УДК 615.454.1:615.218:615.014.2

THE RELEVANCE OF DEVELOPING AN EXTEMPORANEOUS CREAM WITH LEVOCETIRIZINE FOR URTICARIA TREATMENT

Ibtissam Ziati, Volodymyr V. Kovalov, Yulia V. Levachkova, Svitlana V. Oliinyk National University of Pharmacy, Kharkiv, Ukraine

Introduction. The skin represents one of the most significant immunological organs, susceptible to a multitude of external and internal influences, in addition to innate adaptive immune responses. A number of dermatological conditions, including atopic dermatitis, contact dermatitis, urticaria, angioedema, psoriasis and autoimmune blistering disorders, are associated with immune processes. The majority of these diseases are chronic, inflammatory, and proliferative, with both genetic and environmental factors exerting a significant influence. These immunological mechanisms may have implications for potential future therapeutic targets.

It is now relatively commonplace to encounter individuals who exhibit allergic reactions to specific products or who suffer from allergic rhinitis. Indeed, this pathology affects approximately one-third of the global population, ranking as the fifth most prevalent chronic disease worldwide. The risk of developing allergic diseases is increased by a number of factors, including the deterioration of the ecological situation and the emergence of new allergens. The prevalence of disinfectants is also a significant contributing factor, as is acute and chronic stress, which is particularly relevant in our modern, turbulent times.

It is noteworthy that in developed countries, approximately 90% of the population experiences severe stress. For instance, the 2012 global population survey indicated that the average stress level was 4.9 out of 10, with a score of 1 indicating low stress. Furthermore, it is notable that approximately 20% of the population perceives their stress levels to be at an extreme (8-10 points). This is particularly pertinent given the additional stressors that individuals face in the current context, including concerns about the future of the state and their own circumstances.

Urticaria (also known as nettle fever or hives) is an itchy rash characterised by red spots with a raised, swollen centre that appears in various places on the body. Urticaria characterised by the development of blisters and/or angioedema. It should be noted that conditions in which blisters are a symptom, such as skin tests, inflammatory syndromes, diseases caused by mutations in protein-coded genes that play a leading role in the regulation of the inflammatory response, anaphylaxis, and hereditary angioedema, are not classified as urticaria.

It is noteworthy that a universally accepted classification of urticaria has yet to emerge. In practice, however, it is more often divided into allergic and non-allergic categories. In accordance with the "Official Conclusions of the Problem Commission on EAACI Nomenclature," urticaria is regarded as an allergic condition, with its pathogenesis mediated by immunological mechanisms. If there is evidence that it is caused by IgE-dependent mechanisms, it is designated as "IgE-mediated urticaria" [3, 16, 36].

The rash is typically pruritic, but typically resolves within a few hours of onset. Recurrences are often transient and occur in different locations. Additionally, the colour of the rash remains unchanged and there is no scarring to the skin.

Furthermore, 40% of patients present with subcutaneous oedema (angioedema), which typically occurs on the lips, hands, eyelids, and other areas.

Two distinct forms of urticaria have been identified: acute and chronic. Acute urticaria may manifest subsequent to the ingestion of a specific foodstuff or contact with a particular trigger. Additionally, non-allergic causes may be responsible, including elevated temperature, exogenous or endogenous exposure, the use of drugs or certain foods, insect bites, or infections. Urticaria may manifest acutely, lasting from several hours to six weeks. In such instances, a systemic/cutaneous reaction may ensue. Chronic urticaria is rarely caused by specific triggers, rendering allergy tests an ineffective diagnostic tool. Chronic urticaria can persist for an extended period, ranging from months to years. According to the literature, urticaria is observed during the lifetime of 15% to 25% of individuals. While the majority of these cases are readily treatable, approximately 30% of patients experience symptoms for a duration exceeding six weeks. In such instances, urticaria is regarded as a chronic condition.

Chronic urticaria persists for a minimum of six weeks, with some cases lasting for months or even years. In the majority of cases, chronic urticaria is not a manifestation of an allergic reaction, but rather the consequence of an immunological response that results in the activation of mast cells and the release of histamine [16, 31, 42]. Urticaria is finally recognised as an independent disease, but a complete understanding of the mechanisms of its occurrence still eludes researchers. Furthermore, over the past five years, additional evidence has accumulated indicating that patients with urticaria have a significantly impaired quality of life. Consequently, these patients merit the focused attention of medical professionals.

