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Fexofenadine: A review of its use in the treatment of urticaria in pediatric and adult populations

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Urticaria is an inflammatory skin disorder primarily resulting from activation of cutaneous mast cells. The released inflammatory mediators and histamine are responsible for the development of wheals and/or angioedema. Current guidelines recommend non-sedating second generation H_1 antihistamines such as fexofenadine hydrochloride as first-line therapy. A recent review by Ansotegui et al. provides an update on urticaria, both in adult and pediatric populations, and on the safety and efficacy of fexofenadine hydrochloride as a treatment option.

Urticaria is a condition characterized by the appearance of wheals and/or angioedema [1]. A wheal is a sharply circumscribed, superficial swelling accompanied by itching or burning. It may occur abruptly and returns to normal within 30 minutes to 24 hours. Angioedema develops more slowly than wheal and presents with localized edema in the lower dermis and subcutis or mucous membranes. Angioedema is characterized by tingling, burning, and tightness rather than itching. Recovery takes longer than for wheals, up to 72 hours [1, 2].

Approximately one in five people experience urticaria (commonly referred to as hives) at least once during their lifetime, with 50% experiencing wheals only, 40% experiencing wheals and angioedema, and 10% experiencing angioedema only. Acute urticaria is often self-limiting, with episodes resolving within six weeks, whereas chronic urticaria persists longer [2].

Urticaria has a high socioeconomic burden worldwide. It has a strong impact on the quality of life of adult and pediatric sufferers, with significant consequences on sleep, social interaction, and work/school performance [2].

Urticaria is classified according to its duration as acute or chronic and according to the triggers as spontaneous or inducible (see **Tab. 1** and **2**).

The pathogenesis of urticaria is not fully understood. It is a disease primarily driven by mast cells. Effectors react with the membrane of mast cells, activating them and thus leading to the release of inflammatory mediators and stimulation of signaling pathways that cause the formation of wheals and angioedema (see **Fig. 1** and **2**) [2].

Tab. 1. Classification of urticaria by duration [2]

Type of urticaria	Duration
Acute urticaria	Occurrence over a period of less than 6 weeks
Chronic urticaria	Occurrence over a period of more than 6 weeks

Tab. 2. Classification of urticaria by causes [2]

Spontaneous: majority of cases	Inducible: minority of cases	
Causes: ▪ Infections ▪ Food ▪ Drugs ▪ Stress ▪ Autoimmune disorders	Physical causes: ▪ Dermographism ▪ Heat urticaria ▪ Cold urticaria ▪ Solar urticaria ▪ Delayed pressure urticaria ▪ Vibratory angio-edema	Other causes: ▪ Aquagenic urticaria ▪ Cholinergic urticaria ▪ Contact urticaria

Urticaria is often self-diagnosed and self-managed. Current guidelines recommend a diagnostic work-up that focuses on the clinical examination of signs and symptoms associated with urticaria. Since urticaria-like lesions can be the manifestation of various dermatological syndromes, a careful anamnestic examination assessing frequency, circumstances of onset, duration, local or systemic symptoms is essential for the correct diagnosis [2]. The recent guideline [1] lists complete symptom control as the treatment goal. Avoidance

