New Possibilities and Views on The Treatment of Inflammatory and Allergic Dermatoses with External Medications

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ABSTRACT

Currently, there is a steady increase in the frequency and prevalence of allergic skin diseases in the world: atopic dermatitis, contact dermatitis, eczema, which in some countries affects up to 25% of the population. In addition, the severity of the course and tolerance of allergic dermatoses to therapy are increasing everywhere. The unfavorable growth dynamics of this group of diseases is due to a number of reasons. The external factors include, first of all, environmental pollution, especially in industrialized countries, as well as constant contact with a variety of chemicals (household chemicals, cosmetics, construction materials, metals, synthetic materials of clothing and footwear). The rise in the incidence of allergodermatoses is undoubtedly promoted by the use of a large number of drugs, including vitamins and food supplements, canned food and fast food products.

Keywords: allergodermatoses, clinical and epidemiology, age category, gender identity

Introduction. According to modern concepts, the fundamental pathogenetic mechanism of allergodermatoses is the presence of systemic allergic inflammation with active manifestation on the skin. Allergy is a pathological form of immune system response, which results in damage to the body's own cells and tissues. In the implementation of an allergic response in skin diseases, great importance is attached to reagin reactions and disorders in the cell-mediated link of immunity. In atopic conditions, allergic manifestations are characterized by innate hypersensitivity to many environmental factors and the ability to form reagin (IgE) antibodies. Atopy– a hereditary form of allergy, is based on the programmed immune response to an allergen, which is characterized by stimulation of the Th2 population of lymphocytes, hyperproduction of allergen–specific IgE antibodies, degranulation of mast cells, eosinophilic infiltration, which leads to chronic inflammation in the skin and itching. In patients with atopic dermatitis, a sharp increase in total immunoglobulin E is detected, which includes both antigen–specific IgE antibodies to various antigens and IgE molecules. Antigen–specific IgE antibodies to food antigens predominate in childhood, and in older age – to

pollen, household, epidermal, bacterial, viral and fungal allergens. Recently, after the discovery of the Mosmann Th1/Th2 paradigm, new data on the immunological mechanisms of the pathogenesis of atopic dermatitis have been obtained. Until recently, this disease was considered only as a Th2–dependent process. However, the involvement of cytokines produced by Th1 lymphocytes in the pathogenesis of atopic dermatitis has now been proven. In particular, the presence of Th1–type If–g reactions in the pathogenesis of atopic dermatitis is beyond doubt. Increased production of this cytokine is noted in 80% of patients, correlates with the severity of the disease and decreases with successful treatment. The peculiarity of the morphology of skin lesions in atopic dermatitis suggests that other types of hypersensitivity reactions are also realized in this disease. Immediate reactions may occur in the form of cytotoxic, immunocomplex, granulocyte–IgG–mediated, as well as delayed, T–cell reactions. This form of hypersensitivity is observed in many allergodermatoses, in particular in allergic dermatitis, eczema. In the development of delayed–onset hypersensitivity (HRT), the main role is played by T lymphocytes (mainly represented by the Th1 population of lymphocytes), which carry specific antigen receptors on their surface. In this type of reaction, immune T lymphocytes, when interacting with an allergen antigen, secrete a number of proinflammatory cytokines: IL–1, IL–2, TNF, g-interferon. This leads to the initiation of inflammation, the release of biologically active substances (prostaglandins, leukotrienes, histamine, tryptase), which causes the development of tissue inflammatory reactions: in the form of vasodilation and damage, plasma exudation, which is clinically manifested by hyperemia, edema and itching (early allergic response). Another effect of proinflammatory cytokines is the induction of the expression of adhesion molecules on leukocytes and endothelial cells, which results in the influx of leukocytes from the vascular bed into the focus of inflammation by their transendothelial migration. The further advancement and accumulation of immunocompetent cells in the inflammatory focus is controlled by chemokines, which are produced by macrophages and endothelial cells. Recruitment of neutrophils, eosinophils, and macrophages to the site of an allergic reaction forms a cellular infiltrate in the focus of inflammation, which contributes to the further development of allergic inflammation (late allergic response). Thus, type IV allergic reactions involve T lymphocytes (a subpopulation of T helper cells–Th1), macrophages, endothelial cells and cytokines secreted by them .

Pseudoallergic hypersensitivity plays an important role in allergic dermatoses. Unlike true allergic reactions, pseudoallergic ones cause direct degranulation of basophils without the participation of antibodies and immune T–lymphocytes. Bacteria and their toxins, viruses, food products (strawberries, nuts, marinades, smoked meats), medicines, physical agents (cold, etc.), aerogenic and other pollutants can act as provoking exogenous and endogenous factors. In young children, in the presence of a deficiency of digestive enzymes, under-cleaved peptides induce exactly this type of reaction. Pseudoallergia can be provoked by any irritants that directly affect the skin: woolen and synthetic clothing, water treatments (bath, bath), detergents. These changes underlie the non-atopic, pseudoallergic form of blood pressure induced by various factors against the background of blockade of b-adrenergic receptors.

The common pathogenetic mechanisms underlying allergodermatoses make them very similar in clinical terms. This is reflected in the names of individual nosologies: eczematized dermatitis, atopic eczema of the hands, the eczema-like form of atopic dermatitis

Purpose of the study: to investigate the clinical and epidemiological analysis of the indicators of patients with allergodermatoses by age category and sex

Materials and Methods of the Study. During 2021-2022 at the Republican Allergy Centre, we conducted a retrospective study among patients with allergodermatoses who had comorbidities such as diabetes mellitus, chronic diseases of the gastrointestinal tract and ENT organs. Third trimester pregnant patients with

allergodermatoses were also included in the study.