The utilisation of novel pharmaceutical agents for the localised management of urticaria will result in a reduction of bothersome symptoms and a concomitant reduction in the overall duration of treatment. Furthermore, the incidence of adverse effects will be diminished, and the costs associated with the use of expensive, industrially produced pharmaceuticals will be significantly reduced.

Thus, the development of extemporaneous nasal cream and comparison of its antiallergic properties is relevant.

Aim. The objective of study is to provide development actuality of extemporaneous cream composition with Levocetirizine for urticaria treatment.

Materials and methods. To achieve the goal, general scientific methods of research were used: analysis, synthesis, comparison, generalization, comparison, systematization for processing literary data.

Results and discussion. Levocetirizine attracted our attention among antiallergic agents. It is a synthetic drug that is a derivative of piperidine and belongs to the group of antihistamines of the III generation. According to its chemical structure, it is a levorotatory isomer of cetirizine. The mechanism of action of the drug consists in selective blocking of H1-receptors of histamine, prevention of spasms of smooth muscles caused by histamine. With allergic rhinitis, the drug reduces the frequency of sneezing, lacrimation, discharge from the nasal passages, and itching of the nasal mucous membranes.

Levocetirizine is quickly absorbed in the gastrointestinal tract, the bioavailability of the drug is about 100%. The onset of action of the drug in 50% of

patients is observed 12 minutes after oral administration. the simultaneous intake of food does not reduce the degree of absorption of the drug.

The mechanism of action of the drug is selective blocking of histamine H1 receptors, prevention of smooth muscle spasms caused by histamine, including bronchoconstriction in patients with obstructive pulmonary disease, dilation of capillaries and increased permeability, development of angioedema, erythema and itching of the skin and mucous membranes. In allergic rhinitis, the drug reduces sneezing, lacrimation, nasal discharge, and itching of the nasal mucosa.

Levocetirizine is used for seasonal and year-round allergic rhinitis, pollinosis, allergic conjunctivitis, urticaria, Quincke's edema, pruritus, as well as in the complex therapy of atopic dermatitis, chronic eczema and bronchial asthma in both adults and children. The development of the optimal composition of the base will allow to increase the spectrum of the pharmacological action of the drug, thereby expanding the nomenclature of Ukrainian medicines.

Conclusions. Thus, taking into account the wide spectrum of Levocetirizine therapeutic activity, we consider to develop an extemporaneous cream for urticaria treatment including these API.

List of references

- 1. Bauer A, Dickel H, Jakob T, et al. Expert consensus on practical aspects in the treatment of chronic urticaria. Allergo J Int. 2021;30(2):64–75. doi: 10.1007/s40629-021-00162-w
- 2. Britannica, The Editors of Encyclopaedia. "Allergy". Encyclopedia Britannica, 11 Oct. 2024, https://www.britannica.com/science/allergy. Accessed 1 November 2024.
- 3. Godse K, Patil A, De A, et al. Diagnosis and management of urticaria in Indian settings: skin allergy research society's guideline-2022. Indian J Dermatol. 2022;67(6):732–743. doi: 10.4103/ijd.ijd 307 22
- 4. Pal, R.R., Maurya, A.K., Parashar, P. et al. A Comparative Study of Levocetirizine Loaded Vesicular and Matrix Type System for Topical Application: Appraisal of Therapeutic Potential against Atopic Dermatitis. J Pharm Innov 16, 469–480 (2021). https://doi.org/10.1007/s12247-020-09465-x
- 5. Sardana, K., Srinivasan, C., Girdhar, M., Hazarika, N., Patel, K., Rao, N., Agarwal, D. P. (2024). Analyzing the clinical efficacy and safety of levocetirizine based on its receptor occupancy, intraclass comparison and role in the treatment of CSU: an AROG consensus statement. Expert Review of Clinical Pharmacology, 17(10), 875–889. https://doi.org/10.1080/17512433.2024.2401093