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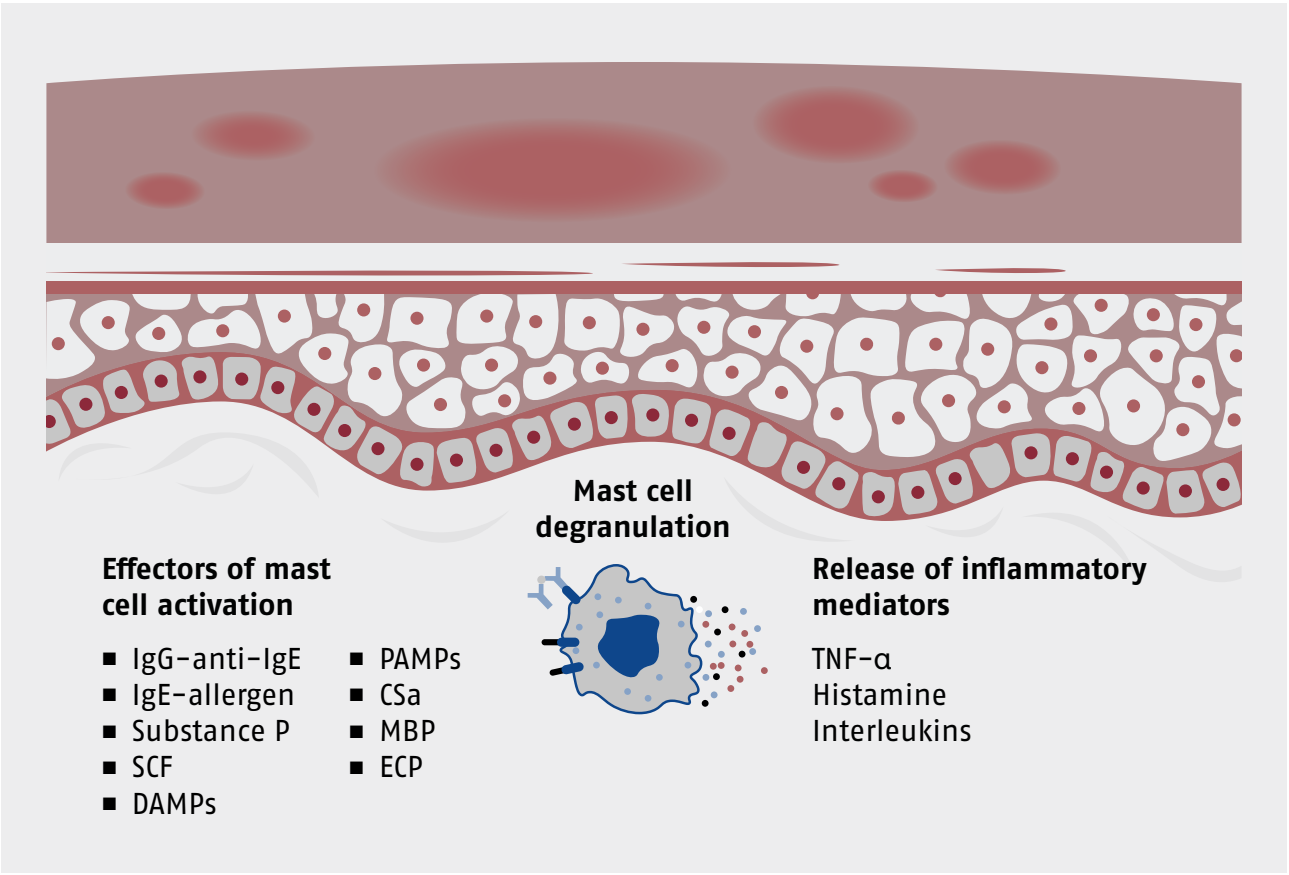

Fig. 1. Mast cell activation.
IgG: immunoglobulin G; IgE: immunoglobulin E; SCF: stem cell factor; DAMPs: damage-associated molecular patterns; PAMPs: pathogen-associated molecular pattern; CSa: Ciclosporin A; ECP: eosinophil cationic proteins; MBP: major basic protein; ECP: eosinophil cationic protein