Results of the study. In the examination of 175 patients, which were 142 females and 33 males, comparative analyses were made by sex, by age category, by etiological factor of allergodermatoses, as well as comparative analysis with the obtained results of my PhD work, defended in 2021.While working on the patients' anamnesis, it was revealed that the main part of them had drug allergy to some drugs from the groups of antibiotics and non-steroidal anti-inflammatory drugs, among women with allergodermatoses, patients in the age category of 21-30 and 31-40 years were more predominant. Further comparative analysis by period of examination revealed that these patients were more in 2022 than in 2021 and accounted for 28% and 23.6% respectively. Sorting out the subjects according to the etiological factor , it was found that the largest proportion of patients were those with aggravated hereditary factor 20.0 %, by medication factor 7.42 %, by seasonality 38.2 %, by food factor 21.11 %, by contact (clothing) factor 25, 7%, allergies caused by cosmetics 30.8%, odour and dust 35.4%, animals 7.42%, bed dust 37.1%, plants 16.5%, and allergies caused by infectious and inflammatory diseases 0.57%.As shown in the table, the female half of the patients, in most cases, had hereditary allergies and this figure was 97.1% of the total number of patients, as well as seasonal allergy 85.0%, plant allergy 93.1%, cosmetic allergy 87.3%. The male half of the patients accounted for only 18.8% of the total number of patients, with a high rate of animal allergy of 23.0%. It should be noted that many patients with allergodermatoses also had a history of allergic predisposition to other allergens.

Thus, currently, due to the appearance in the arsenal of doctors of new highly effective and safe non–fluorinated drugs (hydrocortisone 17-butyrate, mometasone fuorate, methylprednisolone aceponate), topical GCS have taken a leading position in the treatment of these diseases, since other external agents cannot compete with them in terms of anti-inflammatory, antiexudative and antipruritic activity. The anti-inflammatory effect of topical GCS is achieved with the participation of various mechanisms. In tissues and cells of the inflammatory infiltrate, GCS inhibits the formation of lipid mediators such as prostaglandins, leukotrienes and platelet–activating factor by increasing the production of lipocortin-1, which in turn inhibits phospholipase–A2 and cyclooxygenase–2, necessary for the synthesis of arachidonic acid. GCS inhibit the synthesis of several cytokines, including interleukins 1,2,3,4,5,6,10, tumor necrosis factor in various cell types by interacting with the nuclear receptor for GCS, which causes repression of cytokine gene transcription. Another important mechanism of the pro-inflammatory action of steroids is a decrease in the stability of cytokine mRNA and an increase in susceptibility to apoptosis. Topical GCS have a pronounced antiallergic effect by inhibiting the migration of lymphocytes, granulocytes, and Langerhans cells and inhibiting their function in places of inflammation by suppressing the expression of adhesion molecules. The cessation of the synthesis of inflammatory mediators quickly leads to the restoration of impaired permeability of vascular walls, their narrowing, reduction of exudation, and cessation of irritation of nerve receptors. This explains the immediate therapeutic effect of GCS in the form of a rapid decrease in edema, a decrease in erythema and local tissue temperature, as well as a decrease in itching, burning, and paresthesia.

Exhibiting high therapeutic activity at any stage of allergic inflammation, GCS quickly stop the objective and subjective symptoms of allergodermatoses, suppressing the main links of both the early and late phases of allergic inflammation. By providing a rapid therapeutic response, external GCS reduces the treatment time of allergodermatoses many times, and leads to a significant improvement in the quality of life of patients. These circumstances explain their exceptional demand among doctors and patients. The popularity of topical GCS, especially the latest generation, is largely due to their high cosmetic attractiveness, which is largely determined by the basis of the drug. They are well absorbed by the skin, do not leave

traces on clothes and underwear, do not have an untidy smell, do not stain the skin and do not require the use of bandages, which distinguishes them from classic external remedies. Together, these factors determine the high compliance of topical GCS – patients' commitment to choosing these particular drugs for the treatment of both acute and chronic allergodermatoses.

The activity of topical steroids is determined by the chemical structure of the GCS molecule, the concentration of the steroid in the preparation, the composition of its base (the dosage form of the drug), skin permeability, primarily determined by the thickness of the stratum corneum, the bioavailability of the steroid, which is primarily due to its lipophilicity, the distribution coefficient in the skin. The effectiveness and duration of the therapeutic effect of GCS also depends on the speed of binding of the drug molecule to the cytosolic receptors of skin cells and the rate of dissociation of the CS–receptor complex, i.e., the duration of stay at the receptor. The latter circumstance leads to prolonged synthesis of anti-inflammatory proteins and inhibition of inflammatory mediators. Currently, the number of outdoor GCS registered in Russia totals about 40 items represented by 15 companies.Such an abundance of similar medicines creates certain difficulties for the practitioner to choose a specific remedy in a specific clinical situation. In this regard, practical dermatologists should be informed when prescribing external GCS about its potential activity, chemical structure, frequency of use, possible side effects, i.e. safety.

Conclusions: Thus, until recently, this disease was considered only as a Th2–dependent process. However, the involvement of cytokines produced by Th1 lymphocytes in the pathogenesis of atopic dermatitis has now been proven. In particular, the presence of Th1–type If–g reactions in the pathogenesis of atopic dermatitis is beyond doubt. Increased production of this cytokine is noted in 80% of patients, correlates with the severity of the disease and decreases with successful treatment. The ratio of nosological forms of allergic diseases did not undergo changes, and also allergic diseases in dynamics (2021-2022) are characterised by a tendency to increase the number of patients among women with allergodermatoses in the age category of 21-30 and 31-40 years.

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