs in CU.[9] To conjugate the frequent need for long-term treatments aiming to control the disease with the least possible impact in terms of side effects, several therapeutic strategies have been suggested during the last years by scientific panels of experts belonging to national as well as international

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societies, including the European Academy of Allergy and Clinical Immunology; the American Academy of Allergy, Asthma, and Immunology; and the World Allergy Organization.[10–15] Altogether, except for the fact that some new drugs have been introduced in the therapeutic schemes recently, such documents do not show major conceptual differences and are generally organized as a stepwise treatment to be adapted from one patient to another based on the severity of the disease and on the response to therapy. The pharmacologic treatment of CU is critically reviewed here.

GENERAL MEASURES

Besides pharmacologic treatments, CU patients should follow some general measures aiming at the reduction or minimization of a series of cofactors that might induce an exacerbation of the disease. In general, all the conditions causing vasodilation (eg, alcoholic drinks, excessive ambient temperature, heavy clothing, hot baths or showers, and spicy food) should be avoided because they might trigger a flare of wheals. Overtiredness is another condition that can be associated with the appearance of wheal-and-flare skin reactions in these subjects. Finally, up to 15% of CU patients experience an exacerbation of their disease after taking aspirin or other cycloxygenase-1 (COX-1) inhibitors (eg, diclofenac, propionic acid derivatives, indomethacin, oxicams); thus, the tolerability of COX-1-inhibiting drugs should be ascertained, and in the case of a positive history, patients should be advised to use analgesics or anti-inflammatory drugs exerting little or no activity on COX-1, such as paracetamol, etoricoxib, or tramadol. Oral tolerance tests with the latter drugs should be carried out to ascertain their tolerability.

ANTIHISTAMINES

Second-generation antihistamines (bilastine, cetirizine, desloratadine, ebastine, fexofenadine, levocetirizine, loratadine, mizolastine, rupatadine) are unquestionably the cornerstone of treatment of CU. Their effectiveness in patients with mild or moderate urticaria is shown by several randomized controlled trials.[10–15] The different second-generation antihistamines are not equally effective. Based on studies of inhibition of the wheal induced by histamine or by allergens, as well as on double-blind, placebo-controlled studies, cetirizine and its derivative levocetirizine appear to be the most effective compounds of the group,[16–22] although the recently introduced bilastine showed an efficacy similar to levocetirizine in one study,[23] and in another study, rupatadine was superior to levocetirizine.[24] Studies looking at sedation and psychomotor functions produced variable results with no relevant differences between levocetirizine, cetirizine, and loratadine in some cases,[25] and a greater sedative effect of cetirizine over fexofenadine, or loratadine in other cases.[26]

First-generation antihistamines are effective in patients with CU but their efficacy does not seem superior to second-generation antihistamines,[27–29] although they bear a higher degree of sedation and cognitive impairment.[30] Altogether, in most cases there is no reason to use these drugs as first-line treatment or as an add-on treatment for CU patients who do not respond to second-generation antihistamines.[10–15] However, as studies of the negative effects of first-generation antihistamines have almost exclusively been carried out on healthy subjects, not in patients with severe sleep deprivation due to CU, it cannot be excluded that first-generation antihistamines may be beneficial in some CU patients.

In patients with CU who do not respond adequately to second-generation antihistamines at licensed doses, higher than licensed doses can be given. Such approach is supported by studies carried out in both patients with acquired cold urticaria[31] and spontaneous CU,[32,33] showing a greater therapeutic effect without an increase in