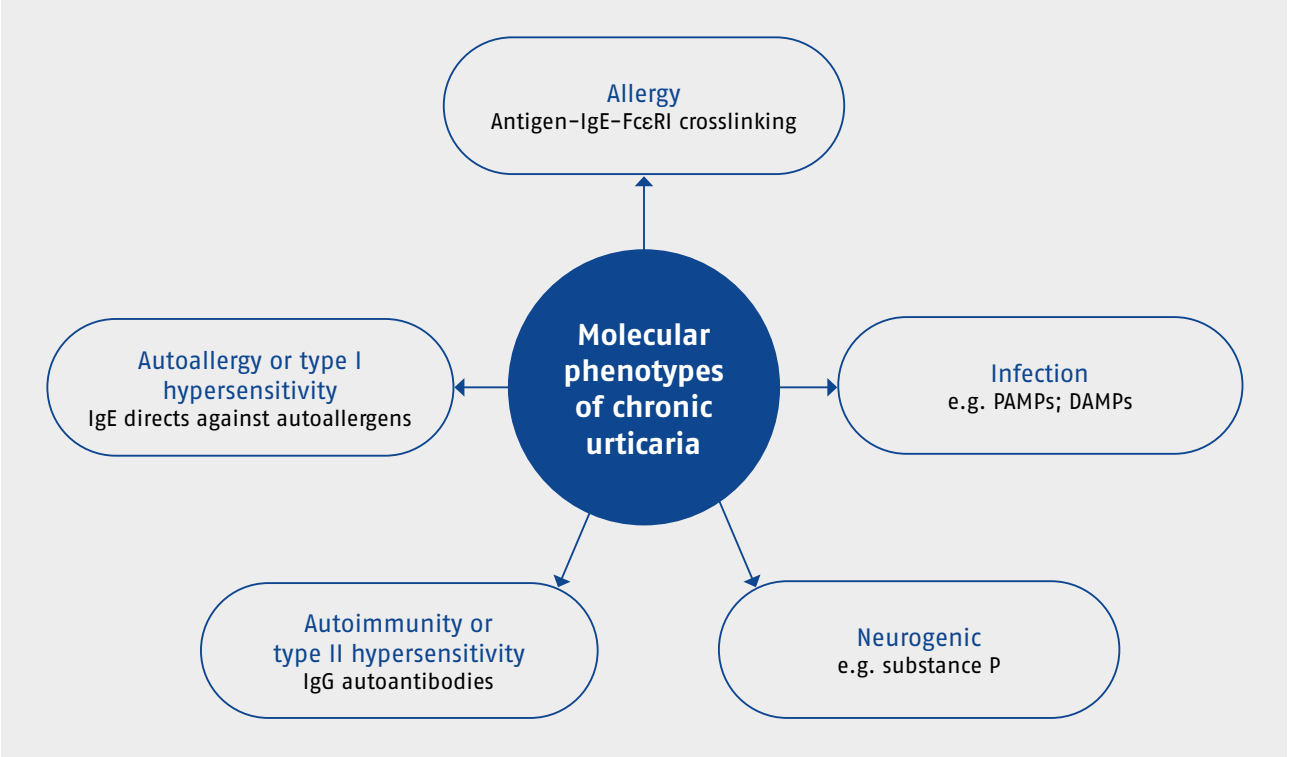

Fig. 2. Molecular phenotypes of chronic urticaria.
IgG: immunoglobulin G; IgE: immunoglobulin E; DAMPs: damage-associated molecular patterns; PAMPs: pathogen-associated molecular pattern. [Adapted from 2]

of triggers is the first suggested recommendation. If this is not possible, a stepwise pharmacological approach is recommended [2].

First-line therapy in children and adults

In urticaria, dysregulation of mast cells and basophiles releases inflammatory mediators. These inflammatory mediators, such as histamine, TNF-α, and interleukins, stimulate signalling pathways that lead to the symptoms of urticaria. In most patients urticaria cannot be avoided. The guidelines strongly recommend treatment with oral second-generation H_1 antihistamines as first line [1]. This group of agents is effective and well tolerated. Second-generation antihistamines do not cross or only minimally cross the blood-brain barrier and therefore only slightly or non-sedating as well as free of anticholinergic adverse side effects. In addition to histamine, other inflammatory mediators are released. In patients who do not respond to histamine, short-term treatment of up to ten days with glucocorticoids can be considered. Other therapeutic options, such as treatment with omalizumab, should be evaluated by specialized centers [2].

The cited review focuses on the use of fexofenadine HCl in urticaria as a representative of the entire drug class [2]. Fexofenadine is available as tablet or suspension and on the market for 25 years in more than 100 countries.

Fexofenadine HCl is a well-tolerated and long-established treatment of urticaria in both adults and children [2]. The approved dose for urticaria treatment in adults and children 12 years of age and older is 180 mg tablets once daily or 60 mg two times daily. Fexofenadine suspension is available for children 6 months of age and older [2, 3]. Second-generation antihistamines pass the blood-brain barrier to a lesser extent than first-generation antihistamines. Central side effects such as a sedative effect therefore occur to a lesser extent. Within the group of second-generation antihistamines, there are significant differences with regard to sedative effects. While fexofenadine does not occupy any of the H_1 receptors of the cerebral cortex, 20 to 50% of these receptors are occupied after ingestion of cetirizine [4].

Fexofenadine is well tolerated as demonstrated in long-term studies in healthy volunteers aged 12 to 65 years and in chronic urticaria patients when doses up to 240 mg were administered once daily for up to 12 months [4].

Summary

Fexofenadine HCl is recommended as first line treatment for the treatment of urticaria. It significantly relieves hives and the itching provoked by hives. Fexofenadine HCl is well tolerated. Discontinuation due to adverse side effects generally occurs in less than 5% of patients. Patients benefit from the improvement of the health-related quality of life and of the performance in daily activities [2].

Patients who do not respond to antihistamines should be referred to a clinical specialist with expertise in the evaluation and treatment of urticaria and/or angioedema [2].

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